AMP

ACTA MÉDICA PORTUGUESA

A Revista Científica da Ordem dos Médicos

ACTA MED PORT. ISSN 0870-399X e-ISSN 1646-0758

5 | 24

Número 5
Série II
Lisboa

Volume 37
Maio 2024
Publicação Mensal

AMP ACTA MÉDICA PORTUGUESA

A Revista Científica da Ordem dos Médicos

Propriedade: Ordem dos Médicos (NIPC 500 984 492)

Sede do Editor / Redação: Av. Almirante Gago Coutinho, 151. 1749-084 Lisboa, Portugal. Tel: +351 21 151 71 00 E-mail: secretariado@actamedicaportuguesa.com

ISSN:0870-399X | e-ISSN: 1646-0758

Assinaturas: Nacional: 300 Euros; Internacional: 350 Euros

AMP37(5) - Maio de 2024

Registo: Inscrito na Entidade Reguladora para a Comunicação Social com o Nº 106 369

Depósito legal: 20 957/88

Estatuto Editorial: http://www.actamedicaportuguesa.com/estatuto-editorial

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Neonatal Resuscitation: Peculiarities and Challenges

Reanimação Neonatal: Particularidades e Desafios

Gabriela MIMOSO✉[1]
Acta Med Port 2024 May;37(5):317-319 ▪ https://doi.org/10.20344/amp.21415

Keywords: Asphyxia Neonatorum; Infant, Newborn; Resuscitation
Palavras-chave: Asfixia Neonatal; Recém-Nascido; Ressuscitação

After birth, most newborn babies (NB) adapt well to extrauterine life, but around 10% need some support,[1] with 3% to 5% of NB requiring ventilatory support and between 0.4% and 2% requiring intubation.[1-3] Even though peripartum asphyxia occurs mostly in low- and middle-income countries, the World Health Organization (WHO) estimates that this occurrence is responsible for around one million neonatal deaths every year,[2] and therefore it is always possible to improve perinatal care even in developed countries.

Supporting NB during the transition to extrauterine life is a major challenge. It is essential to know the underlying physiological processes to recognize NB who need support during the transition.[1,4] Effective communication between all members of the team (obstetricians, neonatologists, and nurses) is essential in identifying signs of fetal distress and ensuring that each step of resuscitation is anticipated and carried out efficiently.[4]

Healthcare professionals with training in basic resuscitation or with experience in advanced resuscitation are essential in all places where births take place.[1,4] All equipment must be regularly checked, easily accessible and ready to use.[1]

In recent years we have seen a significant systematization of guidelines for transition support and neonatal resuscitation by institutions with great international impact [e.g., the European Resuscitation Council (ERC)/International Liaison Committee on Resuscitation (ILCOR)/American Heart Association (AHA)], which has led to the development of normograms that should be used to guide delivery room practices.[5] When a newborn does not show any respiratory movements, it is essential to dry, warm and stimulate them in order to initiate breathing.[2-4,6] Aspiration of secretions is used only when the airway is obstructed, and it should be carried out under visualization.[2-4,6]

All the studies show the benefit of delayed cord clamping in term NB and premature babies who do not need to be resuscitated.[2,4,6] There is no universal definition of the duration of this procedure, but there is consensus that it should take place after 60 seconds. Several studies are ongoing on the approach to premature infants under 28 weeks and newborns requiring resuscitation, particularly on resuscitation with an intact cord.

Unlike in adults, adequate ventilation is the main determinant in neonatal resuscitation, and it is mandatory for healthcare professionals to be trained in mask ventilation techniques.[3] The use of T-piece devices makes it possible to control the positive pressure in the airway and these are considered safer than manual insufflators.[4-6] The use of blenders, which allow air/oxygen mixing, is recommended.[6] In preterm babies who are breathing, continuous positive airway pressure (CPAP) is recommended at a minimum pressure of 6 cmH_2O. If positive pressure ventilation is necessary, a starting inspiratory airway pressure (PIP) of 25 cmH_2O is recommended in preterm babies with a gestational age of less than 32 weeks. In term NB, the initial inspiratory pressure should be 30 cmH_2O. Inspiratory airway pressure is used for initial pulmonary insufflation, to maintain ventilation and prevent alveolar collapse, improve gas exchange and pulmonary compliance. However, the main objective of this stabilization phase is to maintain functional residual capacity, which depends above all on optimizing positive end-expiratory pressure (PEEP).

Endotracheal intubation is indicated when positive pressure ventilation with a face mask is prolonged or ineffective and when cardiac massage is required.[4] The laryngeal mask can be a safe alternative in NB over 34 weeks of gestational age[5] and may become the preferred interface in neonatal resuscitation.[1,4,5] The detection of expired CO_2 is recommended to confirm the position of the tracheal tube.[1] There is also no consensus on the FiO_2 to use in resuscitation. In term NB or premature NB without respiratory distress (RDS), the initial option is to use FiO_2 21%, while FiO_2 30% should be used initially in NB less than 28 weeks of gestational age.

Well-being during the transition should be documented with electrocardiographic monitoring (heart rate) and assessment of transcutaneous oxygen saturation,[3,4,6] which is also used to adjust the FiO_2 to be used later.

1. Serviço de Neonatologia. Maternidade Bissaya Barreto. Centro Hospitalar e Universitário de Coimbra. Coimbra. Portugal.
✉ **Autor correspondente:** Gabriela Mimoso. gmimoso@chuc.min-saude.pt
Recebido/*Received*: 22/02/2024 - **Aceite/*Accepted*:** 04/03/2024 - **Publicado/*Published*:** 02/05/2024

Neonatal mortality - Number of deaths during the first 28 completed days of life per 1000 live births in a given year or other period.
Perinatal mortality - Includes infant deaths less than seven days of age and late fetal deaths at 28 weeks of gestation or more. Perinatal mortality rates are calculated as the number of infant and fetal deaths, divided by the number of live births and fetal deaths.

In the future, the use of videolaryngoscope, simulation and telemedicine will certainly help to improve the education, training, and performance of some of these practices.[1,4]

Historically, the presence of parents at the time of resuscitation has been a source of concern. Today there is a debate about the impact of their presence on the team's performance and how they might be affected by seeing their child being resuscitated. Nowadays, parents want to be actively involved in decisions such as investment in resuscitation/redirection of care or suspension of care. In this context, parents should be informed about the resuscitation maneuvers being carried out and why they are necessary, and early skin-to-skin contact and visual and tactile contact should be promoted in babies who are going to need intensive care, before transferring them to the Intensive Care Unit. When death is imminent, the comfort of the newborn and the well-being of the parents should be promoted, allowing them to establish contact with the baby in accordance with the parents' desires and to collect memories later on. In Portugal, the reform of maternal and neonatal health care in 1990 which promoted the upgrade of delivery rooms and neonatology units, was a pillar in the improvement of perinatal care in Portugal. Since then, the work of devoted and dedicated perinatology professionals has been decisive in improving neonatal and perinatal mortality rates, which in the 1980s was 15‰ and 24‰ respectively, decreasing to half in 1990, and is currently 1.6‰ and 3‰, respectively.

Since our perinatal indicators have improved, we have also successfully invested in increasingly immature newborns. In Portugal, the viability threshold, defined by the gestational age at which more than 50% of the newborns survive, is currently 25 weeks' gestation and 600 g of birthweight. In Portugal, investment is almost generalized in babies at 24 weeks' gestation, but in some countries such as the United Kingdom, the United States of America, Australia, Japan, Canada and Sweden, there is a movement to give the opportunity to even more immature newborns. In each hospital, obstetrics and neonatal teams should be aware of their indicators and make shared decisions about what action to take, and respect the parents' wishes whenever possible.

National neonatal mortality indicators place us among the countries that perform best during birth. The study by Alves *et al*[7] documents the adherence of Portuguese physicians to international recommendations and lists some points where we still need to improve our performance.

Hospitals were assessed based on their type and the primary area for improvement that was identified was communication among team members during team briefings before procedures, during childbirth, and in debriefings afterwards. The aim of these sessions was to analyze both the positive and negative aspects of the team's performance.

Records of the team's performance are essential if the subsequent analysis is to be supported by objective data and should be conducted by someone qualified in neonatal resuscitation. Ideally, all teams should have a physician with experience in advanced resuscitation. The Portuguese Neonatal Society is aware of the need to promote certification in neonatal resuscitation and therefore is training instructors in advanced neonatal resuscitation so that they can then provide training to professionals dedicated to this age group.

The new neonatal resuscitators will respond to some of the weaknesses identified here – newborn temperature control and monitoring with ECG and pulse oximetry, built-in blender device and the possibility of T-piece ventilation. Equipment such as expired CO_2 detectors (to confirm intubation), laryngeal masks, Guedel tubes, videolaryngoscopes and transport incubators with temperature control are essential in modern delivery rooms.

COMPETING INTERESTS

The author declare that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Madar J, Roehr CC, Ainsworth S, Ersdal H, Morley C, Rüdiger M, et al. European Resuscitation Council Guidelines 2021: newborn resuscitation and support of transition of infants at birth. Resuscitation. 2021;161:291-326.
2. Manley BJ, Owen LS, Hooper SB, Jacobs SE, Cheong JL, Doyle LW, et al. Towards evidence-based resuscitation of the newborn infant. Lancet. 2017;389:1639-48.
3. Schmölzer GM, Morley CJ, Kamlin OC. Enhanced monitoring during neonatal resuscitation. Semin Perinatol. 2019;43:151177.
4. Escobedo MB, Shah BA, Song C, Makkar A, Szyld E. Recent recommendations and emerging science in neonatal resuscitation. Pediatr Clin North Am. 2019;66:309-20.
5. Yamada NK, Szyld E, Strand ML, Finan E, Illuzzi JL, Kamath-Rayne BD, et al; American Heart Association and American Academy of Pediatrics.

2023 American Heart Association and American Academy of Pediatrics focused update on neonatal resuscitation: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2024;149:e157-66.
6. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European consensus guidelines on the management of respiratory distress syndrome: 2022 update. Neonatology. 2023;120:3-23.
7. Alves N, Rocha G, Flor-de-Lima F, Rosário M, Pissarra S, Mateus M, et al. Neonatal resuscitation practices in Portuguese delivery rooms: a cross-sectional study. Acta Med Port. 2024;37:342-54.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

A Importância de Brincar

The Importance of Play

Sofia PIRES✉[1], Sandra BORGES[1], Teresa TEMUDO[2]
Acta Med Port 2024 May;37(5):320-322 ▪ https://doi.org/10.20344/amp.20641

Palavras-chave: Brincadeiras e Brinquedos; Criança; Desenvolvimento da Criança
Keywords: Child; Child Development; Play and Playthings

INTRODUÇÃO

O acto de brincar, embutido na existência humana, reveste-se de simbolismo, aprendizagem, construções e representações dependentes da história, da cultura e de características individuais. É um apanágio da vida plena e felicidade das crianças. Será também uma componente essencial na saúde e na conceção de boas práticas médicas?

NA ATUALIDADE

O brincar assume uma posição secundária, perante um mundo centrado no sucesso académico. As escolas, professores, pais e tecnologias tendem a reorientar as brincadeiras, socorrendo-se de estratégias alternativas para conquistar objetivos académicos. Retira-se o lugar à imaginação e criatividade, tornando o brincar um luxo quase inacessível. Importa recordar a sua importância, integrada numa perspetiva de desenvolvimento saudável.

A Convenção sobre os Direitos da Criança (revista em 2019), dita que a criança tem "(...) direito ao repouso e aos tempos livres, o direito de participar em jogos e atividades recreativas".[1] Neurobiologicamente, o brincar está diretamente ligado ao desenvolvimento do córtex pré-frontal que comanda os níveis mais complexos de pensamento e funcionamento.[2] Promove também criação de novas conexões neuronais entre áreas previamente não relacionadas.[2]

NA HISTÓRIA

Os grandes autores do desenvolvimento interpretam o brincar e sublinham a sua importância. Sigmund Freud (1856 - 1939) classificava-o como catártico, ajudando a libertar sentimentos desagradáveis, substituindo-os por outros positivos.[3] Jean Piaget (1896 - 1980) considerou-o como a ferramenta mais importante no desenvolvimento mental da criança, numa perspetiva cognitiva.[3] Erik Erikson (1902 - 1994) discutiu o brincar ao longo dos primeiros anos de vida como parte integrante do processo evolutivo.[3]

O brincar surge de variadas formas, envolvendo objeto ou objetivo, individual ou em grupo, em paralelo ou interação, pode ser passivo, ativo, energético, silencioso, barulhento ou contemplativo, livre ou estruturado. Engloba qualquer atividade escolhida livremente, com motivação intrínseca, desde que realizada com diversão.[4] É a base de toda a civilização.[4]

AO LONGO DO DESENVOLVIMENTO

Consoante a exploração, a interação crescente com o meio e as capacidades adquiridas, o brincar surge em diferentes formas, sendo importante adequar os desafios à idade e etapa desenvolvimental.[5] Esta evolução inicia-se pela exploração do mundo, dando lugar à funcionalidade e, finalmente, ao simbolismo, complexificando-se num brincar social com regras.[5] Identificam-se diferentes tipos de brincar: brincar em sintonia (nos primeiros meses – interação com olhar, trocas de sorrisos, sons e canções), brincar com corpo e movimento (desde o útero, através do desenvolvimento muscular e planeamento motor, até ao controlo da força, andar e correr), brincar com objetos (curiosidade e exploração com mordedores e alimentos podem ser os primeiros), brincar simbólico e faz-de-conta (representação do imaginário e da criatividade), brincar social (competências sociais desde o 'cucu' mais simples), brincar narrativo e histórias (desenvolvimento da comunicação, compreensão, socialização), para além de outros.[6]

OS BENEFÍCIOS

Através da brincadeira, as crianças desenvolvem competências ao variar, repetir e recombinar sequências de comportamento fora do seu contexto primário.[7] Desta forma, este comportamento revela benefícios na esfera do desenvolvimento e da aprendizagem aos níveis emocionais, comportamentais, sociais, cognitivos e físicos.[8]

Brincar é uma linguagem própria que transmite alegrias, frustrações, conquistas, habilidades e dificuldades, expressando-se no mundo, em contacto com a realidade interior.[2] Permite a experiência, treino comportamental e social em ambiente seguro, oportunidade para recriar situações reais, conflitos, dificuldades e desenvolver um reportório

1. Serviço de Psiquiatria da Infância e Adolescência. Centro Hospitalar de Vila Nova de Gaia/Espinho. Vila Nova de Gaia. Portugal.
2. Serviço de Neuropediatria. Centro Hospitalar Universitário de Santo António. Porto. Portugal.
✉ **Autor correspondente:** Sofia Pires. ana.rodrigues.pires@chvng.min-saude.pt
Recebido/*Received*: 04/09/2023 - **Aceite/*Accepted*:** 19/12/2023 - **Publicado/*Published*:** 02/05/2024

emocional diversificado, capacidade de regulação, negociar com outros e gerar uma identidade.[7] Constrói a confiança no outro e a vinculação através da interação.[7,8] Desenvolve relações sociais, aumenta a empatia, cooperação, partilha, cria oportunidade para tomar decisões.[5] Promove a prática de capacidades de comunicação, linguagem e memória, facilita o desenvolvimento da resiliência, adaptabilidade e a capacidade de raciocínio, contribuindo para a resolução de problemas.[8] É útil para processar nova informação (cognitiva e emocional), estimula a fantasia e promove pensamento criativo.[7,8] Potencia capacidades motoras, aumenta a amplitude de movimentos, coordenação, equilíbrio, flexibilidade, melhora o controlo e a força muscular.[7,8] Brincar é também terapêutico: ajuda na diminuição da dor, redução de ansiedade e depressão, reduz risco de psicopatologia e a fadiga associada às doenças crónicas.[7]

COMO BRINCAR?

Relativamente ao processo, pretende-se um brincar saudável e com lugar para o prazer e espontaneidade. É importante a criança deixar-se guiar a um ritmo adequado; deve-se evitar imposição de ideias, estruturar/manipular a brincadeira ou lutas de poder.[6] Deve-se oferecer a oportunidade à criança para exercer controlo, e autonomia, o que por sua vez oferece, autoconfiança e segurança.[4] Deve existir sempre lugar para o elogio, atenção, valorização de conquistas e aquisição de competências, evitando a crítica e encorajando a resolução de problemas autonomamente.[6] No que concerne ao objeto (nunca excluindo a possibilidade de este existir apenas na esfera imaginária da criatividade individual), os brinquedos adequados são aqueles que permitem formas mutáveis e flexíveis de uso, aplicações e simbolismo, permitindo que a criança use a imaginação e crie a sua brincadeira.[5] São apropriados quando ajustados ao nível de desenvolvimento, quando não causam aborrecimento (por não permitirem desafio) ou frustração (quando de nível superior); quando integram vários sentidos ou se desdobram em posições, interpretações, envolvem o uso das mãos ou promovem atividade física e movimento; idealmente laváveis e transportáveis para vários contextos.[5,8]

O MUNDO DIGITAL

Adaptando à atualidade e não esquecendo a versão evolutiva do brincar, constata-se que a tecnologia moderna potenciou profundas alterações nos comportamentos de jogo. No entanto, nem toda a aprendizagem citada é adquirida através do mundo digital. Apesar de proporcionar inegáveis vantagens, impulsionar momentos educativos, promover interação social e aquisição de competências físicas, o digital atua em estreitos limites e capacidades específicas nas escalas de desenvolvimento. Não contribui para um desenvolvimento biopsicossocial dotado de experiências sensoriais enriquecedoras, com todas as sensações e emoções que o contacto com o mundo real comporta (formas, texturas, cores, tamanhos, dinâmica da interação e dos fatores climáticos, experiências multimodais, multissensoriais). Salienta-se que níveis aumentados de atividade física e níveis baixos de tempo de ecrã são favoráveis ao desenvolvimento.[9] Atividades ao ar livre promovem oportunidade para hábitos fisicamente ativos, combatem a obesidade e criam oportunidade para o treino de capacidades sociais.[9] Não sendo possível eliminar o tempo de ecrã, é importante a existência de limites, oportunidade à diversificação de atividades, à exploração e reflexão sobre o digital.[5]

NA CLÍNICA

Convergindo agora ao contexto médico, torna-se, por vezes, difícil avaliar uma criança a brincar. Experiências anteriores traumáticas, o 'medo da bata branca', ambientes hospitalares hostis e despidos do conforto colorido do brincar podem comprometer a observação e podem dificultar a identificação de sintomas. É do conhecimento da comunidade científica que o brincar é terapêutico na redução de ansiedade, *stress* e dor relacionados com procedimentos ou ambientes hospitalares, contribuindo para adaptação à doença/tratamento, uma menor necessidade de administração de fármacos sedativos, maior adesão ao tratamento e evolução clínica com melhores resultados.[10] No campo da decisão terapêutica, promove o empoderamento e a confiança da criança, evitando situações de oposição e recusa.[10] Na área comunicacional floresce como linguagem simbólica repleta de significado e transparência na expressão emocional. Evita rótulos e palavras difíceis, medeia confrontos e acesso ao mundo interior; constrói novas narrativas, permite partilha e negoceia significados.[10]

Neste enquadramento, o brincar oferece a oportunidade ideal para o envolvimento e relacionamento com as crianças, mas, também, como ponte na aproximação e interação em contexto de avaliação ou intervenção médica. Podem ser utilizados brinquedos como reforço positivo, como forma de conseguir a atenção, a autorregulação, o interesse e, consequentemente, a colaboração. O clínico consegue assim identificar sinais de alarme, comunicar, realizar exame físico, observar dificuldades, e realizar leituras de estados emocionais. O clínico é também responsável pela promoção e preservação de um ambiente de observação clínica onde existam brinquedos apropriados às diversas faixas etárias.

O brincar revela-se crucial na existência de qualquer ser humano, permitindo constituir adultos competentes em todas as áreas. É uma indicação de bem-estar mental com potencial evidente no desenvolvimento físico, social,

emocional e cognitivo individual. Apresenta claro benefício e utilidade em contexto médico como utensílio de observação do desenvolvimento psicomotor da criança.

CONTRIBUTO DOS AUTORES

SP: Revisão da literatura e redação do manuscrito.

SB, TT: Revisão crítica do manuscrito.

Todos os autores aprovaram a versão final a ser publicada.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Fundo das Nações Unidas para a Infância. Convenção sobre os direitos da criança e protocolos facultativos. 2019;1-80. [consultado 2023 nov 08]. Disponível em: https://www.unicef.pt/docs/pdf_publicacoes/convencao_direitos_crianca2004.pdf.
2. Yogman M, Garner A, Hutchinson J, Hirsh-Pasek K, Golinkoff RM, Committee on Psychosocial Aspects of Child and Family Health, Council on Communications and Media. The power of play: a pediatric role in enhancing development in young children. Pediatrics. 2018;142:e20182058.
3. Burriss KG, Tsao LL. Review of research: how much do we know about the importance of play in child development? Child Educ. 2002;78:230-3.
4. Hansen J, Macarini SM, Martins GD, Wanderlind FH, Vieira ML. O brincar e suas implicações para o desenvolvimento infantil a partir da psicologia evolucionista. J Hum Growth Dev. 2007;17:133-43.
5. Kang S. The power of play. Am J Health Promot. 2020;34:573-5.
6. National Institute for Play. Play: the basics. 2018. [consultado 2023 nov 08]. Disponível em: https://www.nifplay.org/what-is-play/the-basics/.
7. Nijhof SL, Vinkers CH, van Geelen SM, Duijff SN, Achterberg EJ, van der Net J, et al. Healthy play, better coping: the importance of play for the development of children in health and disease. Neurosci Biobehav Rev. 2018;95:421-9.
8. Ginsburg KR, American Academy of Pediatrics Committee on Communications, American Academy of Pediatrics Committee on Psychosocial Aspects of Child and Family Health. The importance of play in promoting healthy child development and maintaining strong parent-child bonds. Pediatrics. 2007;119:182-91.
9. Hinkley T, Brown H, Carson V, Teychenne M. Cross sectional associations of screen time and outdoor play with social skills in preschool children. PLoS One. 2018;13:e0193700.
10. Perasso G, Camurati G, Morrin E, Dill C, Dolidze K, Clegg T, et al. Five reasons why pediatric settings should integrate the play specialist and five issues in practice. Front Psychol. 2021;12:687292.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Real-World Effectiveness and Safety of Glecaprevir/Pibrentasvir for the Treatment of Chronic Hepatitis C: A Prospective Cohort Study in Portugal

Efetividade e Segurança de Glecaprevir/Pibrentasvir para Tratamento de Hepatite C Crónica: Um Estudo de Coorte Prospetiva em Portugal

José VERA✉[1], André GOMES[2], Diana PÓVOAS[3], Diana SEIXAS[3], Fernando MALTEZ[3], Isabel PEDROTO[4], Luís MAIA[4], Margarida MOTA[5], Maria João VIEIRA[1], Maria José MANATA[3], Paula FERREIRA[6], Sara LINO[3], Tiago PEREIRA GUEDES[4], Vânia BARRADAS[1], Nuno MARQUES[2]

Acta Med Port 2024 May;37(5):323-333 ▪ https://doi.org/10.20344/amp.19178

ABSTRACT

Introduction: Information about pan-genotypic treatments for hepatitis in Portugal is scarce. We aimed to evaluate the effectiveness and safety of glecaprevir plus pibrentasvir (GLE/PIB) treatment for hepatitis C virus (HCV) infection in real-world clinical practice.

Methods: An observational prospective study was implemented in six hospitals with 121 adult HCV patients who initiated treatment with GLE/PIB between October 2018 and April 2019, according to clinical practice. Eligible patients had confirmed HCV infection genotype (GT) 1 to 6 and were either treatment-naïve or had experience with interferon-, ribavirin- or sofosbuvir-based regimens, with or without compensated cirrhosis. Baseline sociodemographic and safety data are described for the total population (N = 115). Effectiveness [sustained virologic response 12 weeks after treatment (SVR12)] and patient-reported outcomes are presented for the core population with sufficient follow-up data (n = 97).

Results: Most patients were male (83.5%), aged < 65 years (94.8%), with current or former alcohol consumption (77.3%), illicit drug use (72.6%), and HCV acquisition through intravenous drug use (62.0%). HIV co-infection occurred in 22.6% of patients. The prevalence of each GT was: GT1 51.3%, GT2 1.7%, GT3 30.4%, GT4 16.5%, and GT5.6 0%. Most patients were non-cirrhotic (80.9%) and treatment-naïve (93.8%). The SVR12 rates were 97.9% (95% CI: 92.8 - 99.4), and > 95% across cirrhosis status, GT, illicit drug use, alcohol consumption, and HCV treatment experience. The adverse event rate was 2.6%, and no patient discontinued treatment due to adverse events related to GLE/PIB.

Conclusion: Consistent with other real-world studies and clinical trials, treatment with GLE/PIB showed high effectiveness and tolerability overall and in difficult-to-treat subgroups (ClinicalTrials.gov: NCT03303599).

Keywords: Genotype; Glecaprevir; Hepatitis C, Chronic/drug therapy; Pibrentasvir; Portugal; Treatment Outcome

RESUMO

Introdução: A informação sobre os tratamentos pan-genotípicos da hepatite em Portugal é escassa. Pretendeu-se avaliar a efetividade e segurança do glecaprevir+pibrentasvir (GLE/PIB) para tratamento da infeção por vírus da hepatite C (VHC), na prática clínica habitual em Portugal.

Métodos: Estudo prospetivo observacional em seis hospitais, com 121 adultos com hepatite C que iniciaram GLE/PIB entre outubro 2018 e abril 2019, conforme a prática clínica habitual. Os doentes elegíveis tinham infeção por VHC de genótipo (GT) 1 a 6, independentemente de ter ou não cirrose compensada e tratamento prévio. Os dados sociodemográficos e de segurança foram descritos para a população total (N = 115). As taxas de resposta virológica sustentada às 12 semanas (RVS12) foram apresentadas para a população com seguimento completo (n = 97).

Resultados: A maioria dos doentes eram homens (83,5%), < 65 anos (94,8%), consumo atual ou anterior de álcool (77,3%) e de substâncias ilícitas (72,6%), e infeção VHC adquirida por agulha contaminada/uso de substâncias intravenosas (62,0%); 22,6% era co-infetado com VIH. A prevalência de GT1 foi de 51,3%, GT2 1,7%, GT3 30,4%, GT4 16,5% e GT5,6 0%. A maioria não tinha cirrose (80,9%) nem tratamento prévio (93,8%). As taxas de RVS12 foram de 97,9% (IC de 95%: 92,8 - 99,4) no geral e > 95% nos subgrupos com cirrose, GT3, uso de substâncias ilícitas, alcoolismo e tratamento prévio. A taxa de eventos adversos foi de 2,6% e nenhum doente interrompeu o tratamento devido a eventos adversos. A qualidade de vida, produtividade e fadiga melhoraram após tratamento.

Conclusão: Em linha com outros estudos, o tratamento com GLE/PIB mostrou alta eficácia e tolerabilidade, no geral e por subgrupos de doentes de difícil tratamento (ClinicalTrials.gov: NCT03303599).

Palavras-chave: Genótipo; Glecaprevir; Hepatite C Crónica/tratamento farmacológico; Pibrentasvir; Portugal; Resultado do Tratamento

INTRODUCTION

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease and liver-related mortality.[1] By 2015, approximately 71 million people were living with HCV infection worldwide, with a higher prevalence in the Eastern Mediterranean (2.3%) and European (1.5%) regions.[2,3] Globally, the most prevalent genotypes (GT) are GT1 (44%), GT3 (25%), and GT4 (15%).[2] About 10% to 20% of individuals with chronic HCV develop extensive fibrosis and cirrhosis over 20 to 30 years, and untreated cases may evolve into hepatic decompensation, liver failure or hepatocellular carcinoma (HCC).[4,5] Treatment of HCV, along with improved access to diagnosis and care,

1. Centro Hospitalar Barreiro-Montijo. Barreiro. Portugal.
2. Hospital Garcia de Orta. Almada. Portugal.
3. Centro Hospitalar Lisboa Central. Lisboa. Portugal.
4. Centro Hospitalar Universitário Porto. Porto. Portugal.
5. Centro Hospitalar Vila Nova de Gaia/Espinho. Vila Nova de Gaia. Portugal.
6. Centro Hospitalar Lisboa Norte. Lisboa. Portugal.
✉ **Autor correspondente:** José Vera. josecvera@chbm.min-saude.pt

Recebido/*Received*: 22/01/2022 - **Aceite/*Accepted*:** 02/06/2023 - **Publicado *Online*/*Published Online*:** 07/02/2024 - **Publicado/*Published*:** 02/05/2024

prevents both disease progression and transmission and is fundamental to achieve the World Health Organization (WHO) targets of 80% reduction in HCV incidence and 65% reduction in HCV-related mortality by 2030.[4,6]

Initial chronic HCV treatments were based on interferon, did not have high cure rates, could not be used to treat all genotypes, and had considerable drug-related adverse events. Therefore, these regimens raised concerns regarding patient adherence, particularly among vulnerable populations such as incarcerated persons and people who inject drugs (PWID).[4,7] Currently, HCV can be treated using pan-genotypic direct-acting antivirals (DAAs), which achieve sustained virological responses post-treatment week 12 (SVR12) over 90%, have a well-established safety profile, and have a treatment duration between eight and 16 weeks.[8]

The combination of glecaprevir (GLE, a NS3/4A protease inhibitor) plus pibrentasvir (PIB, a NS5A inhibitor) is a once-daily, oral, interferon- and ribavirin-free DAA regimen, approved in 2017 for the treatment of HCV GT 1-6 infection. GLE/PIB is the pan-genotypic agent with the shortest treatment duration (i.e., eight weeks) for treatment-naïve patients without cirrhosis or with compensated cirrhosis. Initially, this treatment duration was approved only for naïve non-cirrhotic patients; however, the EXPEDITION-8 study demonstrated that eight-week treatment duration had an overall SVR12 of 97.7% among GT1-6 treatment-naïve patients with compensated cirrhosis.[8,9]

Both clinical trials and real-world evidence (RWE) consistently support GLE/PIB treatment as it has high SVR12 rates and is well tolerated. Indeed, a pooled analysis of phase II and phase III trials evaluating the GLE/PIB regimen in treatment-naïve patients, reported overall SVR12 rates of 97.6% (1218/1248) in the intention to treat (ITT) population and 99.3% (1218/1226) when excluding patients with non-virologic failure (modified ITT). This analysis also showed that only 2.4% of patients reported serious adverse events (AEs) and less than 1% of patients had an AE that led to GLE/PIB discontinuation.[10] Similarly, and according to a pooled analysis from post-marketing observational studies across nine countries (between 13th November 2017 and 31st January 2020), GLE/PIB had a SVR12 of 96.7% in the overall analysis population (N = 1648), and higher than 95% across subgroups of interest including PWID, alcohol users, and those with psychiatric diseases. In addition, DAA-related serious AEs were reported for 0.9% of patients, and the rate of DAA-related AEs leading to treatment discontinuation was 0.3% (N = 2036).[11]

Portugal endorsed the European Union HCV Elimination Manifesto[12] and is one of the first countries in the world to allow universal access to HCV treatment, with relevant health gains in the first year of the program (2015 - 2016).[13] HCV epidemiological data for Portugal are scarce, with estimates for 2015 suggesting a viremic prevalence of 0.8%, and a higher proportion of GT1 (68.1%) followed by GT3 (17.9%) and GT4 (12.5%).[2] Importantly, in 2017 a very high HCV seroprevalence (67.6%) was reported among attendees of a low-threshold methadone program, particularly in the PWID subgroup (94.2%).[14] The INFARMED (Portuguese Authority of Medicines and Health Products) reported that 30 086 treatments had been recorded in the national registry by January 2022.[15] There are no robust data about the current number of untreated HCV infections in Portugal, but experts have recently estimated this number to be around 40 000.[16]

There are no published studies regarding the safety and effectiveness of GLE/PIB in routine clinical practice in Portugal. In addition, data characterizing HCV patients treated in Portuguese hospitals are also sparse. The objective of this prospective observational study is to provide data on the effectiveness and safety of GLE/PIB treatment in specific cohorts of HCV patients in Portugal.

METHODS

Study design and participants

This observational, multicenter, prospective cohort study was conducted to examine the treatment of chronic HCV with GLE/PIB in routine clinical practice in Portugal. The study was part of an international post-marketing project (clinicaltrials.gov: NCT03303599) and was implemented in six hospitals with recognized experience in HCV management from two mainland regions: north (Centro Hospitalar Universitário Porto; Centro Hospitalar Vila Nova de Gaia/Espinho) and south (Centro Hospitalar Barreiro-Montijo; Hospital Garcia de Orta; Centro Hospitalar Universitário Lisboa Central; Centro Hospitalar Universitário Lisboa Norte). The study followed the ethical principles described in the Declaration of Helsinki, was approved by the Ethics Committees of the participating centers and was conducted in compliance with Portuguese and European legislation. All study participants provided written informed consent prior to study procedures.

Eligible participants were adults with confirmed HCV infection GT1 to 6, who were treatment-naïve or treatment-experienced (with regimens based on interferon, ribavirin or sofosbuvir), with or without compensated cirrhosis, with no more than four weeks of GLE/PIB treatment at enrollment, and who provided written informed consent and were not enrolled in any interventional study.

Treatment

The treatment decision was made independently of study procedures and preceded the decision to invite the patient to the study. The prescription of the GLE/PIB regimen was at the discretion of the physician and in

accordance with local clinical practice, international guidelines and/or the summary of product characteristics. During the recruitment period of the study, the GLE/PIB recommended dosage was 300 mg GLE/120 mg PIB once daily for eight weeks (non-cirrhotic, treatment-naïve patients), 12 weeks (all cirrhotic, treatment-naïve patients), and 12 weeks (all treatment-experienced patients, except GT3, which required 16-weeks treatment duration).

The observational period for patients receiving eight weeks of GLE/PIB was approximately 20 weeks (eight weeks treatment and 12 weeks post-treatment), for patients receiving 12 weeks of GLE/PIB the observational period was approximately 24 weeks (12 weeks treatment and 12 weeks post-treatment), and for patients receiving 16 weeks of GLE/PIB the observational period was approximately 28 weeks (16 weeks treatment and 12 weeks post-treatment).

Study variables and endpoints

Demographic, clinical, virological, safety, and treatment-related variables were collected from clinical records. The protocol described five potential visits per patient, regardless of treatment duration: at baseline, during treatment, end of treatment, early post-treatment, and post-treatment week 12 to assess sustained virological response (SVR12). Nevertheless, the number of visits, laboratory tests, and other medical procedures were at the provider's discretion as per routine clinical practice.

HCV RNA tests for SVR12 assessment were performed using a sensitive polymerase chain reaction (PCR) test with a lower limit of quantification < 50 IU/mL, in accordance with the centers' practice. Cirrhosis status was determined by the investigator at baseline according to clinical practice. When available, the results of liver fibrosis assessment through transient elastography (FibroScan®, Echosens, Waltham, MA, USA), the aspartate aminotransferase to platelet ratio index (APRI), and the fibrosis-4 (FIB-4) scores were also collected.

The primary endpoint was the percentage of patients achieving SVR12, defined as HCV RNA detected via PCR test with a lower limit of quantification (LLoQ) of < 50 IU/mL 12 weeks after the last actual dose of GLE/PIB. This was analyzed in the overall population and subpopulations of interest: HCV genotypes, cirrhotic *versus* non-cirrhotic patients, treatment-experienced *versus* treatment-naïve, elderly (≥ 65 years) *versus* non-elderly (< 65 years), illicit substance users *versus* non-users. According to routine clinical practice, SVR12 rates were calculated considering the HCV RNA measurement performed within a time window of 70 to 126 days after the last GLE/PIB dose.

Safety endpoints included the number and percentage of patients with treatment-emergent serious and non-serious adverse events (AEs) and increases in laboratory parameters of interest, namely the hepatic function panel. Safety data were collected at each visit after baseline: AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA; Version 21.1); laboratory parameters were performed as per routine practice.

Patient-reported outcomes (PROs) included the 36-Item Short-Form Health Survey (SF-36), the Work Productivity and Activity Impairment (WPAI) Questionnaire, and the Fatigue Severity Scale (FSS), and were collected at baseline, end of treatment, and SVR12 visit (final visit). The SF-36 consists of eight domains that result in the physical component summary (PCS) and the mental component summary (MCS) scores (range 0 - 100; higher scores indicate better health-related quality of life). The FSS is a nine-item scale that measures fatigue severity and its impact on daily activities and lifestyle. Each item is rated from 1 (completely disagree) to 7 (completely agree), and the FSS total score ranges from 1 (no fatigue) to 7 (very severe fatigue). Minimum clinically important differences (MCID) from baseline to SVR12 were defined as an increase of at least 2.5 points in the PCS or MCS scores and a decrease of at least 0.7 points in the FSS scores. The WPAI questionnaire is a six-item scale measuring work absenteeism, presenteeism, and daily activity impairment during the last seven days. The HCV-specific version, WPAI HepC Version 2.0 was used, and results were expressed as a percentage of overall work impairment due to HCV and percentage of general activity impairment due to HCV.

Statistical methods

Safety data and baseline characteristics were assessed for all patients who received at least one dose of GLE/PIB (total population). The effectiveness analysis (SVR12) was carried out in the core population with sufficient follow-up data (CPSFU), which included all patients who received a GLE/PIB regimen according to their disease characteristics, excluding those patients without an HCV RNA evaluation 70 days after the last dose due to other reasons not related to safety or efficacy (e.g., missing or lost to follow-up).

Comparison of patient characteristics (i.e., current drinkers, illicit drug use, patient on stable opioid substitution therapy) according to the geographical region was performed using the chi-square test with a significance level of 5%. In addition, the comparison of GT frequency by region was performed overall for GT1, GT3, and GT2/4 (chi-square test for independence), and by GT *versus* others (2 x 2 chi-square test except for GT4 *versus* other, where exact Fisher test was used since one expected value was < 5. For the primary SVR12 outcome, 95% confidence intervals (CIs) were provided for both the overall population and the main subgroups of interest. The inclusion of 120 patients would allow a width (i.e., from the lower limit to the upper limit of

the CI) of the 95% CI of the overall estimate of SVR12 of 8.2%, using Wilson's score method. Comparisons between groups with small sample sizes were only done descriptively.

RESULTS

Baseline characteristics

Between 28th September 2018 and 30th April 2019, 121 patients with chronic hepatitis C were enrolled in the study (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18876/15304), with patients receiving at least one dose of GLE/PIB and being included in the safety analysis, and 97 patients comprising the CPSFU and being included in the effectiveness analysis (Fig. 1).

Among the patients that initiated treatment, 94.8% were aged < 65 years and 83.5% were male (Table 1); 73.9% were followed up at centers in southern Portugal. Most patients (77.3%) reported current or former alcohol consumption. Current or former use of illicit drugs was reported by 72.6% of patients, with a significantly higher frequency among patients from the south region (77.6% *vs* 57.1% in the north region; $p = 0.035$, Fig. 2), and 60.2% were PWID (64.7% in the south *vs* 39.3% in the north region; $p = 0.014$). Most patients (62.0%) acquired HCV infection through intravenous (IV) drug use (67.9% in the south *vs* 31.3% in the north region; $p = 0.006$). HIV co-infection was reported in 26 patients (22.6%), of which six presented with an HIV load ≥ 20 copies/mL. There were no patients with chronic HBV infection at baseline.

The most frequent HCV genotype was GT1 (51.3%), followed by GT3 (30.4%), GT4 (16.5%), and GT2 (1.7%), while GT5 and GT6 were not identified in our patients. There were statistically significant differences in the distribution of HCV genotypes by Portuguese region ($p = 0.006$). GT1 was more prevalent in the south (56.5%) *vs* north (36.7%), and GT3 was more prevalent in the north (53.3%) *vs* south (22.4; $p = 0.002$). Overall, 80.9% of patients were non-cirrhotic and 106 patients (93.8%) were treatment-naïve. All cirrhotic patients had a Child-Pugh classification of 5 - 6. Among the seven patients with treatment experience (three patients GT1, two GT3 and two GT4), five had been previously treated with interferon/ribavirin-based regimens (three relapses and two null responses), one had been previously treated with sofosbuvir only (GT3 non-cirrhotic with relapse), and these data were missing for one patient. The mean (± standard deviation) HCV viral load at baseline was 6.0 ± 0.9 $\log_{10}$ IU/mL.

One patient had a history of esophageal varices, and one had ongoing hepatocellular carcinoma. Of 75 patients with available data on renal function, 69.3% had no renal impairment, 29.3% had minor renal impairment (defined as eGFR 60 - 90 mL/min/1.73 m^2) and 1.3% had moderate impairment (eGFR 30-60 mL/min/1.73m^2). Regarding other comorbidities, 10.4% (n = 12) had cardiovascular disease and 7.0% (n = 8) had diabetes mellitus or other metabolic

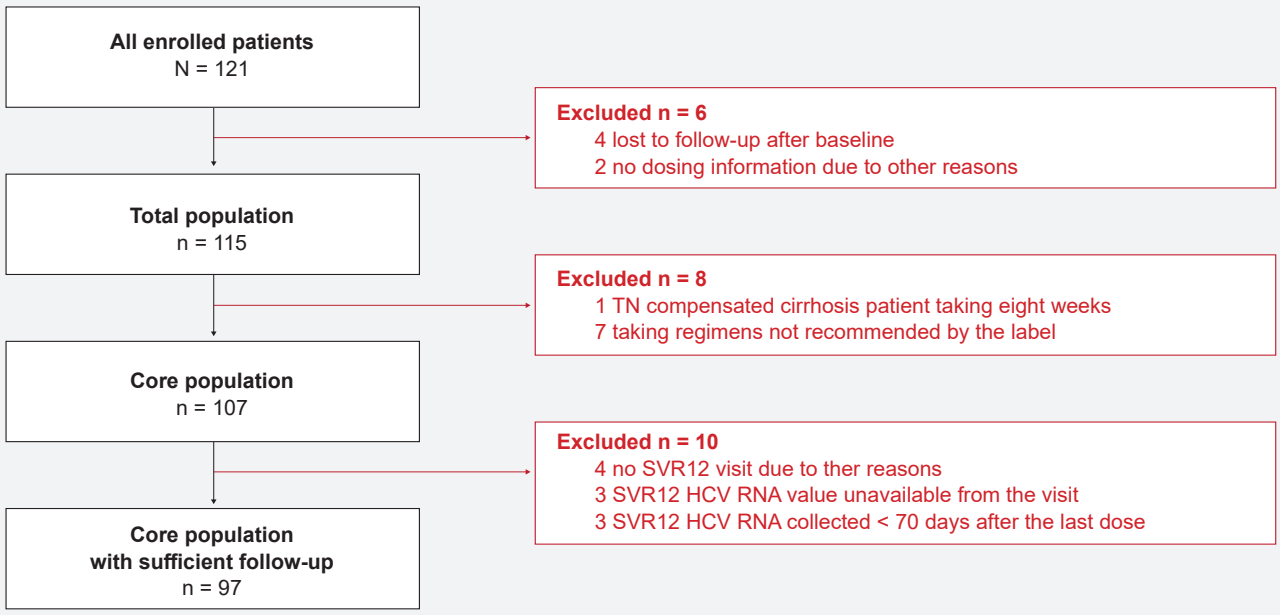


Figure 1 – Patient flowchart

Total population: all patients who received at least one dose of GLE/PIB; Core population: all patients who received a GLE/PIB regimen according to their disease characteristics; Core population with sufficient follow-up: all patients who received a GLE/PIB regimen according to their disease characteristics, excluding those patients without an HCV RNA evaluation 70 to 126 days after the last dose due to other reasons (e.g., missing or lost to follow-up) not related to safety or efficacy.
GLE/PIB: glecaprevir plus pibrentasvir; SVR12: sustained virological response 12 weeks after treatment; TN: treatment-naïve.

Table 1 – Baseline characteristics of the total population

	Total population (n = 115)
Male sex	96 (83.5)
Age (years), mean ± SD	50.6 ± 8.8
Age < 65 years	109 (94.8)
White	111 (96.5)
Current occupational status (n = 85)	
Employed	48 (56.5)
Unemployed	29 (34.1)
Retired/Homemaker	8 (9.4)
Current smoker (n = 84)	57 (67.9)
Any illicit substance use (n = 113)	82 (72.6)
Current use	12 (10.6)
≤ 12 months	7 (6.2)
> 12 months	62 (54.9)
People who inject drugs (current or past) (n = 113)	68 (60.2)
On stable opiate substitution therapy (n = 113)	25 (22.1)
Any history of regular alcohol consumption (n = 88)	68 (77.3)
Current alcohol consumption (any)	41 (46.6)
Current alcohol consumption > 4 drinks/day	16 (18.1)
HCV genotype	
GT1	59 (51.3)
GT2	2 (1.7)
GT3	35 (30.4)
GT4	19 (16.5)
GT5,6	0
Acquisition of HCV infection (n = 100)	
Contaminated needle or IV substance use (current/past)	62 (62.0)
Contact with an infected individual (other than vertical transmission)	4 (4.0)
Blood product transfusion	3 (3.0)
Vertical transmission (mother to child)	2 (2.0)
Surgical procedure	2 (2.0)
Unknown	27 (27.0)
Referral to the hospital for HCV treatment (n = 63)	
Primary care physician	30 (47.6)
Physician at substance dependence treatment center	18 (28.6)
Another physician	15 (23.8)
Years since HCV diagnosis (n = 98), mean ± SD	11.1 ± 9.2
Viral load - HCV RNA (log_{10} IU/mL) (n = 111), mean ± SD	6.0 ± 0.9
< 6.0	44 (39.6)
≥ 6 to < 6.3	15 (13.5)
≥ 6.3	52 (45.6)
Naïve to HCV treatment (n = 113)	106 (93.8)
No history of varices, decompensation, hepatorenal syndrome, or HCC	113 (98.3)
Cirrhosis	22 (19.1)
Liver fibrosis stage* (n = 79)	
F0 to F1	54 (68.4)
F2	3 (3.8)
F3	6 (7.6)
F4	16 (20.3)
APRI score (n = 79), median [min-max]	0.60 [0.17 - 19.48]
APRI > 1	25 (31.6)
FIB-4 score (n = 79), median [min-max]	1.65 [0.41 - 15.79]
Renal function (GFR) (n = 75)	
Normal (≥ 90 mL/min)	52 (69.3)
Mild impairment (≥ 60 to < 90 mL/min)	22 (29.3)
Moderate impairment (≥ 30 to < 60 mL/min)	1 (1.3)
Severe impairment (< 30 mL/min)	0

Data are n (%), except otherwise mentioned. Number of patients in the total population was 115 unless stated otherwise.
APRI: aspartate aminotransferase to platelet ratio index; GFR: glomerular filtration rate; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; SD: standard deviation.
*: Assessed by transient elastography (FibroScan®)

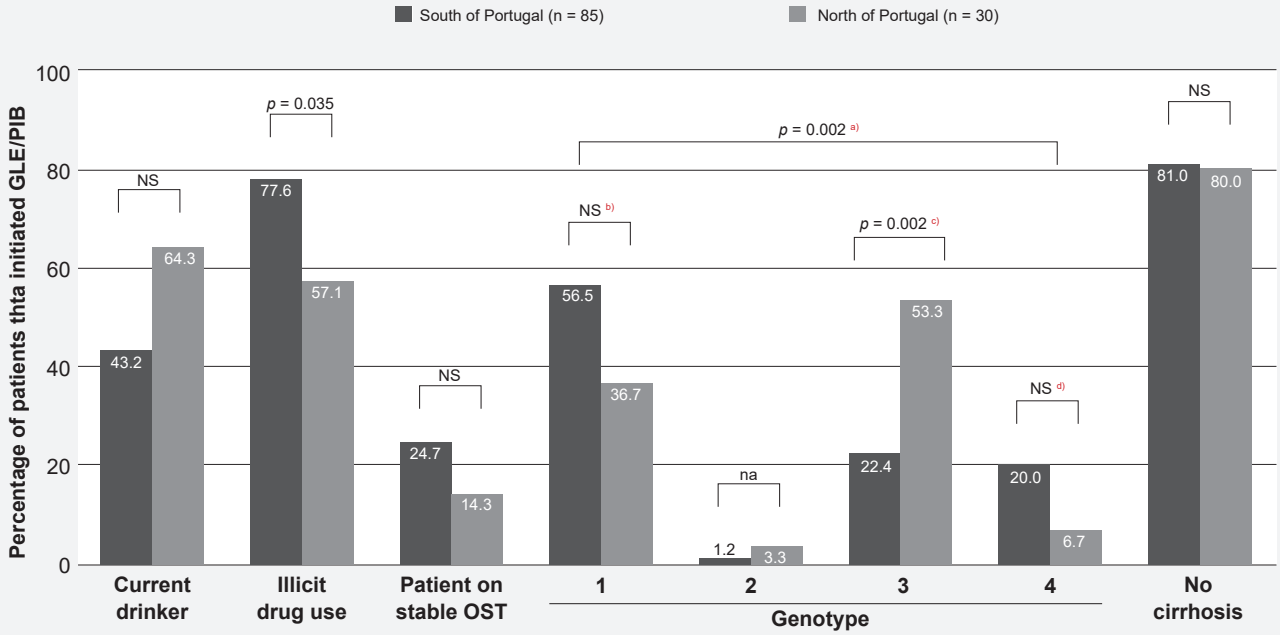


Figure 2 – Main characteristics of the total population (n = 115) at baseline, by Portuguese Region

NS: not statistically significant ($p > 0.05$); n/a: not applicable; OST: opioid substitution therapy.

[a] Chi-square test for independence, after grouping genotypes 2 and 4

[b] Comparison by region of GT1 *versus* other genotypes (chi-square test; *p*-value = 0.062)

[c] GT3 *versus* other (chi-square test; *p*-value = 0.002), and

[d] GT4 *versus* other (exact Fisher; *p*-value = 0.148).

Note: Differences in the number of patients with information available are reported for the following variables: 'Current drinker': north (n = 74) and south (n = 14); 'Illicit drug use': north (n = 28); and 'Patients on stable OST': north (n = 28).

disorders. In addition, 26.1% had a history of depression or suicide attempts/self-injury, 6.1% (n = 7) had depression or bipolar disorder, and 4.3% (n = 5) had a history of anxiety.

During the treatment period, a total of 123 concomitant medications were reported for 60 (52.2%) patients, of whom 43.9% were taking one medicine. The most frequent drug classes (≥ 5% of patients) were anti-HIV drugs (n = 25, 21.7%), drugs used in addictive disorders (n = 18; 15.7%), anxiolytics (n = 10; 8.7%), and antidepressants (n = 6; 5.2%).

Treatment exposure

One hundred and fifteen patients received at least one dose of GLE/PIB, and the most prescribed treatment duration was eight weeks (76.5%), followed by 12 weeks (23.5%). No patient received 16 weeks of treatment. The mean treatment duration was 56.7 ± 3.9 days for the eight-week duration and 82.4 ± 11.5 days for the 12-week regimen. Of the 27 patients with a 12-week regimen, 21 (77.8%) patients had cirrhosis and 15 (55.6%) had GT3 infection (of whom, 12 patients were treatment-naïve with compensated cirrhosis). Of the 35 patients with GT3 infection, 15 (42.9%) initiated a 12-week regimen.

When considering patients that initiated GLE/PIB on-label and according to their disease characteristics (n = 107), 80.4% were assigned to an eight-week treatment duration and 19.6% were prescribed a 12-week treatment. During the study, patients had a median of three in-office appointments (range 2 - 5) with healthcare professionals, including any office visits, emergency room visits, or hospitalizations (based on healthcare resource use data that was available for 88 patients initiating GLE/PIB).

Effectiveness

Of the 97 patients of the CPSFU, 95 (97.9%) achieved SVR12 (95% CI: 92.8% to 99.4%) as shown in Fig. 3. The two patients with virological failure had the following characteristics: < 65 years-old, APRI score ≥ 1, non-cirrhotic, treatment-naïve (HCV viral load ≥ 6.3 $\log_{10}$ IU/mL), history of illicit substance use, no comorbidities/co-infections, and no concomitant medications. Furthermore, one patient had GT1A, and the other patient presented GT3A. Both patients were non-responders due to relapse.

Of the 10 patients who initiated GLE/PIB but had no SVR12 data, nine had unquantifiable/negative HCV RNA at their last measures (five had their last measures during/at the end of treatment, and four had HCV RNA collected ≥ 53 days after the last dose); one patient had only the

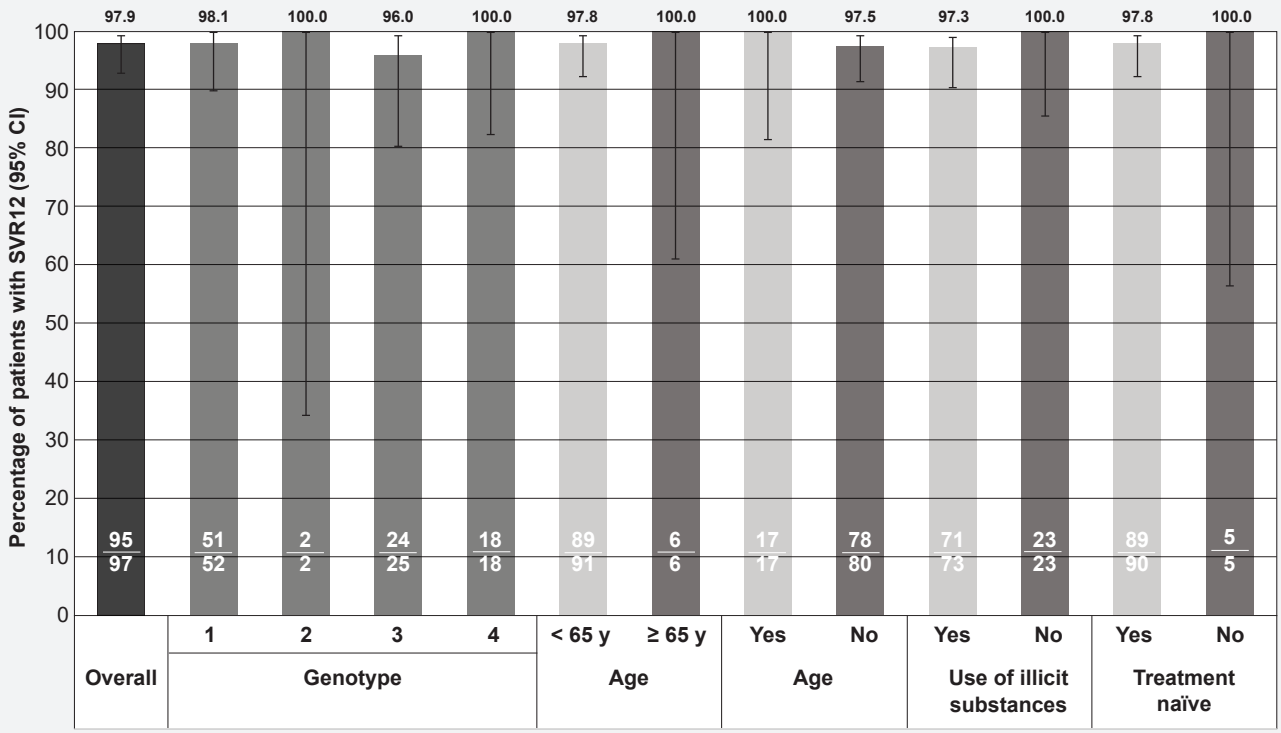


Figure 3 – SVR12 rates after GLE/PIB treatment in the core population with sufficient follow-up: overall and by subgroups of interest

pre-treatment assessment.

Safety evaluation

No serious adverse events were recorded, and the rate of any adverse events was 2.6% (Table 2), namely, headache (n = 2, both treatment-related and one severe), vomiting (n = 2, severe and treatment-related in one case), nausea (n = 1, not treatment-related) and fatigue (n = 1, not treatment-related). One patient discontinued treatment during the first month, after reporting nausea, vomiting, and fatigue (moderate severity and not treatment-related); two patients did not complete treatment and were lost to follow-up, with no reported adverse events. No patient had post-baseline increases of total bilirubin ≥ 2 times the upper limit of normal.

Patient reported outcomes

PROs improved from baseline to the SVR12 visit, presenting MCID in SF36 physical summary score (55% of patients), in SF36 mental summary score (48.3%), and in FSS (31.9%; Table 3).

DISCUSSION

To the best of our knowledge, this is the first observational study to evaluate the safety and effectiveness of GLE/PIB for the treatment of HCV infection in routine clinical practice in Portugal, and the first published study to provide real-world data on the use of pan-genotypic DAAs in this country. We observed an overall SVR12 rate of 97.9% and two virological failures due to relapse (2.1%). This rate is slightly lower than that estimated from the multinational analysis of the same study (98.0%)[17] and from an Italian cohort (99.4%),[18] but is consistent with the results from a Swiss cohort (96.9%),[19] as well as with the pooled analysis of other real-world studies (96.7%).[11] Prospective data of the German Hepatitis C registry (n = 552 patients; 53% GT1, 33% GT3; mostly treatment-naïve, non-cirrhotic and receiving the 8-week GLE/PIB regimen) showed an overall SVR12 rate of 96.7%, with one documented relapse and two HCV reinfections.[20] In our study, the majority of patients were also treatment-naïve and non-cirrhotic; the eight-week regimen was prescribed in more than 75% of cases and more than half of patients presented HCV GT1 infection. Likewise, the results are also similar to the 98% SVR12 reported in a pooled analysis of phase III studies for the GLE/PIB eight-week regimen.[21] When considering patient subgroups, SVR12 results were always higher than 95%, regardless of the cirrhosis status, previous treatment experience, genotype, or use of illicit substances. Even though GT3 infections are considered the most difficult to treat,[1] we observed a 96% SVR12 rate in a total of 25 patients with that genotype.

Table 2 – Adverse events and laboratory abnormalities during the study for the total population

	Total population n = 115
Subjects with AEs	
Any AE	3 (2.6)
Any AE possible related to GLE/PIB treatment*	2 (1.7)
Any AE with a grade of 3 or higher	1 (0.9)
Any treatment-related AE with a grade 3 or higher	1 (0.9)
Any serious AE	0
Any AE leading to treatment discontinuation or interruption	1 (0.9)
Deaths	0
Adverse events reported – preferred term	
Headache	2 (1.7)
Vomiting	2 (1.7)
Fatigue	1 (0.9)
Nausea	1 (0.9)
Laboratory abnormalities, no. of cases/patients evaluated	
Post-nadir ALT > 5x ULN	0/47
Total Bilirubin ≥ 2x ULN	0/47
Post-nadir ALT > 3x ULN and total bilirubin > 2x ULN	0/47

Data are n (%), except otherwise mentioned.
AE: adverse event; ALT: alanine aminotransferase; GLE/PIB: glecaprevir/pibrentasvir; ULN: upper limit of normal.
*: By investigator assessment.

GLE/PIB treatment was well tolerated in our study, with no serious AEs and only 2.6% of patients reporting any AE. This proportion is lower than observed in the Swiss cohort (20.6%) and another German study (26%),[20,21] closer to the 8.3% reported in an Italian real-world study,[22] and higher than the rate observed in the Italian cohort of the same international post-marketing study.[18] Headache was the most common AE as described in clinical trials, and there was no evidence of drug-induced liver injury. An improvement in patients' quality of life was observed during the study, with about half of the patients presenting clinically meaningful improvement in physical or mental dimensions of SF-36. Fatigue improvement (mean decrease of 0.3) was less evident than that observed in the Swiss cohort (mean decrease: 0.8) and in the multinational analysis of the same study.[17] Even so, about a third of patients showed a clinically meaningful improvement in fatigue from baseline to SVR12 visit.

The main study limitation is that the sample was not large enough (safety population: N = 115; evaluable for SVR12: n = 97) to allow robust subgroup analyses for effectiveness, namely for treatment-experienced (n = 5) or elderly (n = 6) patients. Like other real-world studies, safety data may have been underreported, particularly when compared with AE rates from clinical trials (63% for the eight-week duration and 68% for the 12-week duration).[21] Even so, real-world studies enable the evaluation of treatment effectiveness, safety, and prescribing patterns in routine clinical practice with more heterogenous populations, thus providing valuable information for healthcare decision-making. Furthermore, our study sample is likely to represent the Portuguese context, since its demographics are aligned with other national and European reports which described a higher incidence of HCV infection among men and high-risk groups such as PWID.[23-25] GT distribution is also similar to that observed in a larger genomic study in Portugal.[26]

Interestingly, there seem to be regional differences in HCV-infected patients, with a statistically significant higher prevalence rate of illicit drug use in the south and GT3 in the north. We hypothesize that this may result from a different epidemic curve between these regions since subjects with HCV in the south region reflect an older population of PWID associated with a higher frequency of GT1.[26] However, the north region (along with the Azores) presented the highest prevalence of recent and current consumption of any drug and, unless preventive, diagnostic and treatment strategies are reinforced, a rise in the number of patients living with HCV may be observed in this region.[27] A pan-genotypic approach like GLE/PIB has the potential to simplify treatment initiation, e.g., with point-of-care HCV RNA or core antigen testing without genotyping. The ease of use, good safety and tolerability, and short treatment duration may simplify

Table 3 – Summary of patient-reported outcomes during the study

	Baseline	End of treatment	SVR12 visit
SF36 Physical Component Summary score			
n	91	64	60
Mean score at baseline	44.7	44.5	44.0
Mean score at visit		46.9	46.4
Mean ± SD change from baseline		2.5 ± 7.3	2.4 ± 8.4
Increase from baseline ≥ 2.5 points, n (%)		33 (51.6)	33 (55.0)
SF36 Mental Component Summary score			
n	91	64	60
Mean score at baseline	42.6	42.8	43.2
Mean score at visit		46.1	44.6
Mean ± SD change from baseline		3.4 ±10.3	1.3 ±9.8
Increase from baseline ≥ 2.5 points, n (%)		35 (54.7)	29 (48.3)
Work productivity and activity impairment			
% Overall work impairment due to HCV			
n	48	29	24
Mean score at baseline	21.4	15.5	12.5
Mean score at visit		25.3	16.1
Mean ± SD change from baseline		9.8 ± 26.3	3.6 ± 26.4
% Daily activities impairment due to HCV			
n	105	80	64
Mean score at baseline	31.0	33.5	26.4
Mean score at visit		27.6	24.1
Mean ± SD change from baseline		-5.9 ±31.7	-2.3 ± 24.7
Fatigue Severity Scale (FSS) total score			
n	107	83	72
Mean score at baseline	4.4	4.4	4.2
Mean score at visit		3.9	3.9
Mean ± SD change from baseline		-0.4 ± 1.5	-0.3 ± 1.3
Decrease from baseline ≥ 0.7 points, n (%)		28 (33.7)	23 (31.9)

HCV: hepatitis C virus; SD: standard deviation; SF36: 36-Item Short Form Health Survey; SVR12: sustained virological response 12 weeks after completion of treatment.
All scores range from 0 - 100, except FSS total score which ranges from 1 (no fatigue) to 7 (very severe fatigue).

monitoring and reduce healthcare resource use while promoting treatment adherence and patient retention in the cascade of care.[6,9] The shorter GLE/PIB regimens may be particularly relevant in Portugal, considering the high HCV prevalence rate among the difficult-to-treat population of illicit substance users.

CONCLUSION

GLE/PIB administered for eight or 12 weeks was highly effective and well tolerated in the overall sample, regardless of genotype, HCV treatment experience, cirrhosis status, and illicit drug use. In addition, safety and effectiveness results were consistent with those observed in previous clinical trials and real-world studies.[11,21]

ACKNOWLEDGMENTS

The authors would like to thank the study sites, investigators, study coordinators, and patients who participated in the study. Monitoring, data management and medical writing assistance were provided by CTI Clinical Trial & Consulting Services and funded by AbbVie.

PREVIOUS AWARDS AND PRESENTATIONS

Poster “EP-137 - Real World Evidence (RWE) of the Effectiveness and Clinical Practice Use of Glecaprevir Plus Pibrentasvir (G/P) in Patients with Chronic Hepatitis C

Genotypes 1 to 6 in Portugal – Final Results of the Response Study". Semana Digestiva 2020. November 2020.

DATA AVAILABILITY

AbbVie is committed to responsible data sharing, including access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (e.g., protocols, clinical study reports, or analysis plans), as long as the trials are not part of an ongoing or planned regulatory submission. The study data can be requested by any qualified researchers who engage in rigorous, independent, scientific research, and will be provided following review and approval of a research proposal, Statistical Analysis Plan (SAP), and execution of a Data Sharing Agreement (DSA). The data will be accessible for 12 months, with possible extensions considered. For more information on the process or to submit a request, visit the following link: https://www.abbvie.com/our-science/clinical-trials/clinical-trials-data-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html.

AUTHOR CONTRIBUTIONS

JV: Acquisition and interpretation of data for the work; drafting the work; approval of the final version.

AG, DP, DS, FM, IP, LM, MM, MJV, MJM, PF, SL, TPG, VB, NM: Acquisition of data for the work; critical review; approval of the final version.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

AG has received support for training/congresses from AbbVie, and advisory boards fees from ViiV Healthcare;

DP has received support for training/congresses and advisory boards fees from ViiV Healthcare and Roche;

IP has received fees from AbbVie, Merck Sharp & Dohme, and Gilead;

LM has received fees from AbbVie, Gilead Sciences, and Merck Sharp & Dohme;

MJM has received speaker and consultancy fees from AbbVie, Gilead Sciences, Janssen, Merck Sharp & Dohme, and ViiV Healthcare;

SL has received consultancy fees from Gilead Sciences, Merck Sharp & Dohme, and ViiV Healthcare.

All other authors have declared that no competing interests exist.

FUNDING SOURCES

The design, study conduct, analysis, and financial support of the studies were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the content. All authors had access to all relevant data and participated in writing, reviewing, and approval of this abstract. Medical writing support was provided by CTI Clinical Trial & Consulting Services.

REFERENCES

1. Pawlotsky JM, Negro F, Aghemo A, Berenguer M, Dalgard O, Dusheiko G, et al. EASL recommendations on treatment of hepatitis C: final update of the series. J Hepatology. 2020;73:1170-218.
2. Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol. 2017;2:161-76.
3. World Health Organization. Global hepatitis report 2017. [cited 2022 Sep 07]. Available from: https://apps.who.int/iris/handle/10665/255016.
4. AASLD, EASL, APASL, ALEH. Call to action for liver associations to advance progress towards viral hepatitis elimination: a focus on simplified approached to HCV testing and cure. Liver Meeting 2019. [cited 2022 Sep 07]. Available from: https://www.aasld.org/call-action-advance-progress-towards-viral-hepatitis-elimination.
5. Westbrook RH, Dusheiko G. Natural history of hepatitis C. J Hepatol. 2014;61:S58-68.
6. Cooke GS, Andrieux-Meyer I, Applegate TL, Atun R, Burry JR, Cheinquer H, et al. Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol. 2019;4:135-84.
7. Manns MP, Buti M, Gane E, Pawlotsky JM, Razavi H, Terrault N, et al. Hepatitis C virus infection. Nat Rev Dis Primers. 2017;3:17006.
8. Brown RS Jr., Buti M, Rodrigues L, Chulanov V, Chuang WL, Aguilar H, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naïve patients with chronic HCV genotypes 1-6 and compensated cirrhosis: The EXPEDITION-8 trial. J Hepatol. 2020;72:441-9.
9. Spearman CW, Dusheiko GM, Hellard M, Sonderup M. Hepatitis C. Lancet. 2019;394:1451-66.
10. Zuckerman E, Gutierrez JA, Dylla DE, de Ledinghen V, Muir AJ, Gschwantler M, et al. Eight weeks of treatment with glecaprevir/pibrentasvir is safe and efficacious in an integrated analysis of treatment-naïve patients with hepatitis c virus infection. Clin Gastroenterol Hepatol. 2020;18:2544-53.e6.
11. Lampertico P, Carrión JA, Curry M, Turnes J, Cornberg M, Negro F, et al. Real-world effectiveness and safety of glecaprevir/pibrentasvir for the treatment of patients with chronic HCV infection: A meta-analysis. J Hepatol. 2020;72:1112-21.
12. Papatheodoridis GV, Hatzakis A, Cholongitas E, Baptista-Leite R, Baskozos I, Chhatwal J, et al. Hepatitis C: the beginning of the end—key elements for successful European and national strategies to eliminate HCV in Europe. J Viral Hepat. 2018;25:6-17.
13. Velosa J, Macedo G. Elimination of hepatitis c in Portugal: an urban legend? GE Port J Gastroenterol. 2020;27:166-71.
14. Silva MJ, Pereira C, Loureiro R, Balsa C, Lopes P, Água-Doce I, et al. Hepatitis C in a mobile low-threshold methadone program. Eur J Gastroenterol Hepatol. 2017;29:657-62.
15. INFARMED. Hepatite C - Monitorização dos tratamentos, janeiro 2022.

[cited 2022 Sep 07]. Available from: https://www.infarmed.pt/.
16. Marinho RT. Todos contam para travar a transmissão do vírus da Hepatite C até 2030. Raio-X 28 Julho 2020. [cited 2022 Sep 07]. Available from: https://raiox.pt/todoscontam-para-travar-a-transmissao-do-virus-da-hepatite-c-ate-2030/.
17. Aghemo A, Horsmans Y, Bourgeois S, Bondin M, Gschwantler M, Hofer H, et al. Real-world outcomes in historically underserved patients with chronic hepatitis c infection treated with glecaprevir/pibrentasvir. Infect Dis Ther. 2021;10:2203-22;
18. Aghemo A, Alberti A, Andreone P, Angelico M, Brunetto MR, Chessa L, et al. Effectiveness and safety of glecaprevir/pibrentasvir in chronic hepatitis c patients: results of the Italian cohort of a post-marketing observational study. Dig Liver Dis. 2021;53:612-9.
19. Müllhaupt B, Semela D, Ruckstuhl L, Magenta L, Clerc O, Torgler R, et al. Real-world effectiveness and safety of glecaprevir/pibrentasvir therapy in patients with chronic hepatitis c virus infection in Switzerland. Swiss Med Wkly. 2021;151:w20399.
20. Berg T, Naumann U, Stoehr A, Sick C, John C, Teuber G, et al. Real-world effectiveness and safety of glecaprevir/pibrentasvir for the treatment of chronic hepatitis C infection: data from the German Hepatitis C-Registry. Aliment Pharmacol Ther. 2019;49:1052-9.
21. Puoti M, Foster GR, Wang S, Mutimer D, Gane E, Moreno C, et al. High SVR12 with 8-week and 12-week glecaprevir/pibrentasvir therapy: an integrated analysis of HCV genotype 1-6 patients without cirrhosis. J Hepatol. 2018;69:293-300.
22. D'Ambrosio R, Pasulo L, Puoti M, Vinci M, Schiavini M, Lazzaroni S, et al. Real-world effectiveness and safety of glecaprevir/pibrentasvir in 723 patients with chronic hepatitis C. J Hepatol. 2019;70:379-87.
23. Carvalhana SC, Leitão J, Alves AC, Bourbon M, Cortez-Pinto H. Hepatitis B and C prevalence in Portugal: disparity between the general population and high-risk groups. Eur J Gastroenterol Hepatol. 2016;28:640-4.
24. Marinho R, Gíria J, Ferrinho P, Moura M. Aspectos epidemiológicos da hepatite C em Portugal. J Port Gastrenterol. 2000;7:72-9.
25. European Centre for Disease Prevention and Control. Hepatitis C. In: ECDC. Annual epidemiological report for 2021. [cited 2023 May 03]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/AER-HEP-C-2021.pdf.
26. Palladino C, Ezeonwumelu IJ, Marcelino R, Briz V, Moranguinho I, Serejo F, et al. Epidemic history of hepatitis C virus genotypes and subtypes in Portugal. Scientific Reports. 2018;8:12266.
27. SICAD. Relatório Anual 2021 - A situação do país em matéria de drogas e toxicodependências. [cited 2023 May 03]. Available from: https://www.sicad.pt/PT/Publicacoes/Paginas/detalhe.aspx?itemId=178&lista=SICAD_PUBLICACOES&bkUrl=BK/Publicacoes/.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Adaptação e Validação para Português Europeu das Escalas Categories Auditory Performance-II e Infant-Toddler Meaningful Auditory Integration Scale em Crianças com Implante Coclear

Adaptation and Validation for European Portuguese of the Auditory Performance Categories-II and Infant-Toddler Meaningful Auditory Integration Scale for Children with Cochlear Implant

Luís ROQUE REIS✉[1,2], Kaamil GANI[1,2], André SÁ PEREIRA[1,2], Carlota PERES[1], Gonçalo NUNES[1], Ricardo SANTOS[1,2], Assunção O'NEILL[1,2], Pedro ESCADA[1,2]
Acta Med Port 2024 May;37(5):334-341 ▪ https://doi.org/10.20344/amp.20169

RESUMO

Introdução: As escalas *Categories of Auditory Performance II* (CAP-II) e *Infant-Toddler Meaningful Auditory Integration Scale* (IT-MAIS) são questionários simples e de rápida aplicação que permitem avaliar o desempenho auditivo de crianças com implante coclear (IC). O objetivo deste estudo foi a tradução, adaptação e validação da versão em português europeu das escalas CAP-II e IT-MAIS.

Métodos: Um total de 85 participantes completaram a versão em português europeu dos questionários CAP-II e IT-MAIS, dos quais 45 eram pais de crianças com IC pediátrico (9,84 ± 4,22 anos) e outros 40 eram pais de crianças com audição normal (8,35 ± 3,56 anos). Foi avaliada a reprodutibilidade entre avaliadores, a reprodutibilidade teste-reteste, a comparação dos resultados do grupo de estudo *versus* grupo de controlo, a consistência interna e a correlação das novas escalas.

Resultados: As escalas CAP-II e IT-MAIS apresentaram uma elevada confiabilidade e reprodutibilidade, respetivamente com coeficiente de correlação intraclasse (ICC) de 0,979 ($p < 0,001$) e correlação de Spearman de 0,924 para a escala CAP-II, e ICC de 0,932 ($p < 0,001$) e coeficiente de correlação de Spearman de 0,732 para a escala IT-MAIS. As versões do IT-MAIS e do CAP-II apresentaram uma forte consistência interna (valor do coeficiente α de Cronbach de 0,887 para a escala CAP-II e correlação positiva de Spearman de 0,677 para a escala IT-MAIS, respetivamente) e permitem diferenciar entre crianças com audição normal e crianças pós-implantação ($p = 0,001$ e $p < 0,001$ respetivamente para cada uma das escalas). Não se verificou existir associação estatisticamente significativa entre a escolaridade e o resultado nas escalas ($p > 0,05$).

Conclusão: A versão em português europeu destas escalas demonstrou ser uma ferramenta válida e confiável na avaliação do desempenho auditivo em crianças falantes de português europeu com deficiência auditiva.

Palavras-chave: Criança; Implante Coclear; Implantes Cocleares; Inquéritos e Questionários; Qualidade de Vida; Reprodutibilidade dos Resultados; Traduções

ABSTRACT

Introduction: The Categories of Auditory Performance II (CAP-II) scale and the Infant-Toddler Meaningful Audit Integration Scale (IT-MAIS) are simple and quick questionnaires that allow assessment of the auditory performance of children with cochlear implant (CI). The aim of this study was to translate, adapt and validate the European Portuguese version of the CAP-II and IT-MAIS scales.

Methods: A total of 85 participants completed the European Portuguese version of the CAP-II and IT-MAIS questionnaires, of which 45 were parents of children with pediatric cochlear implants (9.84 ± 4.22 years) and another 40 were parents of children with normal hearing (8.35 ± 3.56 years). Inter-rater reproducibility, test-retest reproducibility, comparison of study group *versus* control group results, internal consistency and correlation of the new scales were evaluated.

Results: The CAP-II and IT-MAIS scales showed high reliability and reproducibility, respectively, with an intraclass correlation coefficient (ICC) of 0.979 ($p < 0.001$) and a Spearman's correlation of 0.924 for the CAP-II scale, and an ICC of 0.932 ($p < 0.001$) and Spearman's correlation coefficient of 0.732 for the IT-MAIS scale. The IT-MAIS and CAP-II versions showed strong internal consistency (Cronbach's α coefficient value of 0.887 for the CAP-II scale and Spearman's positive correlation of 0.677 for the IT-MAIS scale, respectively) and allowed for the differentiation between children with normal hearing and post-implantation children ($p = 0.001$ and $p < 0.001$ respectively for each of the scales). There was no association between parental education and the results on the scales ($p > 0.05$).

Conclusion: The findings demonstrated that the European Portuguese version of these scales is a valid and reliable tool for assessing auditory performance in European Portuguese-speaking children with hearing loss.

Keywords: Child; Cochlear Implantation; Cochlear Implants; Quality of Life; Reproducibility of Results; Surveys and Questionnaires; Translations

INTRODUÇÃO

A implantação coclear é considerada uma forma de tratamento muito eficaz em crianças com surdez de grau severo a profundo. A precocidade da intervenção parece desempenhar um papel importante no desempenho pós-implantação e a avaliação do desenvolvimento auditivo pré-lingual é essencial na identificação precoce e no estabelecimento de intervenções para tratar a surdez.[1-4] Várias escalas foram desenvolvidas para avaliar este desenvolvimento em entrevistas estruturadas com os pais, que são provavelmente a melhor fonte para obter esta informação, uma vez que os indivíduos a avaliar são habitualmente lactentes ou crianças muito pequenas.[5-9]

1. Serviço de Otorrinolaringologia. Hospital Egas Moniz. Centro Hospitalar de Lisboa Ocidental (CHLO). Lisboa. Portugal.
2. Faculdade de Ciências Médicas | NOVA Medical School. Universidade NOVA de Lisboa. Lisboa. Portugal.
✉ **Autor correspondente:** Luis Roque Reis. roque-reis@sapo.pt
Recebido/*Received*: 15/05/2023 - **Aceite/*Accepted*:** 07/09/2023 - **Publicado *Online*/*Published Online*:** 18/03/2024 - **Publicado/*Published*:** 02/05/2024

Dado que o desenvolvimento auditivo pré-lingual ocorre antes do início da linguagem falada, habitualmente cerca dos 18 – 24 meses em crianças com audição normal, é necessário utilizar escalas que possam ser utilizadas na infância até ao início da linguagem falada.[10-14] É o caso das escalas *Categories of Auditory Performance* II (CAP-II)[5] e *Infant-Toddler Meaningful Auditory Integration Scale* (IT-MAIS),[6] cuja utilização é recomendada até aos três anos de idade, mas que podem ser usadas até aos 18 anos. O CAP-II e o IT-MAIS são questionários amplamente utilizados em muitos países e permitem uma avaliação prospetiva do desempenho auditivo em crianças com implante coclear (IC).[8,15-22] São preferidos a outras ferramentas de avaliação por serem pequenos, fáceis de realizar e porque refletem o progresso da criança na vida real com elevada reprodutibilidade e confiabilidade.[23] Além disso, podem ser administrados por médicos e outros profissionais de saúde, mas também por outros profissionais, como educadores ou professores, que lidam frequentemente com crianças com IC.

O desempenho auditivo de crianças com IC precisa de ser avaliado regularmente por pessoas próximas, como pais ou professores. Esta necessidade reflete a importância da validação de uma versão em português europeu destes questionários. O objetivo deste estudo foi traduzir, adaptar e validar uma versão em língua portuguesa europeia o CAP-II e o IT-MAIS para ser usada por médicos, terapeutas da fala, audiologistas, pais, professores de educação especial e outros profissionais que lidam com crianças com IC.

MÉTODOS

Este estudo foi submetido e aprovado pela Comissão de Ética para a Saúde (CES) do Centro Hospitalar de Lisboa Ocidental (CHLO) em 17 de outubro de 2020, tendo sido atribuído o n.º 20170700050 no Registo Nacional de Estudos Clínicos (RNEC). O estudo foi conduzido segundo os princípios da Declaração de Helsínquia (revisão de 2013) e os pais deram consentimento informado para que seus filhos participassem no estudo, assinando o termo de consentimento informado.

Amostra

O grupo de pacientes implantados foi recrutado do Serviço de Otorrinolaringologia do Centro Hospitalar de Lisboa Ocidental durante o período de janeiro de 2017 a janeiro de 2022. Todas as crianças foram implantadas no Serviço de Otorrinolaringologia do Centro Hospitalar de Lisboa Ocidental, que é um centro de referência nacional na área dos implantes cocleares aprovado pelo Ministério da Saúde. Incluímos pacientes pediátricos (idade de 18 meses a 18 anos) com surdez pré-lingual e implantados com IC unilateral ou bilateral. Foram excluídos deste estudo pacientes com idade superior a 18 anos, pacientes que desenvolveram linguagem antes do implante, e pacientes com problemas neurológicos e psicológicos ou outros distúrbios que poderiam afetar a sua comunicação. O grupo de controlo (crianças sem histórico de qualquer problema auditivo) foi uma amostra de conveniência recrutado na consulta externa de Pediatria da mesma instituição, durante o mesmo período, sem história de patologia auditiva e otoscopia normal. Este estudo transversal incluiu um total de 85 participantes pediátricos, 45 pacientes pós-IC e 40 participantes no grupo de controlo. A versão em português europeu do CAP-II e do IT-MAIS foi preenchida e avaliada pelos pais e terapeutas da fala para o grupo de pacientes, enquanto para o grupo de controlo foi avaliado apenas pelos pais.

Tradução, retrotradução e adaptação cultural

A validação do CAP-II e do IT-MAIS em português europeu foi realizada seguindo as recomendações para adaptação transcultural[24] e após o pedido da autorização e das normas para a tradução aos autores das escalas. Dois tradutores profissionais bilíngues fluentes em inglês (cujo idioma nativo era o português europeu) traduziram a versão original em inglês do CAP-II e do IT-MAIS para português europeu. As traduções foram revistas por uma comissão de revisão constituída por dois otorrinolaringologistas, um audiologista e um terapeuta da fala. Por consenso, reduziram as diferenças encontradas nas traduções, escolhendo as melhores expressões e palavras para cada questão, e adaptaram o texto ao conhecimento cultural português. Obteve-se um novo e único questionário em português europeu para cada uma das escalas CAP-II e IT-MAIS. Após a revisão, as novas versões do CAP-II e do IT-MAIS em português europeu foram posteriormente retrotraduzidas para o inglês por outros dois profissionais de tradução (cujo idioma nativo era o inglês), desconhecedores do texto original e do estudo, bem como dos tradutores iniciais, para evitar qualquer influência na tradução. O CAP-II e o IT-MAIS originais e as versões retrotraduzidas foram comparadas para garantir que o significado original fosse mantido. Este processo avaliou a semelhança entre a versão original em inglês e a versão em inglês traduzida.

Procedimentos

Cada paciente foi entrevistado e avaliado por uma terapeuta da fala com um dos pais. A terapeuta da fala aplicou os questionários, lendo oralmente cada questão que suscitasse dúvidas, a fim de localizar eventuais dúvidas que surgissem na interpretação das perguntas. A equivalência cultural é estabelecida quando no mínimo 80% dos indivíduos não mostram qualquer tipo de dificuldade em compreender e responder a cada questão formulada.[25] A versão em português europeu dos questionários foi respondida na

sua totalidade, não tendo sido encontradas dificuldades na compreensão das questões. Os questionários foram repetidos com o mesmo progenitor 14 dias depois para avaliar a reprodutibilidade (teste-reteste). Esta medida foi avaliada pela determinação do coeficiente de correlação intraclasse (ICC). A validade convergente concorrente também foi usada medindo a força da correlação do CAP-II e do IT-MAIS em português europeu. Por outro lado, a validade foi avaliada através da capacidade do CAP-II e do IT-MAIS de diferenciar entre pacientes pós-implantação e as crianças do grupo de controlo.

Pontuação

A escala CAP-II permite uma classificação linear e hierárquica de 10 categorias para avaliar os resultados do IC pediátrico na vida quotidiana [Apêndice 1, Tabela 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/20169/15355)]. Difere de medidas mais técnicas por ser prontamente aplicada e facilmente compreendida por profissionais não especialistas e pelos pais. Está organizada numa hierarquia de categorias de desempenho, associadas à perceção auditiva, e que aumentam em dificuldade. A pontuação varia desde o nível mais baixo de desconhecimento dos sons ambientais até o nível mais alto de ter a capacidade de conversar ao telefone com uma pessoa familiar. Gilmour *et al*[17] adicionaram mais duas categorias e pontuações à escala original CAP e que representam as capacidades de conversa em grupo e ao telefone com um desconhecido. Esta escala CAP-II consiste assim em 10 categorias e permite uma capacidade de avaliar completamente o benefício máximo do IC, especialmente na implantação bilateral. A pontuação varia desde o nível mais baixo de desconhecimento dos sons ambientais (0) até o nível mais alto de ter a capacidade de conversar ao telefone com uma pessoa familiar (9).

A escala IT-MAIS é composta por 10 itens que se destinam a avaliar o comportamento auditivo da criança [Apêndice 1, Tabela 2 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/20169/15355)]. Os dois primeiros itens avaliam o comportamento vocal da criança, além da aceitação e confiança da criança no dispositivo. Os quatro itens seguintes avaliam a deteção e resposta espontânea da criança ao seu próprio nome e a sons e sinais ambientais. Os quatro itens finais avaliam a capacidade da criança de reconhecer e discriminar sons como as diferenças entre vozes masculinas e femininas, sons de fala e outros, ou ainda as diferenças no tom vocal que transmitem as emoções. Para cada uma das questões existe a possibilidade de cinco respostas, sendo que cada questão é pontuada pela frequência de ocorrência do comportamento que varia de 0 ("nunca demonstrou este comportamento") a 4 ("sempre demonstrou este comportamento"). A possibilidade total de pontuação na escala IT-MAIS é de 40, sendo que uma pontuação mais alta na escala corresponde a um melhor desempenho. No primeiro item da escala IT-MAIS ("o comportamento vocal da criança é afetado enquanto usa o aparelho?"), realizámos um ajuste na pontuação desta pergunta na população controlo e atribuímos o valor máximo (4) em todos os indivíduos. A escala IT-MAIS deriva de uma escala anterior, a *Meaningful Auditory Integration Scale* (MAIS).[26] Estas duas versões diferem entre si nos dois primeiros itens do questionário, que avaliam o comportamento vocal e a confiança da criança no dispositivo e, da forma como foram elaboradas, os itens da MAIS só são possíveis de ser aplicados em crianças mais velhas com IC.

Métodos estatísticos

Os dados foram analisados usando o *Statistical Package for Social Sciences* (SPSS) versão 28.0 (SPSS Inc, IBM, Armonk, NY). Os dados categóricos foram expressos em números e percentagens e os dados contínuos foram expressos em média, desvio padrão e variação. O teste qui-quadrado foi utilizado para comparar duas proporções categóricas. O teste exato de Fisher e o teste *t* foram usados para comparar duas médias. As estatísticas Kappa foram utilizadas para determinar as discrepâncias nos diferentes questionários. A avaliação da reprodutibilidade (teste-reteste) através do teste de Spearman, a correlação interclasses e o teste de α Cronbach foram calculados para determinar os níveis de concordância entre questionários. Foi também utilizado o teste α de Cronbach para avaliar a consistência interna da IT-MAIS. Como os dados não seguem a distribuição normal (teste Kolmogorov-Smirnov) foi usado o teste não paramétrico Mann-Whitney para comparar as duas amostras independentes ao nível da idade e do total das escalas. Para avaliar a consistência do CAP-II, e tendo em conta que não é possível o cálculo do α de Cronbach dado que esta escala tem só um item, calculou-se a validade concorrente através da correlação de Spearman com a escala IT-MAIS. A validade discriminante foi realizada comparando os resultados do grupo de estudo e do grupo de controlo. Um valor de $p < 0,05$ foi considerado como estatisticamente significativo.

RESULTADOS

Um total de 85 participantes completaram a versão em português europeu dos questionários CAP-II e IT-MAIS, dos quais 45 eram pais de crianças com IC e outros 40 eram pais de crianças sem histórico de qualquer problema auditivo (grupo de controlo). A média da idade das crianças implantadas foi de 5,46 ± 4,48 anos (intervalo de 1 - 16 anos), enquanto a idade média das crianças do grupo de controlo foi de 8,35 ± 3,56 anos (intervalo de 3 - 17 anos).

Tabela 1 – Características demográficas das crianças com implante coclear (n = 45)

Características	
Idade em anos, média (DP)	5,46 (4,48)
Idade em anos, intervalo	1 - 16
Género	
Masculino, n (%)	20 (44,4%)
Feminino, n (%)	25 (55,6%)
Tempo após a implantação coclear em anos, média (DP)	5.96 (4,48)
Implante coclear	
Unilateral, n (%)	16 (35,6%)
Bilateral, n (%)	29 (64,4%)
Nível educacional do progenitor	
Sem informação, n (%)	6 (13,3%)
4.º ano, n (%)	1 (2,2%)
6.º ano, n (%)	2 (4,4%)
9º ano, n (%)	2 (4,4%)
Escolaridade obrigatória, n (%)	24 (53,3%)
Licenciatura, n (%)	10 (22,3%)

DP: desvio padrão

Não houve diferença estatisticamente significativa na média de idades entre os dois grupos (p = 0,078). O grupo implantado foi composto por 20 crianças do sexo masculino (44,4%) e 25 do sexo feminino (55,6%), enquanto o grupo de controlo tinha 19 crianças do sexo masculino (47,5%) e 21 do sexo feminino (52,5%). A maioria da nossa amostra tinha implantação coclear bilateral (29 crianças, 64,4%). O tempo médio após a implantação coclear foi de 49,09 ± 31,74 meses (intervalo de 3 - 110 meses) (Tabela 1). A maioria dos pais tinha a escolaridade obrigatória ou inferior (29, 64,4%), 10 dos progenitores tinham licenciatura ou equivalente (22,3%) e em seis não foi possível obter esta informação (13,3%).

Os resultados do questionário da escala CAP-II estão sumarizados na Tabela 2. O item 7 do questionário ("compreensão da conversa com um interlocutor familiar sem leitura labial") foi o que obteve mais respostas, enquanto o item 2 do questionário ("perceção dos sons do ambiente circundante") foi o que obteve menos respostas. A média do questionário CAP-II foi de 6,58 ± 2,37 numa possibilidade de total de pontuação de 10.

Os resultados do questionário da escala IT-MAIS estão sumarizados na Tabela 3. Os itens 1, 4, 6 e 7 do questionário obtiveram mais respostas na opção de resposta "frequentemente", enquanto os itens 2, 3, 5, 8, 9 e 10 do questionário obtiveram mais respostas na opção de resposta "sempre". A média do questionário IT-MAIS foi de 27,62 ± 8,84 numa possibilidade total de pontuação de 40.

As versões em português europeu dos questionários CAP-II e IT-MAIS apresentaram um excelente desempenho no teste-reteste (superior a 0,9). A confiabilidade foi avaliada com o modelo *two-way mixed* porque teve em consideração que os examinadores eram fixos e os sujeitos randomizados. A escala CAP-II apresentou uma confiabilidade ICC = 0,979 (95% CI = 0,949 - 0,991, p < 0,001) e um coeficiente de correlação de Spearman de 0,924 (p < 0,01). A escala IT-MAIS apresentou uma confiabilidade ICC = 0,932 (95% CI = 0,838 - 0,971, p < 0,001) e um coeficiente de correlação de Spearman de 0,732 (p < 0,001).

A escala IT-MAIS apresentou uma boa consistência interna, com um coeficiente α de Cronbach 0,887. Para avaliar a consistência do CAP-II, dado esta escala ter só um

Tabela 2 – Resultados do questionário da escala CAP-II nas crianças com implante coclear

Item	n	%
1	2	4,4
2	1	2,2
3	1	2,2
4	4	8,9
5	5	11,1
6	8	17,8
7	9	20,0
8	4	8,9
9	5	11,1
10	6	13,3

A cinzento escuro está assinalada a resposta mais frequente

Tabela 3 – Resultados do questionário da escala *Infant-Toddler Meaningful Auditory Integration Scale* (IT-MAIS) nas crianças com implante coclear

Item	Nunca		Raramente		Às vezes		Frequentemente		Sempre	
	n	%	n	%	n	%	n	%	n	%
1	8	17,8	8	17,8	10	22,2	12	26,7	7	15,6
2	5	11,1	4	8,9	4	8,9	6	13,3	26	57,8
3	2	4,4	1	2,2	6	13,3	5	11,1	31	68,9
4	3	6,7	6	13,3	7	15,6	18	40,0	11	24,4
5	3	6,7	2	4,4	8	17,8	13	28,9	19	42,2
6	3	6,7	5	11,1	8	17,8	15	33,3	14	31,1
7	3	6,7	2	4,4	11	24,4	16	35,6	13	28,9
8	3	6,7	2	4,4	8	17,8	15	33,3	17	37,8
9	3	6,7	3	6,7	12	26,7	10	22,2	17	37,8
10	9	20,0	1	2,2	10	22,2	9	20,0	16	35,6

A cinzento escuro estão assinaladas as respostas mais frequentes para cada item

item e não é possível o cálculo do α de Cronbach, calculou-se a sua correlação com a escala IT-MAIS. Para a validade concorrente, as pontuações do CAP-II mostraram uma correlação positiva com as pontuações IT-MAIS, com um valor de correlação de Spearman de 0,677 e $p < 0,001$ (Fig. 1).

A validade discriminante foi realizada comparando a avaliação dos pais do grupo de estudo e do grupo de controlo e mostrou que a versão portuguesa das escalas CAP-II e IT-MAIS permite diferenciar entre crianças com audição normal e crianças pós-implantação (Tabela 4).

Apenas 22,3% dos progenitores tinham licenciatura ou equivalente e tentou-se perceber se existia uma relação entre a escolaridade parental e o nível de desempenho auditivo das crianças. Não se verificou existir associação estatisticamente significativa entre a escolaridade e o resultado nas escalas CAP-II e IT-MAIS ($p > 0,05$)

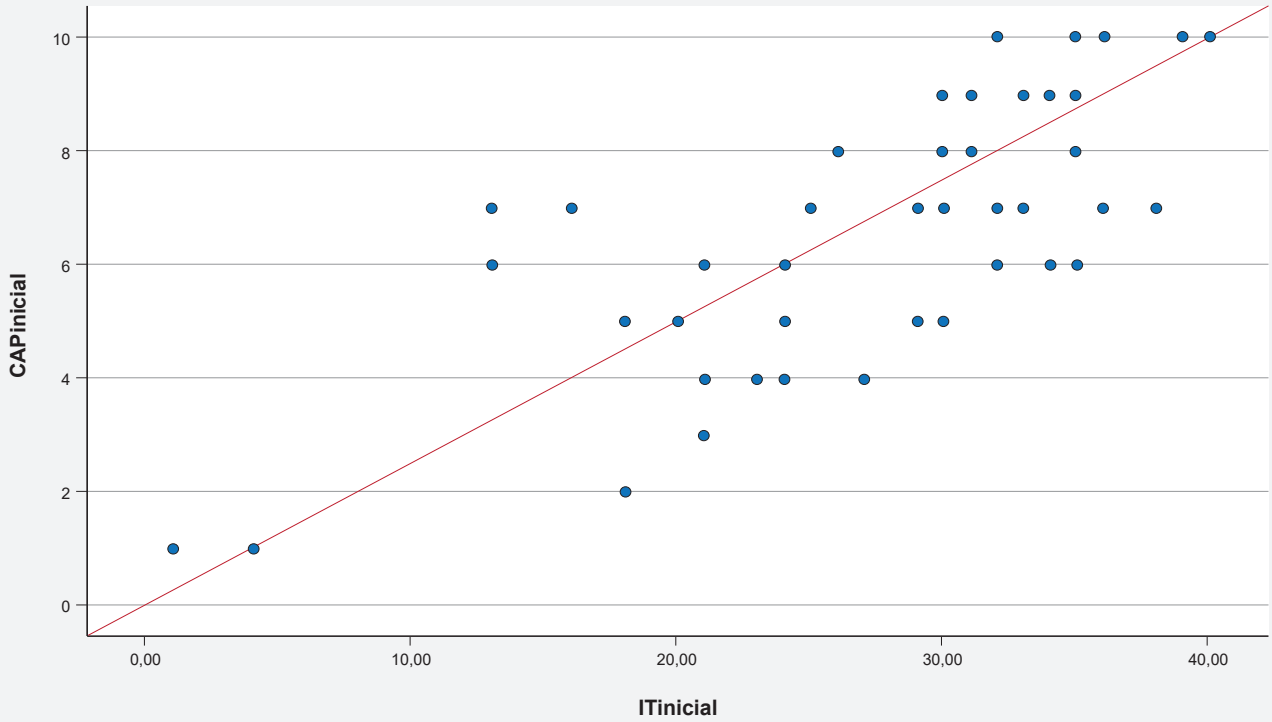
DISCUSSÃO

O objetivo deste estudo foi desenvolver uma versão para o português europeu das escalas CAP-II e IT-MAIS. Estas escalas constituem uma ferramenta útil para capacitar os pais, professores e profissionais de saúde na avaliação do desempenho auditivo diário das crianças após o IC, melhoria após a implantação e acompanhamento do seu progresso. Além disso, as escalas CAP-II e IT-MAIS são uma ferramenta popular e amplamente utilizada para avaliar a qualidade de vida após o IC, atribuindo-se ao fato de ambas poderem ser facilmente administradas e permitirem resultados confiáveis nas crianças implantadas.

As versões do IT-MAIS e do CAP-II para o português europeu apresentaram uma forte consistência interna (valor do coeficiente de α de Cronbach de 0,887 e correlação positiva de Spearman de 0,677, respetivamente). Todos os sujeitos completaram totalmente os questionários, indicando que entenderam todas as perguntas e ficaram à vontade para responder a todas elas. Houve pontuações significativamente mais baixas do CAP-II e IT-MAIS nas crianças com IC em comparação com as do grupo de controlo ($p < 0,001$). Esses resultados demonstraram a capacidade da versão em português europeu destas escalas de discriminar entre crianças com audição normal e com IC, bem como a sua potencial capacidade no acompanhamento do seu progresso. Não se verificou existir associação estatisticamente significativa entre a escolaridade e o resultado nas escalas CAP-II e IT-MAIS ($p > 0,05$).

Com este estudo, os autores deste trabalho completam um ciclo que se iniciou com a adaptação e a validação para o português europeu de uma escala para os utilizadores de próteses auditivas (SADL),[27] posteriormente de uma escala para os utilizadores adultos de IC (Nijmegen)[28] e agora, e por fim, de duas escalas para os utilizadores pediátricos de IC (CAP-II e IT-MAIS). A decisão de validar estas duas escalas para os doentes pediátricos com IC justificou-se pelo facto de serem escalas de fácil utilização, complementares, e apesar de ambas avaliarem o desempenho auditivo, uma delas avalia sobretudo a componente auditiva (IT-MAIS) e a outra sobretudo a componente da fala (CAP-II).

A escala IT-MAIS apresentou uma consistência interna e confiabilidade semelhantes em diversas línguas como o persa, italiano, mandarim, alemão e polaco. Estas semelhanças foram observadas em populações com características culturais e linguísticas diversas, sugerindo que o início do desenvolvimento auditivo pré-lingual tem uma evolução similar em todas as crianças.[29,30] A versão persa do IT-MAIS apresentou uma correlação intraclasse sobreponível à versão portuguesa (ICC = 0,96, IC 95% = 0,93 - 0,98), com uma confiabilidade aceitável (α de Cronbach = 0,74) e uma boa consistência interna dos itens do questionário.[31]



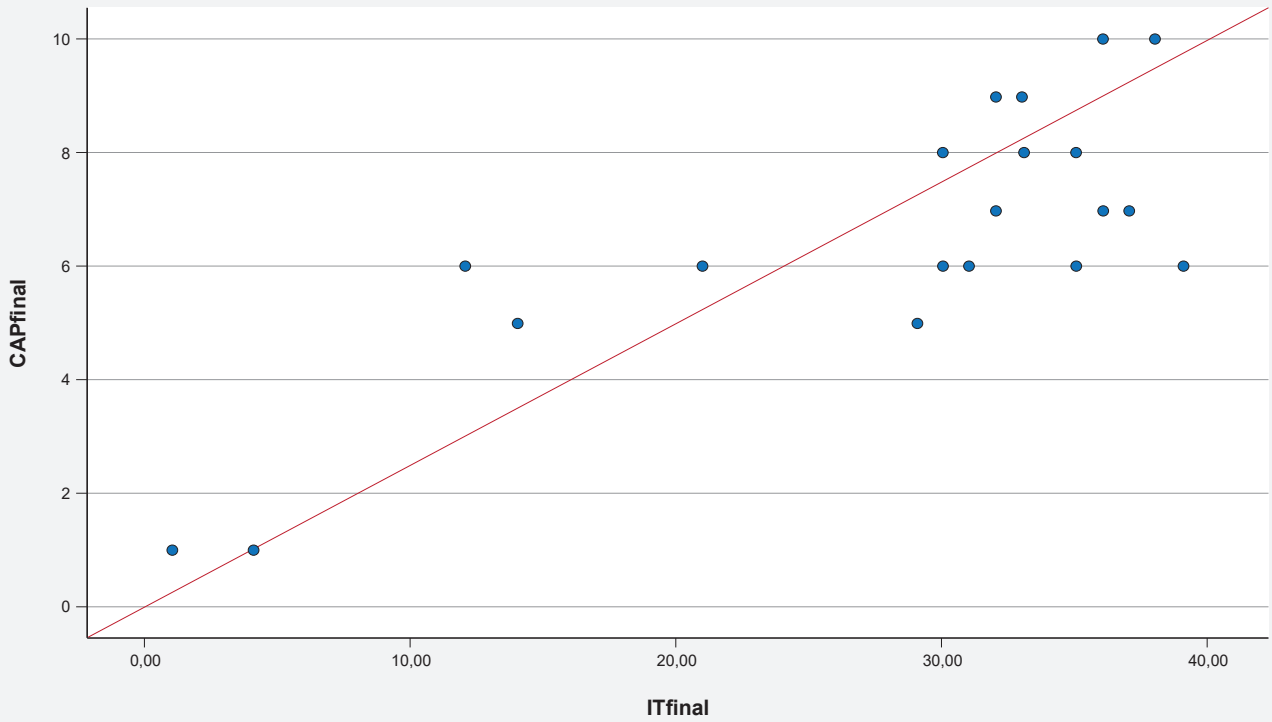


Figura 1 – As pontuações do CAP-II mostraram uma correlação positiva e forte com as pontuações IT-MAIS, indicando que a valores mais altos de uma variável correspondem valores mais altos da outra. Na figura de cima (primeiro momento de avaliação), valores mais altos avaliados do CAP-II correspondem a valores mais altos no IT-MAIS. Na figura de baixo (avaliação final) verifica-se a mesma correspondência.

Zhong *et al* avaliaram as propriedades psicométricas do questionário IT-MAIS em mandarim, com resultados do ICC e α de Cronbach de 0,92 e 0,83, respetivamente.[8] As propriedades psicométricas do IT-MAIS em italiano apresentaram igualmente uma boa confiabilidade intraclasse (ICC = 0,93), sendo que o α de Cronbach total foi de 0,91.[19] Existem também várias versões validadas do teste CAP-II em diversos idiomas. A versão árabe do CAP-II mostrou uma forte confiabilidade teste-reteste, traduzida por alto ICC (0,9), bem como uma alta correlação de Spearman de 0,9 ao correlacionar as pontuações do teste-reteste.[15] Estes resultados foram sobreponíveis aos da versão em mandarim do CAP-II que relataram achados semelhantes em relação aos valores do ICC (0,924), do índice de correlação de Spearman (0,842) e do Kappa (0,688).[32]

Apesar dos bons resultados obtidos, é importante referir que a satisfação sentida com o IC pode variar com diversos fatores tais como a causa da surdez, o tempo de privação sensorial, a idade do diagnóstico e da intervenção, a diferenciação escolar parental, a motivação e o apoio familiar.[33-35] Uma das limitações do estudo é o tempo variável de implantação, bem como a dimensão da amostra. Outra limitação foi a não realização de exames de triagem audiológica nos participantes do grupo de controlo, pois foram recrutados no mesmo centro hospitalar e apenas a avaliação auditiva subjetiva foi realizada.

Contudo, estas crianças não tinham histórico de problemas auditivos ou de atraso de desenvolvimento da linguagem relatado por seus pais. Abordaremos estas limitações em estudos futuros. O IT-MAIS e o CAP-II são as primeiras escalas validadas para português europeu que permitem avaliar o desempenho auditivo de crianças com IC, podem ser aplicadas em crianças de qualquer idade, são simples e de fácil aplicação quer por profissionais de saúde ou outros profissionais que lidem com estas crianças, são complementares entre si e apresentaram uma forte consistência interna e confiabilidade.

CONCLUSÃO

As versões em português europeu dos questionários CAP-II e IT-MAIS são ferramentas válidas e confiáveis para a avaliação do desempenho auditivo em crianças de língua portuguesa com deficiência auditiva e implantação coclear. Estas escalas permitem avaliar o desempenho auditivo da criança na vida real e monitorizar o seu progresso ao longo do tempo após a implantação.

CONTRIBUTO DOS AUTORES

LRR: Desenho do estudo, recolha de dados, redação do manuscrito.

KG, ASP, CP, GN: Desenho do estudo, recolha de dados, redação do manuscrito.

RS: Recolha de dados, redação do manuscrito.

AO, PE: Desenho do estudo, redação e revisão crítica do manuscrito.

PROTEÇÃO DE PESSOAS E ANIMAIS

Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial atualizada em 2013.

CONFIDENCIALIDADE DOS DADOS

Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação de dados.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Zhou H, Chen Z, Shi H, Wu Y, Yin S. Categories of auditory performance and speech intelligibility ratings of early-implanted children without speech training. PLoS One. 2013;8:e53852.
2. Carlson ML, Sladen DP, Haynes DS, Driscoll CL, DeJong MD, Erickson HC, et al. Evidence for the expansion of pediatric cochlear implant candidacy. Otol Neurotol. 2015;36:43-50.
3. Svirsky MA, Teoh SW, Neuburger H. Development of language and speech perception in congenitally, profoundly deaf children as a function of age at cochlear implantation. Audiol Neurootol. 2004;9:224-33.
4. Hemmingson C, Messersmith JJ. Cochlear implant practice patterns: the U.S. trends with pediatric patients. J Am Acad Audiol. 2018;29:722-33.
5. Archbold S, Lutman ME, Nikolopoulos T. Categories of auditory performance: inter-user reliability. Br J Audiol. 1998;32:7-12.
6. Zimmerman-Phillips S, Robbins AM, Osberger MJ. Assessing cochlear implant benefit in very young children. Ann Otol Rhinol Laryngol Suppl. 2000;185:42-3.
7. Allen C, Nikolopoulos TP, Dyar D, O'Donoghue GM. Reliability of a rating scale for measuring speech intelligibility after pediatric cochlear implantation. Otol Neurotol. 2001;22:631-3.
8. Zhong Y, Xu T, Dong R, Lyu J, Liu B, Chen X. The analysis of reliability and validity of the IT-MAIS, MAIS and MUSS. Int J Pediatr Otorhinolaryngol. 2017;96:106-10.
9. Coninx F, Weichbold V, Tsiakpini L, Autrique E, Bescond G, Tamas L, et al. Validation of the LittlEARS® Auditory Questionnaire in children with normal hearing. Int J Pediatr Otorhinolaryngol. 2009;73:1761-8.
10. May-Mederake B. Early intervention and assessment of speech and language development in young children with cochlear implants. Int J Pediatr Otorhinolaryngol. 2012;76:939-46.
11. Yang Y, Chen M, Zheng J, Hao J, Liu B, Liu W, et al. Clinical evaluation of cochlear implantation in children younger than 12 months of age. Pediatr Investig. 2020;4:99-103.
12. Ruben RJ. Language development in the pediatric cochlear implant patient. Laryngoscope Investig Otolaryngol. 2018;3:209-13.
13. Mitchell RM, Christianson E, Ramirez R, Onchiri FM, Horn D L, Pontis L, et al. Auditory comprehension outcomes in children who receive a

cochlear implant before 12 months of age. Laryngoscope. 2020;130:776-81.
14. Liu H, Jin X, Li J, Liu L, Zhou Y, Zhang J, et al. Early auditory preverbal skills development in Mandarin speaking children with cochlear implants. Int J Pediatr Otorhinolaryngol. 2015;79:71-5.
15. Al-Shawi Y, Mesallam TA, Alfallaj R, Aldrees T, Albakheet N, Alshawi M, et al. Inter-rater reliability and validity of the arabic version of Categories of Auditory Performance-II (CAP-II) among children with cochlear implant. Otol Neurotol. 2020;41:e597-602.
16. Wang L, Shen M, Liang W, Dao W, Zhou L, Zhu M. Validation of the Mandarin versions of CAP and SIR. Int J Pediatr Otorhinolaryngol. 2020;139:110413.
17. Gilmour L. The inter-rater reliability of categories of auditory performance-II (CAP)-II. Southampton: Institute of Sound and Vibration Research: University of Southampton; 2010: p.135.
18. Bustos-Rubilar MK, Tapia-Mora D, Hormázabal-Reed X, Mahon M. Chilean Spanish transcultural adaptation of CAP-II and SIR scales in an online format for parents of children with hearing aids or cochlear implants. Revista Chilena de Fonoaudiología. 2022;21:1-14.
19. Cavicchiolo S, Mozzanica F, Guerzoni L, Murri A, Dall'Ora I, Ambrogi F, et al. Early prelingual auditory development in Italian infants and toddlers analysed through the Italian version of the Infant-Toddler Meaningful Auditory Integration Scale (IT-MAIS). Eur Arch Otorhinolaryngol. 2018;275:615-22.
20. Yoon MS. Validity and reliability of the IT-MAIS Korean version in children with normal hearing. Commun Sci Disord. 2011;16:494-502.
21. Özses M, Batuk MO, Isikhan SY, Cinar BC. Validity and reliability of Turkish version of the Auditory Behavior in Everyday Life Questionnaire. Am J Audiol. 2022;31:155-65.
22. Ueda CH, Magalhães AT, Sadowski T, Tsuji RK, Goffi-Gomez MV. Desenvolvimento de habilidades auditivas de crianças no primeiro ano após o implante coclear unilateral e bilateral. Audiol Commun Res. 2022;27.
23. Eiser C, Morse R. The measurement of quality of life in children: past and future perspectives. J Dev Behav Pediatr. 2001;22:248-56.
24. Lohr KN, Aaronson NK, Alonso J, Burnam MA, Patrick DL, Perrin EB, et al. Evaluating quality-of-life and health status instruments: development of scientific review criteria. Clin Ther. 1996;18:979-92.
25. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. J Clin Epidemiol. 1993;46:1417-32.
26. Robbins AM, Renshaw JJ, Berry SW. Evaluating meaningful auditory integration in profoundly hearing-impaired children. Am J Otol. 1991;12:S144-50.
27. Roque Dos Reis L, Donato M, Sousa R, Escada P. Translation, cultural adaptation and validation of the Satisfaction with Amplification in Daily Life Scale for European Portuguese. Acta Med Port. 2017;30:115-21.
28. Roque Reis L, Castelhano L, Gani K, Correia F, Nunes G, Santos R, et al. Translation, cultural adaptation and contributions to the validation of the Nijmegen Cochlear Implant Questionnaire (NCIQ) for European Portuguese. Acta Med Port. 2022;35:866-73.
29. Yang F, Zhao F, Zheng Y, Li G. Modification and verification of the Infant-Toddler Meaningful Auditory Integration Scale: a psychometric analysis combining item response theory with classical test theory. Health Qual Life Outcomes. 2020;18:367.
30. Zheng Y, Soli SD, Wang K, Meng J, Meng Z, Xu K, et al. A normative study of early prelingual auditory development. Audiol Neurootol. 2009;14:214-22.
31. Geravand R, Mehrkian S, Hassanzadeh S, Bakhshi E. The Persian version of infant-toddler meaningful auditory integration scale. Audit Vestib Res. 2019;28:235-41.
32. Xu T, Zhong Y, Wang H, Chen X. A normative study of auditory perception in Mandarin-speaking children with categories of Auditory Performance-II. Int J Pediatr Otorhinolaryngol. 2021;145:110705.
33. Hirschfelder A, Grabel S, Olze H. The impact of cochlear implantation on quality of life: the role of audiologic performance and variables. Otolaryngol Head Neck Surg. 2008;138:357-62.
34. Damen GW, Beynon AJ, Krabbe PF, Mulder JJ, Mylanus EA. Cochlear implantation and quality of life in postlingually deaf adults: long-term follow-up. Otolaryngol Head Neck Surg. 2007;136:597-604.
35. Damen GW, Pennings RJ, Snik AF, Mylanus EA. Quality of life and cochlear implantation in Usher syndrome type I. Laryngoscope 2006;116:723-8.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Neonatal Resuscitation Practices in Portuguese Delivery Rooms: A Cross-Sectional Study

Práticas Atuais de Reanimação Neonatal nas Salas de Parto em Portugal: Um Estudo Transversal

Natacha ALVES[1], Gustavo ROCHA[2], Filipa FLOR-DE-LIMA[2,3], Marta ROSÁRIO[2,3], Susana PISSARRA[2], Mário MATEUS[2], Inês AZEVEDO[3,4], Henrique SOARES✉[2,3]
Acta Med Port 2024 May;37(5):342-354 ▪ https://doi.org/10.20344/amp.20009

ABSTRACT

Introduction: Data from previous studies have demonstrated inconsistency between current evidence and delivery room resuscitation practices in developed countries. The primary aim of this study was to assess the quality of newborn healthcare and resuscitation practices in Portuguese delivery rooms, comparing current practices with the 2021 European Resuscitation Council guidelines. The secondary aim was to compare the consistency of practices between tertiary and non-tertiary centers across Portugal.

Methods: An 87-question survey concerning neonatal care was sent to all physicians registered with the Portuguese Neonatal Society via email. In order to compare practices between centers, participants were divided into two groups: Group A (level III and level IIb centers) and Group B (level IIa and I centers). A descriptive analysis of variables was performed in order to compare the two groups.

Results: In total, 130 physicians responded to the survey. Group A included 91 (70%) and Group B 39 (30%) respondents. More than 80% of participants reported the presence of a healthcare professional with basic newborn resuscitation training in all deliveries, essential equipment in the delivery room, such as a resuscitator with a light and heat source, a pulse oximeter, and an O_2 blender, and performing delayed cord clamping for all neonates born without complications. Less than 60% reported performing team briefing before deliveries, the presence of electrocardiogram sensors, end-tidal CO_2 detector, and continuous positive airway pressure in the delivery room, and monitoring the neonate's temperature. Major differences between groups were found regarding staff attending deliveries, education, equipment, thermal control, umbilical cord management, vital signs monitoring, prophylactic surfactant administration, and the neonate's transportation out of the delivery room.

Conclusion: Overall, adherence to neonatal resuscitation international guidelines was high among Portuguese physicians. However, differences between guidelines and current practices, as well as between centers with different levels of care, were identified. Areas for improvement include team briefing, ethics, education, available equipment in delivery rooms, temperature control, and airway management. The authors emphasize the importance of continuous education to ensure compliance with the most recent guidelines and ultimately improve neonatal health outcomes.

Keywords: Delivery Rooms; Infant, Newborn; Portugal; Resuscitation; Surveys and Questionnaires

RESUMO

Introdução: Estudos previamente publicados demonstraram discordância entre as práticas de reanimação neonatal nas salas de partos e as recomendações internacionais em países desenvolvidos. O objetivo primário deste estudo foi avaliar a qualidade dos cuidados de saúde neonatais e de reanimação neonatal nas salas de partos portuguesas, comparando as práticas atuais com as diretrizes de 2021 do European Resuscitation Council. O objetivo secundário foi comparar a consistência das práticas entre centros terciários e centros não-terciários em Portugal.

Métodos: Um questionário com 87 perguntas foi enviado por correio eletrónico aos médicos inscritos na Sociedade Portuguesa de Neonatologia. Para comparar as práticas entre centros terciários e não-terciários, os participantes foram divididos em dois grupos: Grupo A (centros nível III e nível IIb) e Grupo B (centros nível IIa e nível I). Para comparar as práticas entre os grupos A e B foi efetuada uma análise descritiva das variáveis.

Resultados: No total, 130 médicos responderam ao questionário. O Grupo A incluiu 91 (70%) e o Grupo B 39 (30%) participantes. Mais de 80% relataram a presença de um profissional com treino básico em reanimação neonatal em todos os partos, realização de clampagem tardia do cordão a todos os recém-nascidos que nascem sem complicações, e a presença de alguns equipamentos essenciais nas salas de partos. Menos de 60% relataram a realização de *team briefing*, controlo da temperatura dos recém-nascidos, e a presença de sensores de eletrocardiograma, sensores de CO_2 expirado e máquinas geradoras de pressão positiva contínua da via aérea (CPAP). As áreas de maior divergência entre os grupos incluíram os recursos humanos presentes nas salas de partos, educação, equipamento, controlo térmico, manipulação do cordão umbilical, monitorização de sinais vitais, administração profilática de surfactante e transporte do recém-nascido.

Conclusão: De um modo geral, os médicos portugueses revelaram uma elevada adesão às diretrizes internacionais. Ainda assim, foram encontradas algumas diferenças entre as diretrizes internacionais e as práticas atuais, bem como entre as práticas em centros com diferentes níveis de diferenciação. Os aspetos a melhorar incluem o *team briefing*, questões éticas, educação, equipamentos disponíveis, monitorização da temperatura e abordagem à via aérea. Os autores salientam a importância da formação contínua, de modo a garantir adesão às diretrizes mais recentes e a melhorar os outcomes na saúde neonatal.

Palavras-chave: Inquéritos e Questionários; Portugal; Ressuscitação; Recém-Nascido; Salas de Partos

1. Faculdade de Medicina. Universidade do Porto. Porto. Portugal.
2. Serviço de Neonatologia. Centro Hospitalar e Universitário de São João. Porto. Portugal.
3. Departamento de Ginecologia-Obstetrícia e Pediatria. Faculdade de Medicina. Universidade do Porto. Porto. Portugal.
4. Serviço de Pediatria. Centro Hospitalar e Universitário de São João. Porto. Portugal.
✉ **Autor correspondente:** Henrique Soares. hecsoares@europe.com
Recebido/*Received*: 06/07/2023 - **Aceite/*Accepted*:** 11/09/2023 - **Publicado/*Published*:** 02/05/2024

INTRODUCTION

The transition from fetal to neonatal life involves major physiological changes.[1] Although most neonates do not need help and are able to start breathing spontaneously, approximately 10% will require simple stimulation in order to start breathing, 5% will need positive pressure ventilation, 0.4% to 2% will require endotracheal intubation, and < 0.3% will receive chest compressions to restore cardiorespiratory function.[2]

According to the World Health Organization (WHO), approximately 75% of all neonatal deaths occur during the first week of life, and a significant proportion of neonates die within the first 24 hours. Intrapartum-related events are still a leading cause of neonatal mortality.[3] Although most neonatal deaths take place in low and middle-income countries,[3] there is still room to improve newborn care in developed countries.

Data from previous studies suggested inconsistency between current evidence and the delivery room (DR) resuscitation practices in developed countries,[4] as well as significant differences in practices among hospitals with different levels of care within the same country.[5,6] International guidelines on newborn resuscitation practices are updated regularly according to the most recent clinical evidence and should serve as a basis for the development of national guidelines to optimize clinical practice.[4] Consistency of clinical practice in early DR management should be assessed regularly to identify sources of variation and improve the quality of newborn health care in the DR.

The last study to assess the quality of neonatal resuscitation practices in the DR in Portugal was published in 2011 and showed that there was still room for improvement concerning medical equipment and human resources. It pointed out the need to update practices on oxygen therapy and prophylactic surfactant use.[7] This study also highlighted the need to improve team communication and reduce newborn transport after delivery.[7] Since then, the European Resuscitation Council (ERC) guidelines for newborn resuscitation and support of transition of infants at birth have been updated twice (in 2015 and 2021), and significant changes have been made.[2,8]

Therefore, the primary aim of this study was to assess the quality of newborn healthcare and resuscitation practices in the DR in Portugal, comparing current practices with the 2021 ERC guidelines. The secondary aim of this study was to compare the consistency of practices between tertiary centers and non-tertiary centers across the country.

METHODS

Study design

In this cross-sectional study, an 87-question web-based survey [Appendix 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/20009/15399)] was developed to assess neonatal care practices in Portuguese DR. The survey included both multiple choice and short answer questions and was divided into five main sections: (I) demographic data of participants; (II) human resources, ethics and education; (III) available equipment and temperature control in the delivery room; (IV) medical practices regarding support with transition and newborn resuscitation; (V) characterization of the neonatal center. The questionnaire was developed by experts in the field of neonatology and was organized on the basis of the 2021 ERC Guidelines on newborn resuscitation and transition support for infants at birth.[2]

The levels of neonatal care considered in this study were as follows: level I – provides care for neonates with a gestational age (GA) greater that 34 weeks; level IIa – provides care for neonates over 32 weeks; level IIb – provides care for neonates over 23 weeks; level III – provides all levels of neonatal care (full range of medical and surgical specialties).

Participants

The survey was sent to all neonatologists and pediatricians registered with the Portuguese Neonatal Society (PNS). To be eligible, all participants had to be practicing clinicians. This approach was preferred over questioning the heads of department in order to avoid a potential bias in the responses. The physicians were invited to participate in the study via email, which included a link to answer the questionnaire via Google Forms, and a participant information document [Appendix 2 (Appendix 2: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/20009/15400)]. The participant information document provided an overview of the study's objectives and informed participants of their anonymity throughout the study. Participation was strictly voluntary, and participants could withdraw at any time.

Data collection

The email was sent two times, with a one-month interval, in order to maximize response rates. Responses were collected between December 19, 2022, and February 20, 2023. All answers were stored in a Microsoft Excel datasheet.

Data analysis

Data analysis was performed using SPSS statistical software (SPSS for Windows, version 28, IBM SPSS statistics, Inc., Chicago, IL, USA). Categorical variables were described as absolute and relative frequencies and continuous variables with asymmetric distribution by median

(minimum – maximum). To investigate potential differences in clinical practice between tertiary and non-tertiary centers, the participants were categorized into two groups based on the gestational age limits of their respective centers. The first group (Group A) comprised participants working in level III and level IIb centers, and the second group (Group B) included those working in level IIa and level I centers. Descriptive analysis of variables was performed in order to

Table 1 – Demographic data of participants

	Total (n = 130)
(a) Age (years)	
< 40	41 (31.5)
40 - 49	38 (29.2)
50 - 59	22 (16.9)
≥ 60	29 (22.3)
Median age (minimum - maximum)	45 (29 - 69)
(b) Sex	
Female	98 (75.4)
Male	31 (23.8)
NA	1 (0.8)
(c) Specialty/subspecialty	
Pediatrician	46 (35.4)
Neonatologist	84 (64.6)
(d) Years of practice	
< 10	36 (27.7)
10 - 19	36 (27.7)
20 - 29	21 (16.1)
≥ 30	37 (28.5)
(e) Administrative sector	
Public	91 (70)
Private	2 (1.5)
Both public and private	37 (28.5)
(f) Region	
North	75 (57.7)
Center	23 (17.7)
South	30 (23.1)
Islands (Madeira or Azores)	2 (1.5)
(g) Level of care	
Level III (with neonatal intensive care unit, neonatal surgery, hemodynamic monitoring and induced hypothermia)	42 (32.3)
Level IIb (> 23 week-gestation)	49 (37.7)
Level IIa (> 32 week-gestation)	17 (13.1)
Level I (> 34 week-gestation)	22 (16.9)
(i) Deliveries per year	
> 2500	37 (28.5)
1500 - 2500	57 (43.8)
1000 - 1500	26 (20)
500 - 1000	6 (4.6)
< 500	4 (3.1)

Data are expressed as n(%).
NA : not applicable.

compare the two groups.

Ethical approval

This study was approved by the Ethics Committee of Centro Hospitalar Universitário de São João, Porto, with the license number CE 264-22.

RESULTS

In total, 130 neonatologists and pediatricians registered with the Portuguese Neonatal Society answered the survey and all met the eligibility criterion. It should be noted that the PNS membership list comprised 457 members, including retired physicians and some who have passed away. For confidentiality reasons, these individuals could not be quantified and excluded from the total count, and consequently, an accurate response rate could not be determined.

The median age [min - max] of respondents was 45 [29 - 69] years old, 98 (75.4%) participants were female and 84 (64.6%) were neonatologists. Group A included 91 (70%) respondents and Group B, 39 (30%). Table 1 presents the demographic data of all participants in the study.

Staff attending delivery, team briefing, ethics, and education (Table 2)

In total, 112 (86.2%) physicians reported that a healthcare professional with expertise in basic newborn resuscitation was present in all deliveries. Regarding team briefing, 73 (56.2%) respondents stated that it took place before each delivery or each high-risk delivery. During advanced resuscitation, 55 (42.3%) participants reported allowing the presence of the other parent in the DR. Concerning education, 96 (73.8%) respondents stated that their institution conducts periodic training sessions on neonatal resuscitation.

Equipment and temperature control in the delivery room (Table 3)

Devices reported as being present in the DR by more than 80% of participants were: pulse oximeter (98.5%), vital signs monitor (83.1%), plastic bag or polyethylene film (91.5%), resuscitator with light and heat source (99.2%), oxygen and compressed air in all DRs (90.8%), Guedel tubes (87.7%), face masks (96.2%), laryngoscope (100%), controlled pressure ventilatory support device with O_2 blender (81.5%), self-inflating device with pressure valve connected to O_2 source (81.5%), T-piece resuscitator with PIP and PEEP control (90.8%) and umbilical catheters (96.9%).

Devices that were reported to be present less often included electrocardiogram (ECG) sensors (54.6%), end-tidal CO_2 detector (30%), self-inflating bag with pressure valve connected to O_2 blender (59.2%), CPAP (46.2%), nasal CPAP (43.1%), and intraosseous needle (43.8%).

Concerning DR temperature control, 62 (47.7%) respondents reported its monitoring.

Newborn's thermal control, umbilical cord management and vital signs monitoring (Table 4)

Newborn temperature control was reported by 64 (49.2%) physicians. Among those who reported controlling the neonate's temperature, a target temperature of 36.5º - 37.5ºC was indicated by 39 (60.9%) participants. Drying and stimulation immediately after delivery for > 32 week-gestation neonates was performed by 125 (96.2%) participants of the study, and skin-to-skin contact with the mother for all > 32 week-gestation neonates born without complications was documented by 66 (50.8%) respondents.

Delayed cord clamping (> 60 s) for all neonates born without complications was performed by 113 (86.9%) of the respondents.

Intermittent monitoring combined with pulse oximetry was reported by 64 (49.2%) participants for vital signs monitoring in term infants and by 74 (56.9%) in preterm infants.

Transition support and neonatal resuscitation practices (Table 5)

Routine suctioning in all non-vigorous/apneic/inefficiently breathing infants was reported by 64 (49.2%) participants.

The use of an oxygen blender in assisted ventilation was reported by 113 (86.9%) participants. Air was the initial inflation gas mixture of choice for term infants in 101 (77.7%) participants. In Group A, 51 (56%) used a FiO_2 of 21% - 29% as the initial inflation gas mixture for the preterm newborns (< 32 weeks GA). An initial inflation pressure of 30 cmH_2O for term infants was reported by 75 (57.7%) participants. However, for preterm newborns, a 25 cmH_2O pressure was documented by 77 (84.6%) respondents in Group A. A total of 85 (65.4%) respondents chose auscultation only as the method to confirm correct endotracheal tube placement.

The compression/insufflation ratio of 3:1 was chosen by 99 (76.1%) participants. The umbilical access was the primary vascular access reported by 122 (93.8%) respondents. Fifteen (11.5%) physicians reported administering prophylactic surfactant routinely to neonates at risk of respiratory distress syndrome (RDS).

Transporting the newborn from the DR to the neonatal intensive care unit (NICU) was stated as being easy by 119 (91.5%) participants and access to a transport incubator with a fully controlled environment was noted by 106 (81.5%) physicians.

Comparison between Group A and Group B

Regarding staff attending deliveries and education

(Table 2), the presence of a professional with expertise in basic neonatal resuscitation in all deliveries was documented by 75 (82.4%) participants in Group A and by 37 (94.9%) in Group B. Fifty physicians (54.4%) in Group A confirmed the presence of a nurse specialized in neonatal care in the DR for all high-risk deliveries, compared with 14 (35.9%) in Group B. Seventy-two (79.1%) physicians in Group A reported attending periodic training sessions on neonatal resuscitation in their respective center, compared with 24 (61.5%) in Group B.

Concerning the available equipment in the delivery room (Table 3), Group A participants more frequently reported the presence of equipment such as a plastic bag or a polyethylene film, quick access to videolaryngoscopy, end-tidal CO_2

Table 2 – Staff attending delivery, team briefing, ethics, and education

		Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(a) Staff attending deliveries				
A neonatologist or a pediatrician with expertise in advanced newborn resuscitation is present at every delivery		58 (44.6)	36 (39.6)	22 (56.4)
If not at every delivery, there is a neonatologist or a pediatrician with expertise in advanced newborn resuscitation available in the institution for all high-risk deliveries		68 (94.4)	55 (100)	13 (76.5)
A health professional with expertise in basic newborn resuscitation is present at all deliveries		112 (86.2)	75 (82.4)	37 (94.9)
Two health professionals with expertise in advanced neonatal resuscitation are present in all high- risk deliveries		90 (69.2)	64 (70.3)	26 (66.7)
A nurse specialized in neonatal care is present at all high-risk deliveries		64 (49.2)	50 (54.9)	14 (35.9)
(b) Team briefing				
A pre-delivery checklist is verified before every delivery to clarify responsibilities and check equipment		113 (86.9)	79 (86.8)	34 (87.2)
Team briefing takes place before every delivery or every risk delivery		73 (56.2)	47 (51.6)	26 (66.7)
Debriefing takes place after every delivery where newborn resuscitation was performed	Always	24 (18.5)	17 (18.7)	7 (17.9)
	Sometimes	97 (74.6)	66 (72.5)	31 (79.5)
	Never	9 (6.9)	8 (8.8)	1 (2.6)
(c) Ethics				
The decision to attempt resuscitation of an extremely preterm or clinically complex infant is taken in consultation with the parents and other health professionals?	Yes	123 (94.6)	88 (96.7)	35 (89.7)
	No	6 (4.6)	2 (2.2)	4 (10.3)
	NR	1 (0.8)	1 (1.1)	0 (0)
During advanced resuscitation, the presence of the other parent is allowed in the DR.	Yes	55 (42.3)	35 (38.5)	20 (51.3)
	No	61 (46.9)	44 (48.3)	17 (43.6)
	Other	14 (10.8)	12 (13.2)	2 (5.1)
During advanced resuscitation with bad prognosis, the parent is involved in the decision to withdraw resuscitation.		29 (22.3)	19 (20.9)	10 (25.6)
(d) Education				
Your health institution conducts periodic training sessions on neonatal resuscitation?	Yes	96 (73.8)	72 (79.1)	24 (61.5)
Do those sessions take place in simulation centers?	Yes	40 (41.7)	30 (41.7)	10 (41.7)
	Sometimes	15 (15.6)	9 (12.5)	6 (25)
	No	41 (42.7)	33 (45.8)	8 (33.3)

Data are expressed as n(%).
NR: non respondents.

detector, controlled pressure ventilatory support device with O_2 blender, CPAP, nasal CPAP, and umbilical catheters in the delivery rooms of their respective centers, compared with Group B physicians.

In Group A, 51 physicians (56%) reported controlling the temperature of all newborns, compared with 13 physicians (33.3%) in Group B (Table 4). Performing skin to skin contact with the mother for all > 32 week-gestation neonates

Table 3 – Equipment and temperature control in the delivery room (section 1 of 2)

	Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(a) Equipment and drugs			
Stopwatch	124 (95.4)	85 (93.4)	39 (100)
Scalpel/scissors	129 (99.2)	90 (98.9)	39 (100)
Pulse oximeter	128 (98.5)	89 (97.8)	39 (100)
ECG sensors	71 (54.6)	48 (52.7)	23 (59)
Stethoscope	129 (99.2)	91 (100)	38 (97.4)
Vital signs monitor	108 (83.1)	75 (82.4)	33 (84.6)
Plastic bag or polyethylene film	119 (91.5)	89 (97.8)	30 (76.9)
Resuscitator with light and heat source	129 (99.2)	91 (100)	38 (97.4)
Oxygen and compressed air in all DR	118 (90.8)	81 (89)	37 (94.9)
Guedel tubes	114 (87.7)	76 (83.5)	38 (97.4)
Face masks	125 (96.2)	87 (95.6)	38 (97.4)
Laryngoscope	130 (100)	91 (100)	39 (100)
Quick access to videolaryngoscope	42 (32.3)	38 (41.8)	4 (10.3)
Orotracheal tubes	128 (98.5)	90 (98.9)	38 (97.4)
Laryngeal masks	89 (68.5)	64 (70.3)	25 (64.1)
Aspiration endotracheal tubes	82 (63.1)	54 (59.3)	28 (71.8)
End-tidal CO_2 detector	39 (30)	33 (36.3)	6 (15.4)
Controlled pressure ventilatory support device	94 (72.3)	71 (78)	23 (59)
Controlled pressure ventilatory support device with O_2 blender	106 (81.5)	81 (89)	25 (64.1)
Self-inflating device with pressure valve	124 (95.4)	87 (95.6)	37 (94.9)
Self-inflating device with pressure valve connected to O_2 source	106 (81.5)	75 (82.4)	31 (79.5)
Self-inflating bag with pressure valve connected to O_2 blender	77 (59.2)	58 (63.7)	19 (48.7)
CPAP	60 (46.2)	51 (56)	9 (23.1)
Nasal CPAP	56 (43.1)	46 (50.5)	10 (25.6)
T-piece resuscitator with PIP and PEEP control	118 (90.8)	86 (94.5)	32 (82.1)
Umbilical catheters	126 (96.9)	91 (100)	35 (89.7)
Intraosseous needle	57 (43.8)	39 (42.9)	18 (46.2)
Material for thoracentesis	62 (47.7)	47 (51.6)	15 (38.5)
Chest drain	49 (37.7)	40 (44)	9 (23.1)
Adrenaline	129 (99.2)	90 (98.9)	39 (100)
10% glucose	124 (95.4)	88 (96.7)	36 (92.3)
Sodium bicarbonate	117 (90)	82 (90.1)	35 (89.7)
Naloxone	127 (97.7)	88 (96.7)	39 (100)
Physiological saline	129 (99.2)	90 (98.9)	39 (100)
Surfactant	71 (54.6)	46 (50.5)	25 (64.1)

Table 3 – Equipment and temperature control in the delivery room (section 2 of 2)

		Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(b) Temperature control				
Controls the temperature of the DR		62 (47.7)	41 (45.1)	21 (53.8)
If the answer to the previous question was yes, what DR target temperature do you use for newborns > 28 weeks?	21º - 23ºC	7 (11.3)	2 (4.9)	5 (23.8)
	23º - 25ºC	40 (64.5)	29 (70.7)	11 (52.4)
	25º - 27ºC	13 (21)	8 (19.5)	5 (23.8)
	NR	2 (3.2)	2 (4.9)	0 (0)
If the answer to the previous question was yes, what target temperature do you use for newborns ≤ 28 weeks?	21 - 23ºC	-	1 (2.4)	-
	23º - 25ºC	-	5 (12.2)	-
	> 25ºC	-	33 (80.5)	-
	NR	-	2 (4.9)	-
	NA	21 (33.9)	0 (0)	21 (100)

Data are expressed as n(%).
NR : non respondents; NA : not applicable.

was reported by 40 participants (44%) in Group A and 26 (66.7%) in Group B. Performing delayed cord clamping for all neonates born without complications was documented by 83 physicians (91.2%) in Group A and 30 (76.9%) in Group B (Table 4).

As for the neonate's airway approach (Table 5), 84 physicians (92.3%) in Group A reported using an O_2 blender in assisted ventilation compared with 29 (74.4%) in Group B. The administration of prophylactic surfactant to all neonates at risk for RDS was reported by four physicians (4.4%) in Group A, and 11 (28.2%) in Group B (Table 5).

Regarding the neonate's transportation (Table 5), 90 physicians (98.9%) in Group A described the transportation of the newborn out of the delivery room to a neonatal intensive care unit as being easy compared with 29 (74.4%) in Group B. Access to a transport incubator with a fully controlled environment was reported by 80 physicians (87.9%) in Group A and 26 (66.7%) in Group B.

DISCUSSION

Overall, the results of this study suggest there was good compliance of Portuguese neonatologists and pediatricians with the 2021 ERC guidelines for newborn resuscitation and support of transition, in both centers with the highest and the lowest level of differentiation of care. However, some differences between the current practices and international recommendations were identified.

Staff attending delivery and team briefing

According to a Canadian audit, the need for neonatal resuscitation is not anticipated in 76% of cases.[9] Ongoing in-house coverage by a neonatologist or pediatrician has been shown to reduce the need for chest compressions, admissions to the NICU, and hospital stay duration in term infants with poor transition at birth.[10] The 2021 ERC guidelines recommend that staff members competent in newborn life support should be available for every delivery.[2] In this study, 86.2% of respondents reported the presence of a professional with expertise in basic neonatal resuscitation in all deliveries. This finding highlights the need for improving the skills of staff members attending deliveries in Portugal, as a professional with basic neonatal resuscitation skills should be present in all delivery rooms, and 100% compliance should be the aim.

The results suggest that team briefing was not consistently adopted by participating physicians, both in Group A and in Group B, which could negatively affect team dynamics. Although there is no current evidence suggesting that team briefing improves clinical outcomes,[2] this is an aspect that could improve neonatal care in Portugal. There was, however, good compliance with the use of pre-delivery checklists.

Ethics and education

Family-witnessed resuscitation is a controversial issue that is still discussed widely, and this topic urgently needs high quality research to measure the actual impact of family presence on patient and family outcomes.[11,12] However, the 2021 ERC guidelines support the presence of family presence during cardiovascular resuscitation and advocate for facilitating the presence of parents during resuscitation whenever possible.[2] This study's findings suggest that Portuguese neonatologists and pediatricians have not widely adhered to the current recommendations, as 46.9% of respondents reported not allowing the other member of the couple to be present in the DR during advanced resuscitation. This is in line with the results of other studies,[13] highlighting the need for increased awareness of ethical issues

in Portuguese delivery rooms, as well as the need of further research to support current recommendations.

Overall, the adherence of the Portuguese medical centers to periodic training sessions on neonatal resuscitation appears to be adequate, as reported by 73.8% of respondents. However, there is room for improvement, particularly in Group B centers where physicians reported less frequent training than physicians in Group A. This highlights the need

Table 4 – Newborn's thermal control, umbilical cord management and vital signs monitoring

		Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(a) Newborn's thermal control				
Controls newborn's temperature	Yes	64 (49.2)	51 (56)	13 (33.3)
	No	60 (46.2)	36 (39.6)	24 (61.5)
	NR	6 (4.6)	4 (4.4)	2 (5.1)
Target temperature for the participants that responded "yes" to the previous question	< 36.5ºC	24 (37.5)	15 (29.4)	9 (69.2)
	36.5º - 37.5ºC	39 (60.9)	35 (68.6)	4 (30.8)
	> 37.5ºC	0 (0)	0 (0)	0 (0)
	NR	1 (1.6)	1 (2)	0 (0)
Performs drying and stimulation immediately after delivery for > 32-week-gestation newborns		125 (96.2)	89 (97.8)	36 (92.3)
Performs skin-to-skin contact with mother for all > 32 week-gestation newborns born without complications		66 (50.8)	40 (44)	26 (66.7)
Uses plastic bag or polyethylene wrapping in < 32 week-gestation preterms		90 (69.2)	90 (98.9)	-
(b) Umbilical cord management				
Performs delayed cord clamping (> 60s) for all newborns born without complications		113 (86.9)	83 (91.2)	30 (76.9)
Performs cord milking when delayed cord clamping is not possible in infants > 28 week-gestation		49 (37.7)	36 (39.6)	13 (33.3)
Routinely performs assessment of umbilical cord blood (arterial and venous) pH		23 (17.7)	18 (19.8)	5 (12.8)
(c) Vital signs monitoring				
Full-term newborns	Intermittent monitoring with stethoscope/ pulse palpation	40 (30.8)	25 (27.5)	15 (38.5)
	Intermittent + continuous monitoring with pulse oximeter	64 (49.2)	43 (47.2)	21 (53.8)
	Intermittent + continuous monitoring with pulse oximeter + ECG	24 (18.5)	22 (24.2)	2 (5.1)
	NR	2 (1.5)	1 (1.1)	1 (2.6)
Preterm newborns	Intermittent monitoring with stethoscope/ pulse palpation	1 (0.8)	0 (0)	1 (2.6)
	Intermittent + continuous monitoring with pulse oxymeter	74 (56.9)	49 (53.8)	25 (64.1)
	Intermittent + continuous monitoring with pulse oximeter + ECG	52 (40)	40 (44)	12 (30.8)
	NR	3 (2.3)	2 (2.2)	1 (2.6)

Data are expressed as n(%).
NR : non respondents.

for greater investment in training programs for neonatal resuscitation in these centers, as well as in the country, as research has shown that intermittent, infrequent training without periodic refreshment may lead to a decline in skills related to neonatal resuscitation.[2]

Table 5 – Transition support and neonatal resuscitation practices (section 1 of 2)

		Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(a) Newborn's airway approach				
Ventilation support for < 30 weeks newborns born with spontaneous breathing	CPAP	-	84 (92.3)	-
	Endotracheal intubation	-	2 (2.2)	-
	NR	-	5 (5.5)	-
	NA	39 (30)	0	39 (100)
Performs routine airway aspiration in all non-vigorous/apneic/ineffective respiratory pattern newborns		64 (49.2)	45 (49.5)	19 (48.7)
Use of O_2 blender in assisted ventilation		113 (86.9)	84 (92.3)	29 (74.4)
Initial inflation gas mixture for the full-term newborn	Air	101 (77.7)	70 (76.9)	31 (79.5)
	21 - 29% O_2	24 (18.5)	19 (20.9)	5 (12.8)
	30% O_2	1 (0.8)	0 (0)	1 (2.6)
	> 30% O_2	4 (3.1)	2 (2.2)	2 (5.1)
	NR	0 (0)	0 (0)	0 (0)
	NA	0 (0)	0 (0)	0 (0)
Initial inflation gas mixture for the preterm newborn (<32 weeks)	Air	-	14 (15.4)	-
	21 - 29% O_2	-	51 (56)	-
	30% O_2	-	26 (28.6)	-
	> 30% O_2	-	0 (0)	-
	NR	-	0 (0)	-
	NA	39 (30)	0(0)	39 (100)
Initial inflation pressure for the full-term newborn	< 25 cmH_2O	4 (3.1)	3 (3.3)	1 (2.6)
	25 cmH_2O	44 (33.8)	27 (29.7)	17 (43.6)
	30 cmH_2O	75 (57.7)	59 (64.8)	16 (41)
	≥ 35 cmH_2O	1 (0.8)	0 (0)	1 (2.6)
	NR	3 (2.3)	2 (2.2)	1 (2.6)
	NA	3 (2.3)	0 (0)	3 (7.7)
Initial inflation pressure for the preterm newborn (< 32 week-gestation)	< 25 cmH_2O	-	10 (11)	-
	25 cmH_2O	-	77 (84.6)	-
	30 cmH_2O	-	3 (3.3)	-
	≥ 35 cmH_2O	-	0 (0)	-
	NR	-	1 (1.1)	-
	NA	39 (30)	0 (0)	39 (100)
Confirmation of correct endotracheal tube placement	Auscultation with stethoscope	85 (65.4)	57 (62.6)	28 (71.8)
	End tidal CO_2 device	3 (2.3)	2 (2.2)	1 (2.6)
	Auscultation + end tidal CO_2 device	37 (28.5)	32 (35.2)	5 (12.8)
	Thoracic X-ray	4 (3.1)	0 (0)	4 (10.3)
	NR	1 (0.8)	0 (0)	1 (2.6)

Table 5 – Transition support and neonatal resuscitation practices (section 2 of 2)

		Total (n = 130)	Group A (n = 91)	Group B (n = 39)
(b) Chest compressions				
Chest compressions/insuflations ratio	15 compressions to 2 insuflations	29 (22.3)	17 (18.7)	12 (30.8)
	30 compressions to 2 insuflation	1 (0.8)	1 (1.1)	0 (0)
	3 compressions to 1 insuflation	99 (76.1)	72 (79.1)	27 (69.2)
	NR	1 (0.8)	1 (1.1)	0 (0)
(c) Vascular access				
First line vascular access if needed	Umbilical access	122 (93.8)	87 (95.6)	35 (89.7)
	Periferal venous access	8 (6.2)	4 (4.4)	4 (10.3)
	Intraosseous access	0 (0)	0 (0)	0 (0)
(d) Prophylactic surfactant in the DR				
Routinely performs administration of prophylactic surfactant to all newborns at risk of respiratory distress syndrome		15 (11.5)	4 (4.4)	11 (28.2)
(e) Glycemic control of the newborn				
Routinely performs glycemic monitoring to all newborns who underwent resuscitation		87 (66.9)	56 (61.5)	31 (79.5)
(f) Transportation of the newborn after resuscitation				
Easy access/transportation of the newborn to a neonatal intensive care unit (NICU)		119 (91.5)	90 (98.9)	29 (74.4)
Access to short-duration invasive ventilation in the DR before transportation to differentiated care		116 (89.2)	84 (92.3)	32 (82.1)
Access to a transport incubator with fully controlled environment		106 (81.5)	80 (87.9)	26 (66.7)
Access to a transport incubator with humidified air		65 (50)	44 (48.4)	21 (53.8)

Data are expressed as n(%).
NR : non respondents; NA : not applicable.

Equipment

The availability and suitability of appropriate equipment is critical for successful neonatal resuscitation, and the use of checklists can help to ensure that.[14] Based on the findings of this study, the Portuguese delivery rooms appear to be well-equipped for adequate neonatal resuscitation, as the presence of most of the essential equipment was reported among participants. However, end-tidal CO_2 detector, CPAP and nasal CPAP were underreported in both groups, despite being significantly more reported by the Group A physicians, which is to be expected given the gestational age limit of these centers. The ERC guidelines advocate for exhaled CO_2 detector as the preferred method for confirmation of the correct endotracheal tube placement, and for CPAP as the preferred method of ventilatory support after delivery of preterm infants who are breathing spontaneously.[2] Therefore, improving the availability of these devices in the Portuguese DRs should be considered.

Temperature

Both hypothermia and hyperthermia increase the risk of neonatal morbidity and mortality in both term and preterm infants.[15] A high incidence of postnatal hypothermia has been reported in both high and low resource countries and preterm infants are especially vulnerable.[15] According to the ERC guidelines, the temperature of newly born infants should be maintained between 36.5ºC and 37.5ºC. In order to achieve this, European guidelines advise keeping the delivery room temperature between 23º – 25ºC for neonates ≥ 28 week-gestation and > 25°C for preterm infants < 28 week-gestation.[2] Skin-to-skin contact with the mother may be effective in maintaining thermal stability (low

quality evidence) in infants > 32 week-gestation where resuscitation was not required.[16] Portuguese physicians seem to have not yet adopted these recommendations widely, which is in line with results of other studies.[13] Only 47.7% reported monitoring the DR temperature, and only 49.2% indicated monitoring the temperature for all neonates, with participants in Group B reporting it less often. Given these findings, it would be appropriate to increase awareness in Portugal regarding the need to control the temperature of neonates and the DR's temperature, as well as re-establishing target temperatures according to the current international guidelines, especially in level I and in level IIa centers.

Umbilical cord management

The act of clamping the umbilical cord immediately after birth is associated with a reduction in preload, which subsequently causes a decrease in the neonate's cardiac output.[17] This effect can be reduced by ventilating the lungs and increasing pulmonary blood flow before clamping the cord.[17] A recent systematic review and meta-analysis has shown that delayed cord clamping in term infants was associated with significantly reduced hospital mortality (high-quality evidence).[18] For these reasons, the ERC guidelines clearly advise delaying cord clamping for at least 60 seconds when immediate resuscitation is not required.[2] Overall, Portuguese neonatologists and pediatricians appeared to follow the international guidelines for umbilical cord management. However, Group B physicians seem to have a lower adherence to this practice, despite the majority still being compliant. This finding suggests there is room for improvement in these centers.

Heart rate monitoring

The neonate's heart rate is an important indicator of the effectiveness of spontaneous breathing, and it guides the need of further interventions and serves as a marker of response to resuscitative interventions.[1] For these reasons, a reliable method of measuring it is crucial in neonatal care.[1] The ERC guidelines advocate the determination of the heart rate with auscultation and pulse oximetry monitoring ± ECG for later continuous assessment. For preterm infants it is suggested that continuous rather than intermittent monitoring be considered.[2] Portuguese physicians appear to be aligned with these recommendations, as the combination of auscultation and continuous monitoring using a pulse oximeter appears to be the most commonly used strategy for vital signs monitoring both in term and preterm infants. However, the use of ECG in term infants in Portugal, particularly among Group B participants, seems limited.

Airway, ventilation and circulation

Routine suctioning of the oro- or nasopharynx of newborns is currently not recommended in those born with meconium-stained fluid,[2] since it does not decrease the incidence of meconium aspiration syndrome or newborn deaths[19] and is likely to delay initiation of ventilation. However, some studies show that following this recommendation is associated with an increase in admissions to the NICU.[19] In this study, a significant percentage of participants (49.2%) reported to perform routine airway aspiration in all non-vigorous/apneic/ineffective breathing neonates. This emphasizes the need of raising awareness about this recommendation among Portuguese neonatologists and pediatricians, as well as the need to conduct additional research to reinforce existing guidelines.

According to the ERC guidelines, pulse oximeters and oxygen blenders should be used when resuscitating newborns in the DR.[2] Portuguese physicians showed good compliance with this recommendation. However, Group B physicians reported less often the use of oxygen blenders in assisted ventilation, suggesting that this could be an area of improvement in these centers.

The findings of this study suggest that in terms of ventilation of term infants, Portuguese physicians mostly initiate ventilation with air and with an inflation pressure of 30 cmH_2O. This shows good compliance with international guidelines.[2] However, there was some variation between the groups regarding the initial inflation pressures used for these neonates, with Group A predominantly reporting pressures of 30 cmH_2O and Group B predominantly reporting pressures of 25 cmH_2O. In fact, the evidence supporting the optimal initial inflation pressure for lung ventilation in term infants remains limited,[2] and these results highlight the importance of further research.

Regarding the ventilation of newborns < 32 week-gestation, Portuguese physicians also appear to be in line with the current recommendations, as most participants who deal with these infants reported initiating ventilation with 21% - 29% O_2 and an inflating pressure of 25 cmH_2O. Nevertheless, there was some variation in responses regarding the gas mixture used during the initial inflation of these neonates, which may be explained by the fact that the O_2 concentration used for preterm infants depends on the gestational age, according to ERC guidelines.[2]

Prophylactic administration of surfactant consists of its administration to infants at risk of RDS, while selective surfactant treatment occurs in infants with established RDS.[20] With the increasing use of CPAP in the stabilization of preterm infants, the evidence showed that prophylactic use of surfactant was no longer beneficial.[20] The 2022 European Consensus Guidelines on the management of RDS advocate for surfactant administration in the DR when intubation is needed for stabilization.[21] The Portuguese neonatologists and pediatricians are in line with this recommendation, as

only 11.5% of respondents reported performing routine prophylactic administration of surfactant. However, Group B physicians appear to be less compliant with current recommendations, so further investment should be made in education towards this matter in these centers.

Chest compressions are a crucial part of the neonatal resuscitation algorithm, but circulatory support with chest compressions is only effective if the lungs have been successfully ventilated.[2] The ERC guidelines advocate for a 3:1 compression ratio to be used,[2] and most Portuguese physicians seem to be compliant with these recommendations. The intraosseous needle is considered a reasonable alternative to the umbilical vein catheterization when this access is not feasible[1] and the presence of this device in Portuguese DRs is still limited, suggesting there is a need to increase its availability.

Strengths and limitations

The present study has several strengths. Firstly, the questionnaire was carefully designed, covering most aspects of neonatal resuscitation in accordance with the ERC guidelines. Moreover, the questionnaire was approved by experts in the field of neonatology, ensuring its validity and reliability. Thirdly, the use of an online survey facilitated participation, and the dissemination through the Portuguese Neonatal Society increased the response rate compared with the 30 responses obtained in the 2011 survey.[7]

However, this study also has some limitations. Firstly, the use of a survey comes with the risk of inducing response bias, as well as a limited response rate. The fact that the response rate could not be determined limited the generalizability of the findings, although 130 responses represent a substantial absolute count. Moreover, physicians working in level IIb and level III centers may be overrepresented in this study, as the Portuguese Neonatal Society has a larger number of physicians working in these centers, which limited making statistical inferences when comparing the groups. Nonetheless, the results are consistent with what would be expected both in higher and in lower-level units. This study did not include all neonatologists in Portugal as not all are registered with the Portuguese Neonatal Society. Lastly, the questionnaire did not cover the use of positive end-expiratory pressure (PEEP) during positive pressure ventilation (PPV) administration to neonates, which is an important measure to evaluate as it has been demonstrated to be beneficial, particularly in preterm infants, and it is advocated by the 2021 ERC guidelines. Moreover, the questionnaire did not cover the methods for administering surfactant in the delivery room.

Future studies should consider these limitations and address them to provide a more comprehensive understanding of the current practices in neonatal resuscitation in Portugal as well as in other countries.

CONCLUSION

Overall, adherence to neonatal resuscitation international guidelines was high among Portuguese physicians. However, there was some variation between guidelines and current practice, as well as between centers with different levels of care. Areas for improvement include team briefing, ethics, education, available equipment in delivery rooms, temperature control and airway management. The findings of this study are relevant, as this is one of the few studies assessing the quality of neonatal resuscitation practices in Portugal. The authors of this study emphasize the importance of continuous training and educational updates, particularly in level I and level IIa centers, in order to ensure compliance with the most recent guidelines and ultimately improve neonatal health outcomes in Portugal.

ACKNOWLEDGEMENTS

We extend our acknowledgements towards the Portuguese Neonatal Society, it's president and the participating physicians, whose contributions were crucial to the success of this study.

AUTHOR CONTRIBUTIONS

NA: Literature search, data collection, analysis, and interpretation, drafting of the manuscript.

GR, FFL: Study design, literature search, data collection, analysis, and interpretation, critical review of the manuscript.

MR: Study design, literature search, critical review, approval of the final version of the manuscript.

SP: Literature search, data collection, analysis, and interpretation, critical review, approval of the final version of the manuscript.

MM: Study design, literature search, critical review, approval of the final version of the manuscript.

IA: Literature search, data interpretation, critical review, approval of the final version of the manuscript.

HS: Study design, literature search, data interpretation, critical review, approval of the final version of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Wyckoff MH, Wyllie J, Aziz K, de Almeida MF, Fabres JW, Fawke J, et al. Neonatal life support 2020 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2020;156:A156-87.
2. Madar J, Roehr CC, Ainsworth S, Ersdal H, Morley C, Rudiger M, et al. European resuscitation council guidelines 2021: newborn resuscitation and support of transition of infants at birth. Resuscitation. 2021;161:291-326.
3. World Health Organization. Newborns: improving survival and well-being. 2020. [cited 2023 Jan 14]. Available from: https://www.who.int/news-room/fact-sheets/detail/newborns-reducing-mortality.
4. Mann C, Ward C, Grubb M, Hayes-Gill B, Crowe J, Marlow N, et al. Marked variation in newborn resuscitation practice: a national survey in the UK. Resuscitation. 2012;83:607-11.
5. El-Naggar W, McNamara PJ. Delivery room resuscitation of preterm infants in Canada: current practice and views of neonatologists at level III centers. J Perinatol. 2012;32:491-7.
6. Iriondo M, Thió M, Burón E, Salguero E, Aguayo J, Vento M, et al. A survey of neonatal resuscitation in Spain: gaps between guidelines and practice. Acta Paediatr. 2009;98:786-91.
7. Rocha G, Saldanha J, Macedo I, Areias A, Graça A, Tomé T. Condições de assistência ao recém-nascido na sala de partos: inquérito nacional (2009). Acta Med Port. 2011;2:213-22.
8. Wyllie J, Bruinenberg J, Roehr CC, Rudiger M, Trevisanuto D, Urlesberger B. European Resuscitation Council guidelines for resuscitation 2015: section 7. Resuscitation and support of transition of babies at birth. Resuscitation. 2015;95:249-63.
9. Mitchell A, Niday P, Boulton J, Chance G, Dulberg C. A prospective clinical audit of neonatal resuscitation practices in Canada. Adv Neonatal Care. 2002;2:316-26.
10. Bensouda B, Boucher J, Mandel R, Lachapelle J, Ali N. 24/7 in house attending staff coverage improves neonatal short-term outcomes: a retrospective study. Resuscitation. 2018;122:25-8.
11. Fulbrook P, Latour J, Albarran J, de Graaf W, Lynch F, Devictor D, et al. The presence of family members during cardiopulmonary resuscitation: European federation of Critical Care Nursing associations, European Society of Paediatric and Neonatal Intensive Care and European Society of Cardiology Council on Cardiovascular Nursing and Allied Professions Joint Position Statement. Eur J Cardiovasc Nurs. 2007;6:255-8.
12. Dainty KN, Atkins DL, Breckwoldt J, Maconochie I, Schexnayder SM, Skrifvars MB, et al. Family presence during resuscitation in paediatric and neonatal cardiac arrest: a systematic review. Resuscitation. 2021;162:20-34.
13. Gizzi C, Trevisanuto D, Gagliardi L, Vertecchi G, Ghirardello S, Di Fabio S, et al. Neonatal resuscitation practices in Italy: a survey of the Italian Society of Neonatology (SIN) and the Union of European Neonatal and Perinatal Societies (UENPS). Ital J Pediatr. 2022;48:81.
14. Sawyer T, Lee HC, Aziz K. Anticipation and preparation for every delivery room resuscitation. Semin Fetal Neonatal Med. 2018;23:312-20.
15. Trevisanuto D, Testoni D, de Almeida MF. Maintaining normothermia: why and how? Semin Fetal Neonatal Med. 2018;23:333-9.
16. Moore ER, Bergman N, Anderson GC, Medley N. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database Syst Rev. 2016;11:CD003519.
17. Hooper SB, Polglase GR, Roehr CC. Cardiopulmonary changes with aeration of the newborn lung. Paediatr Respir Rev. 2015;16:47-50.
18. Fogarty M, Osborn DA, Askie L, Seidler AL, Hunter K, Lui K, et al. Delayed vs early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. Am J Obstet Gynecol. 2018;218:1-18.
19. Sheikh M, Nanda V, Kumar R, Khilfeh M. Neonatal outcomes since the implementation of no routine endotracheal suctioning of meconium-stained nonvigorous neonates. Am J Perinatol. 2022 (in press). doi: 10.1055/a-1950-2672.
20. Ng EH, Shah V. Guidelines for surfactant replacement therapy in neonates. Paediatr Child Health. 2021;26:35-41.
21. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European Consensus guidelines on the management of respiratory distress syndrome: 2022 Update. Neonatology. 2023;120:3-23.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Needs for Care, Service Use and Quality of Life in Dementia: 12-Month Follow-Up of the Actifcare Study in Portugal

Necessidades de Cuidados, Utilização de Serviços e Qualidade de Vida na Demência: Reavaliação da Amostra Portuguesa no Estudo Actifcare após 12 Meses

Manuel GONÇALVES-PEREIRA✉[1,2], Maria J. MARQUES[2,3], Regina F. ALVES[3], Ana VERDELHO[4], Conceição BALSINHA[1,2], Luísa ALVES[1,5], Teresa ALVES REIS[2,6], Bob WOODS[7], Marjolein de VUGT[8], Frans VERHEY[8], on behalf of the Actifcare Consortium [Corporate Author]

Acta Med Port 2024 May;37(5):355-367 ▪ https://doi.org/10.20344/amp.20427

ABSTRACT

Introduction: The intermediate stages of dementia are relatively under-researched, including in Portugal. The Actifcare (ACcess to TImely Formal Care) EU-JPND project studied people with mild-moderate dementia, namely their needs, access to and use of community services (e.g., day centers, home support). In our baseline assessment of the Portuguese Actifcare cohort, the unmet needs of some participants would call for formal support, which was not always accessible or used. We now report the main results of the 12-month follow-up, analyzing changes in needs, service (non)use, quality of life and related variables.

Methods: This was a longitudinal, observational study using a convenience sample of 54 dyads of people with dementia and their family carers. Our main outcomes were the Camberwell Assessment of Need for the Elderly (CANE) and the Resources Utilization in Dementia. Clinical-functional, quality of life, psychological distress and caregiving-related assessments were also used.

Results: At follow-up, the cognitive and functional status of people with dementia declined ($p < 0.001$), and their neuropsychiatric symptoms increased ($p = 0.033$). Considering CANE interviewers' ratings, the total needs of people with dementia increased at follow-up ($p < 0.001$) but not the unmet needs. Quality of life was overall stable. The use of formal care did not increase significantly, but informal care did in some domains. Carers' depressive symptoms increased ($p = 0.030$) and perseverance time decreased ($p = 0.045$). However, carers' psychological distress unmet needs were lower ($p = 0.007$), and their stress and quality of life remained stable.

Conclusion: People with dementia displayed complex biopsychosocial unmet needs. Their cognitive-functional decline over one year was not accompanied by a corresponding increase in any pattern of unmet need, nor of service use. Reliance on informal care (namely supervision) may have contributed to this. Caregiving-related outcomes evolved according to different trends, although stability was almost the rule. Primary carers were even more present at follow-up, without an apparently heavier toll on their own needs, burden, and quality of life. Overall, this longitudinal study comprehensively assessed Portuguese community-dwelling people with dementia. Despite the lack of generalizability, participants' needs remained overall stable and partly unmet over one year. Longer follow-up periods are needed to understand such complex processes.

Keywords: Caregivers; Dementia; Health Services Accessibility; Needs Assessment

RESUMO

Introdução: As fases intermédias da demência têm sido menos investigadas. O projecto EU-JPND Actifcare (*ACcess to TImely Formal Care*) estudou as necessidades de pessoas com demência ligeira-moderada e o acesso/utilização de serviços na comunidade (v.g., centros de dia, apoio domiciliário). Na avaliação inicial da subamostra portuguesa, as necessidades não cobertas de alguns participantes exigiriam apoio formal, nem sempre disponível ou procurado. Apresentamos agora resultados do estudo longitudinal (12 meses), analisando necessidades, utilização dos serviços, qualidade de vida e variáveis relacionadas.

Métodos: Estudo longitudinal de uma amostra de conveniência (54 díades doente/familiar-cuidador). Além dos principais instrumentos (Camberwell Assessment of Need for the Elderly - CANE, Resources Utilization in Dementia), foram realizadas avaliações complementares: clínico-funcionais, qualidade de vida, sofrimento psicológico, experiência de cuidar.

Resultados: No *follow-up*, o estado cognitivo e funcional das pessoas com demência piorou ($p < 0,001$) e os sintomas neuropsiquiátricos aumentaram ($p = 0,033$). O total de necessidades aumentou ($p < 0,001$), mas o total de necessidades não cobertas e a qualidade de vida permaneceram estáveis. A utilização de cuidados formais não aumentou significativamente, mas os cuidados informais sim (nalguns domínios). Os sintomas depressivos dos familiares-cuidadores aumentaram ($p = 0,030$), diminuindo o tempo de perseverança ($p = 0,045$). Porém, as suas necessidades não cobertas de sofrimento psicológico foram menores ($p = 0,007$), enquanto o *stress* e a qualidade de vida permaneceram estáveis.

Conclusão: Estas pessoas com demência apresentavam necessidades biopsicossociais complexas e não cobertas. O declínio cognitivo-funcional ao longo de um ano não foi, aparentemente, acompanhado por um aumento de necessidades não cobertas, nem da utilização de serviços. A maior utilização dos cuidados informais (supervisão) pode ter contribuído para tal. A análise das dimensões da experiência de cuidar sugere tendências não inteiramente uniformes, embora a estabilidade fosse quase a regra. Os familiares-cuidadores 'primários' estavam ainda mais presentes no *follow-up*, sem que isso pareça ter alterado as suas próprias necessidades, sobrecarga e qualidade de vida. Em suma, apresentamos uma análise longitudinal abrangente de uma amostra comunitária de famílias de pessoas com demência ligeira-moderada. Não sendo os resultados generalizáveis, ao fim de um

1. Faculdade de Ciências Médicas | NOVA Medical School. Universidade NOVA de Lisboa. Lisbon. Portugal.
2. Comprehensive Health Research Center (CHRC). Laboratório Associado REAL. Universidade NOVA de Lisboa. Lisbon. Portugal.
3. NOVA School of Public Health. Universidade NOVA de Lisboa. Lisbon. Portugal.
4. Faculdade de Medicina da Universidade de Lisboa. Centro Hospitalar Universitário Lisboa Norte. Instituto de Saúde Ambiental. Lisbon. Portugal.
5. Hospital de Egas Moniz. Centro Hospitalar de Lisboa Ocidental. Lisbon. Portugal.
6. Hospital do Espírito Santo. Évora. Portugal.
7. Dementia Services Development Centre Wales. Bangor University. Bangor. United Kingdom.
8. Alzheimer Centrum Limburg. Maastricht University. Maastricht. The Netherlands.

✉ **Autor correspondente:** Manuel Gonçalves Pereira. gpereira@nms.unl

Recebido/*Received*: 21/07/2023 - **Aceite/*Accepted*:** 02/11/2023 - **Publicado *Online*/*Published Online*:** 08/03/2024 - **Publicado/*Published*:** 02/05/2024

ano as necessidades dos participantes mantiveram-se globalmente estáveis e parcialmente não cobertas. Para compreender processos tão complexos, necessitamos de estudos com tempos de seguimento maiores.
Palavras-chave: Acessibilidade aos Serviços de Saúde; Avaliação das Necessidades; Cuidadores; Demência; Prestação de cuidados

INTRODUCTION

Dementia is a major public health problem. Its global burden of disease substantially increased in recent years and will most probably continue to increase likewise.[1] The number of people with dementia worldwide is estimated to reach 131.5 million by 2050.[2] In Europe, the enormous economic costs associated with dementia tend to follow a North-South gradient, with Mediterranean countries more reliant on informal, family care.[3,4]

Regarding Portugal, knowledge about the prevalence of dementia has improved considerably compared to a decade ago, and fieldwork strongly supports estimates exceeding 200 000 people living in the community with this condition.[1,5] These are probably underestimates, as they do not include institutionalized people with dementia[5]; furthermore, numbers are expected to increase up to 350 000 in 2050.[1] In a recent study, the global estimated cost of Alzheimer's disease amounted to 2 billion euros in 2018 (1% of the GDP[6]). Informal care represents more than half of these costs[6] and is a heavy burden on family income.[4]

In Portugal, a Dementia National Strategy was approved.[7] However, there are complex barriers to its implementation, including poor resources and organization. Some mainly relate to primary health care,[8] others to secondary and tertiary healthcare, social security and the third sector.[9] There is a convoluted system of fragmented care which is hard to navigate, because its components are poorly articulated. Regarding community services, as day centers or home care, timely access is difficult and close-to-home care coordination or case management are lacking. Support for carers and families remains inadequate, to say the least.[9] Like everywhere,[10] stigma additionally contributes to delays in diagnosis and access to care, family exhaustion and premature institutionalization. Mental health stigma and a tendency towards family caregiving obligations seem more influential in Southern Europe than barriers to access and use of services.[11] Despite the recognition of these challenges, we know little about patterns of service (under)use by people with dementia and their families, as related to their unmet needs.

In this context, the Actifcare (ACcess to TImely Formal Care) EU-JPND project focused on needs for care, access, and use of services by people living with intermediate stages of dementia in the community and their families. By 'intermediate' we mean mild (beyond immediate postdiagnosis) and moderate stages, still relatively neglected in psychosocial research as compared with more advanced phases. The project included a cohort study of a large sample from eight European countries,[12] for which a baseline analysis of the Portuguese subsample has been published.[13] We were interested in analyzing the transition from situations in which people can rely on family informal care only, to more advanced levels of disability where formal community services (e.g., day centers, home care) become necessary to meet emerging needs. At baseline, unmet needs were more frequently psychosocial in nature (e.g., company, psychological distress, daily activities). Some would call for formal support, were it not for problems regarding access or use of community services. Problems with access or use of these services, when present, were frequently due to attitudinal issues or lack of knowledge regarding the condition or available services (influencing levels and types of unmet needs).[13]

We now report the 12-month follow-up results of the same Portuguese cohort, aiming to analyze changes in participants' needs for care, service (non)use, and related clinical, functional, and psychosocial variables over time.

METHODS

Study design

The Actifcare EU-JPND cohort study protocol is available elsewhere,[12] and has been detailed regarding the Portuguese subsample recruitment, study procedures and baseline assessments.[13] Here, we refer to the 12-month follow-up results.

Ethical considerations

Written informed consent was provided by all participants (persons with dementia and their family carers). Permission was granted by local ethics committees [Comissão de Ética da Faculdade de Ciências Médicas; Comissões de Ética para a Saúde do Centro Hospitalar de Lisboa Ocidental, Administração Regional de Saúde (ARS) de Lisboa e Vale do Tejo and ARS Alentejo] and by the Portuguese data protection authority (Comissão Nacional de Proteção de Dados).

Sample

The EU Actifcare sample was composed of 451 dyads of people with a diagnosis of DSM-IV-TR dementia[14] and their primary (main) family caregivers, henceforth called 'carers'. According to the inclusion criteria, participants should have mild or moderate dementia (Clinical Dementia Rating-CDR),[15] or score below 25 on the Mini Mental State Examination (MMSE),[16] no relevant formal assistance with

personal care relating to dementia (e.g., paid home carer) for the previous six months, and a clinical impression that such formal care would be needed within the 12-month follow-up. People with significant comorbidities (severe somatic/mental disorders or sensory impairments) were excluded.[12,13] In Portugal, we recruited 66 dyads from different regions and clinical and social settings (primary care, public or private neurology and psychiatry outpatient clinics, and the third sector, including Alzheimer Portugal).

Instruments

Our study assessments were comprehensive. An overview of all variables included may be found in Table 1, along with the corresponding measures and references to original and Portuguese validation studies.[12,13]

Assessments of people with dementia

Following our baseline report, we remained focused on needs for care and service use, and the corresponding measures: the Camberwell Assessment of Need for the Elderly (CANE)[17] and the Resources Utilization in Dementia (RUD).[18] The CANE interview assesses care needs (unmet, met, or non-existent) across 24 biological and psychosocial domains, allowing for the comparison of users', carers' and interviewers' perspectives on each domain. For each user, a total score is computed by summing up all domains where an existing need is recognized. Its validity and reliability have been documented internationally[17,19] and in Portugal.[20] Regarding RUD, it measures the use of formal and informal care in dementia, and its psychometric properties were also documented.[18] Additionally, an *ad hoc* checklist described access to and use of formal services more in depth.[12]

We also used the Quality of Life-Alzheimer's Disease Scale (QOL-AD),[21] both self and proxy-rated. Its thirteen domains (physical health, energy, mood, living situation, memory, family, marriage, friends, chores, fun, money, self, and life overall) are evaluated on four-point Likert scales (poor, fair, good, excellent). Higher scores indicate better quality of life (range 13 - 52). The QOL-AD demonstrated favorable validity and reliability in Portugal.[22] Participants' clinical-functional characterization further included: dementia severity,[15] cognitive function,[16] neuropsychiatric symptoms,[23] comorbidity[24] and overall functioning[25] (Table 1).

Assessment of family carers

We assessed carers' specific needs with the two corresponding items of the CANE interview (information about dementia and psychological distress),[17] use of resources with the RUD,[18] and quality of life with the CarerQol scale. This last scale was specifically developed to gauge the impact of providing informal care. It consists of seven items, rated on three-point scales; here we used the sum score (range 0 - 14), with higher scores meaning higher quality of life.[26,27] Additional assessments included e.g., anxiety and depression symptoms,[28] family burden,[29] perseverance time[30] (Table 1).

Procedures

All interviewers were psychologists with clinical and/or research experience. Reliability training for the study measures has already been reported.[13]

The assessments took place at home or elsewhere, as convenient. They were conducted separately with the person with dementia and their carer. If necessary, conjoint conversations would take place, mainly if the person with dementia felt more secure in the presence of their loved one. Furthermore, interviews would be interrupted due to tiredness or assessment burden, to be completed within short timeframes.

Data analysis

For this longitudinal analysis of our Portuguese cohort, only the 54 dyads completing the 12-month follow-up were considered. Beforehand, the variables' distributional properties were examined, using means with standard deviations (SD) for continuous variables and frequencies with percentages for categorical variables (n, %). The data were tested for normality (Shapiro-Wilk) before all analyses were carried out. Chi-square (with Fisher's correction when necessary) or *t*-Student test were used to analyze socio-demographic and clinical differences between baseline and dropout participants. All variables were compared at baseline and at the 12-month follow-up. In order to compare means, we used specific tests: *T*-tests for related samples; two-way repeated measures ANOVA, with the Bonferroni test for the multiple pairwise comparisons. To analyze categorical variables, we used McNemar or Wilcoxon tests. When the results showed statistically significant differences the effect size (Cohen's d) was calculated. A significance level of 0.05 was used. All analyses were performed with Statistical Package for the Social Sciences/SPSS, v28.0 for Windows.

Data availability

The complete dataset is available upon reasonable request to the corresponding author. Consent for dataset availability has not been obtained from participants, but data was anonymized.

RESULTS

After recruitment and baseline assessment, 12 of the 66 dyads of people with dementia and their carers were lost to the 12-month follow-up. Attrition was due to carer withdrawal (not willing to collaborate, stating exhaustion) (six dyads), person with dementia death (four) or

Table 1 – Overview of the EU-Actifcare project instruments specifically used in this longitudinal analysis

Instrument	Variable	Respondents[a]	**Author** (year) **/ Portuguese translation** (year) **and/or reference of validation study in Portugal**
Sociodemographic, clinical and functional characteristics of people with dementia			
Sociodemographic questionnaire	Sociodemographic data	1,2	Actifcare Workgroup in Portugal (2015)
Clinical Dementia Rating (CDR)	Dementia severity	1,2	Morris (1993) / *Grupo de Estudos de Envelhecimento Cerebral e Demência* (2008)
Mini Mental State Examination (MMSE)	Cognitive Status	1	Folstein *et al* (1975) / Guerreiro *et al* (1994); Portuguese version obtained from Psychological Assessment Resources, via MAPI Research Trust – PROQOLID (2014)
Neuropsychiatric Inventory Questionnaire (NPI-Q)	Neuropsychiatric symptoms	2	Kaufer *et al* (2000) / Adapted from *Grupo de Estudos de Envelhecimento Cerebral e Demência* (2008); online approval obtained from the website http://www.npitest.net/ (2014)
Charlson Index	Comorbility	4	Charlson *et al* (1994) / Actifcare Workgroup in Portugal (2015)
Lawton Instrumental Activities of Daily Living (IADL)	Instrumental activities of daily living	2	Lawton & Brody (1969) / Araújo *et al* (2008)
Physical Self-Maintenance Scale (PSMS)	Activities of daily living	2	Lawton & Brody (1969) / Araújo *et al* (2008)
Needs for care			
Camberwell Assessment of Need for the Elderly (CANE)	Needs for care	1,2,4	Reynolds *et al* (2000) / Gonçalves-Pereira *et al* (2007); Fernandes et al (2009)
Service access and utilization			
Checklist of service utilization	Access and reasons for (no) utilization of services	1,2	Actifcare Workgroup in Portugal (2015)
Resources Utilization in Dementia (RUD) 5.0	Service utilization	1,2	Wimo *et al* (2013) / Portuguese version obtained online from the website http://rudinstrument.com (2015)
Quality of life and relationship quality			
Quality of Life-Alzheimer's Disease (QOL-AD)	Quality of life of people with dementia	1,3	Logsdon *et al* (1999) / Bárrios *et al* (2013)
CarerQoL-7D	Quality of life of carers	2	Brouwer *et al* (2006) / Actifcare Workgroup in Portugal (2015)
Positive Affect Index (PAI)	Quality of the relationship between carers and people with dementia	1,2	Bengtson & Schrader (1982) / Actifcare Workgroup in Portugal (2015)
Carers' psychological distress, caregiving experiences and social support			
Hospital Anxiety and Depression Scale (HADS)	Anxiety and depression	2	Zigmond & Snaith (1983) / Pais-Ribeiro *et al* (2007); Portuguese version obtained from GL Assessment, via MAPI Research Trust – PROQOLID (2014)
Relative Stress Scale (RSS)	Disease-related family burden	2	Greene *et al* (1982) / Actifcare Workgroup in Portugal (2015)
Lubben Social Network Scale (LSNS-6)	'Perceived' social support	2	Lubben, 1988 / Ribeiro *et al* (2012)
Perseverance time	Single question[b]	2	Kraijo *et al* (2014) / Actifcare Workgroup in Portugal (2015)
Carers' dispositional variables			
Locus of Control Behavior Scale (LOC)[c]	Locus of control	2	Craig *et al* (1984) / Actifcare Workgroup in Portugal (2015)
Orientation to Life Questionnaire (SOC-13)	Sense of coherence	2	Antonovsky (1987) / Saboga-Nunes (1999)

[a] Respondents: people with dementia (1); informal carers/family (2); informal carers (as a proxy, giving an opinion on the status of the person with dementia or providing an approximate response that person would give) (3); researchers/interviewers (4);
[b] In case the current situation remains unchanged, how long would you be able to keep on with caregiving? ('*Se a situação de cuidados se mantiver tal como está, quanto tempo será capaz de continuar a prestar cuidados*?');
[c] Only used in baseline assessments.

institutionalization (one), and carer death (one). In three other dyads, the person with dementia was no longer able to participate in follow-up assessments due to cognitive decline; these were not dropouts since the carer remained willing and able to participate.

We first compared the 12 dyads lost to follow-up and the 54 that could be reassessed after 12 months (Table 2). There were no statistically significant differences between these two groups regarding individuals' demographic and clinical-functional characteristics, dyads' caregiving arrangements, or locus of control (a measure that was only completed at baseline).

Regarding people with dementia who completed the study, mean age was 77 years (SD = 6.4) and around two thirds (34 participants) were women. More than one third of the sample (20 participants) had a diagnosis of Alzheimer's disease, which was the most frequent dementia subtype, and two thirds (34 participants) had high comorbidity levels with the Charlson Index. Only two lived alone. Regarding carers, mean age was 64 years (SD = 15.1), 35 of them (around two thirds) were women and 32 were spouses of the person with dementia.

Table 3 concerns other clinical, functional, and psychosocial assessments of people with dementia and their carers, showing the corresponding differences between baseline and 12-month follow-up.

There was a decrease in MMSE scores, in Lawton IADL function and in basic ADL function. These differences were

Table 2 – Baseline demographic characteristics, clinical diagnoses of dementia and multimorbidity of participants completing the study versus lost to follow-up

	Completing the study (54 dyads)	**Lost to follow-up** (12 dyads)	***p*-value**
People with dementia			
Age, years, mean (SD)	76.9 (6.4)	79.1 (5.4)	0.273[b]
Women, n (%)	34 (63.0)	7 (58.3)	0.737[c]
Education, years, mean (SD)	6.9 (6.6)	4.4 (2.9)	0.215[b]
Living alone, n (%)	2 (3.7)	0 (0.0)	0.498[c]
Type of dementia, n (%)			0.882[c]
Alzheimer's Type	20 (37.0)	5 (41.7)	
Vascular	6 (11.1)	2 (16.7)	
Mixed (Alzheimer's and Vascular)	6 (11.1)	1 (14.3)	
Lewy Body	2 (3.7)	0 (0.0)	
Frontotemporal dementia	4 (7.4)	0 (0.0)	
Unspecified	16 (29.6)	4 (33.3)	
Comorbidity (Charlson), mean (SD)	3.1 (1.5)	3.0 (1.3)	0.785[b]
			0.658[c]
None, n (%)[a]	8 (14.8)	1 (8.3)	
Low comorbidity, n (%)[a]	12 (22.2)	4 (33.3)	
High comorbidity, n (%)[a]	34 (63.0)	7(58.3)	
Family carers			
Age, years, mean (SD)	64.2 (15.1)	68.2 (14.7)	0.408[b]
Women, n (%)	35 (64.8)	9 (75.0)	0.498[c]
Education, years, mean (SD)	9.4 (6.5)	7.3 (5.0)	0.300[b]
Relationship to person with dementia, n (%)			0.884[c]
Spouse/partner	32 (59.3)	8 (66.7)	
Adult children	16 (29.6)	4 (33.3)	
Other (e.g., son/daughter in law; sibling)	6 (11.1)	0 (0.0)	
Locus of control, mean (SD)	57.3 (6.5)	55.5 (5.4)	0.321[b]

SD: standard deviation.
[a] Charlson index – none: 0-1 conditions; low comorbidity: 2 conditions; high comorbidity: ≥ 3 conditions.
[b] *t*-Student test.
[c] Chi square test with Fisher's correction

statistically significant and had moderate effect sizes. Accordingly, seven cases converted from CDR 1 to CDR 2 dementia severity. Neuropsychiatric symptoms increased, but the level of significance and effect size were lower. People with dementia did not report significant differences in their quality of life over time, the same happening with proxy perceptions. Furthermore, when accounting for the interaction between time and respondent in a two-way repeated measures ANOVA, QOL-AD scores were not significantly different at baseline and follow-up ($F = 0.176$, $p > 0.05$).

Regarding carers' assessments (Table 3), depressive symptoms increased, and perseverance time decreased, but the effect size was modest for both changes. We found no other significant differences between carers' baseline and follow-up assessments.

Table 4 depicts changes in levels of need of people with dementia, according to their own views, their carers' and the interviewers' (overall perspective). The mean total number of needs decreased according to people with dementia ($p = 0.010$) but increased according to both carers ($p = 0.015$) and interviewers ($p < 0.001$). The mean total number of unmet needs decreased according to people with dementia

Table 3 – Clinical, functional and secondary outcome assessments of people with dementia and their family carers: differences between baseline and follow-up (12 months)

	Baseline	Follow-up	*p*-value	Effect size[d]
People with dementia				
Dementia severity (CDR)			**0.016**[a]	
Category 1, n (%)	50 (92.6)	43 (79.6)		
Category 2, n (%)	4 (7.4)	11 (20.4)		
MMSE (range: 0 - 30)	18.3 (4.8)	16.2 (5.7)	**< 0.001**[b]	**0.753**
Neuropsychiatric symptoms (NPI-Q) (range: 0 - 12)	6.9 (5.9)	8.4 (4.5)	**0.033**[b]	-0.297
Lawton IADL function (range: 0 - 8)	3.9 (2.0)	2.9 (2.1)	**< 0.001**[b]	**0.669**
Basic ADL function (PSMS) (range: 0 - 6)	3.9 (1.8)	3.2(1.9)	**< 0.001**[b]	**0.580**
QOL-AD (range: 13 - 52)	31.1 (5.9)	31.3 (5.7)	0.791[b]	
Relationship Quality (PAI) (range: 5 - 30)	22.0 (4.6)	21.7 (3.5)	0.567[b]	
Proxy				
QOL-AD (range: 13 - 52)	29.4 (5.8)	30.1 (6.5)	0.397[a]	
Family carers				
CarerQoL-7D (range: 0 - 13)	10.2 (2.6)	9.7 (2.3)	0.109[b]	
Relationship Quality (PAI) (range: 5 - 30)	21.0 (4.6)	20.2 (4.1)	0.114[b]	
Anxiety symptoms (HADS) (range: 0 - 21)	6.3 (3.7)	6.6 (4.0)	0.477[b]	
Depressive symptoms (HADS) (range: 0 - 21)	6.2 (4.5)	7.3 (4.4)	**0.030**[b]	-0.309
Subjective burden (RSS) (range: 0 - 60)	21.0 (11.4)	22.8 (10.0)	0.202[b]	
Social Support (LSNS-6) (range: 0 - 30)	16.3 (4.3)	16.7 (4.7)	0.503[b]	
Perseverance Time, n (%)			**0.045**[c]	-0.213
Less than one week	0 (0.0)	0 (0.0)		
More than one week but less than one month	0 (0.0)	0 (0.0)		
More than one month but less than six months	2 (3.9)	4 (8.5)		
More than six months but less than one year	5 (9.8)	5 (10.6)		
More than one year but less than two years	5 (9.8)	8 (17.0)		
More than two years	39 (76.5)	30 (63.8)		
Sense of Coherence (SOC-13) (range: 13 - 91)	65.0 (11.2)	67.4 (12.6)	0.078[b]	

Mean (SD) for all, unless noted otherwise.
CDR: Clinical Dementia Rating Scale; MMSE: Mini Mental State Examination; NPI: Neuropsychiatric Inventory; IADL: Instrumental Activities of Daily Living; PSMS: Physical Self-Maintenance Scale; QOL-AD: Quality of Life-Alzheimer's Disease; PAI: Positive Affect Index; HADS: Hospital Anxiety Depression Rating Scale; RSS: Relative Stress Scale; LSNS-6: Lubben Social Network Scale; SOC-13: Sense of Coherence Scale-13.
[a] Related-samples McNemar test;
[b] Paired Samples *T*-test;
[c] Wilcoxon test;
[d] Cohen's d

Table 4 – CANE ratings by people with dementia, family carers and interviewers (overall perspective): differences between baseline and follow-up (12 months)[a]

CANE	Perspective (type of rating)	Baseline (n = 54) Mean (SD)	Follow-up (n = 54) Mean (SD)	Effect Time[b] *p*-value	Effect Time x perspective[c] *p*-value
Unmet needs	People with dementia	1.4 (1.9)	0.8 (1.4)	**0.029**	**0.018**
	Family carers	1.4 (1.5)	1.0 (1.5)	**0.019**	
	Interviewers	6.4 (2.8)	5.2 (3.1)	0.775	
Met needs	People with dementia	5.0 (2.7)	4.5 (2.6)	0.251	**< 0.001**
	Family carers	7.9 (2.6)	9.0 (3.0)	**< 0.001**	
	Interviewers	9.3 (3.1)	10.0 (3.0)	**< 0.001**	
Total needs	People with dementia	6.4 (2.8)	5.2 (3.1)	**0.010**	**< 0.001**
	Family carers	7.6 (2.8)	9.2 (2.8)	**0.015**	
	Interviewers	8.8 (3.1)	10.4 (2.4)	**< 0.001**	

[a] The two CANE items on carers' needs are not included here;
[b] Paired Samples *T*-test;
[c] Two-way repeated measures ANOVA.

(p = 0.029) and their carers (p = 0.019). In contrast, the total number of unmet needs according to interviewers did not change significantly from baseline to follow-up. The two-way repeated measures ANOVA showed a significant interaction between type of CANE ratings and time, in the unmet (F = 5.999, p = 0.018), met (F = 20.394, p < 0.001) and total number of needs (F = 35.592, p < 0.001), suggesting that changes over time varied depending on the type of rating considered. At follow-up, there were significant differences between people with dementia and carers' ratings (met needs: p < 0.001; total needs: p < 0.001) and between people with dementia and interviewers' ratings (unmet needs: p = 0.022; met needs: p < 0.001; total: p < 0.001). Carers and interviewers' ratings did not differ significantly at follow-up.

Going into more detail, Table 5 shows the ratings of unmet needs compared to 'no needs' and 'met needs', by domain, now only from the interviewers' integrative perspective. Item-by-item analyses showed no statistically significant differences between baseline and follow-up in any person with dementia need domain. 'Company', 'psychological distress' and 'daytime activities' were the most common unmet needs at baseline. The number of participants with these unmet needs decreased at follow-up ('company' and 'psychological distress') or remained stable ('daytime activities'). On the contrary, the number of participants with unmet needs increased in other domains, namely 'memory', 'medicines', 'mobility' and 'behavior'. Regarding the two carer-related need domains, there was an increase in information and a decrease in psychological distress unmet needs, with the latter being statistically significant.

Finally (Table 6) there was a general trend towards an increase in access/use of formal and informal care. However, the only statistically significant differences were an increase in time spent in supervision by carers and in their level of contribution to care provision, as primary carers.

DISCUSSION

We conducted a longitudinal study of dyads of community-dwelling people with mild to moderate dementia and their family carers, over one year. This small sample had been recruited to integrate a large cohort from eight countries. Notwithstanding, cross-country comparisons were not a primary aim of the EU project and that is why we undertook this analysis of Portuguese participants. To our knowledge, this is the first study of a Portuguese sample in which needs for care, service use, and quality of life in dementia were comprehensively assessed over time. We additionally considered carers' variables such as anxiety and depressive symptoms and family burden.

As expected, we documented cognitive and functional decline in people with dementia and a relative increase in their neuropsychiatric symptoms. However, regarding needs assessment, total unmet needs did not change significantly at follow-up, according to interviewers. This was a surprising result. First, because unmet needs are more important to consider in health services research than the crude mean of overall needs (met plus unmet), which was significantly higher at follow-up (interviewers' ratings) owing to the met needs' component. Second, in order to rate each CANE item, interviewers take into consideration users' and carers' views, aiming to provide an integrated perspective over each need domain: that is why this specific CANE score is more often reported. That users', carers' and interviewers' views did not exactly coincide is not surprising: research has widely illustrated such discrepancies.[19,31,32] Our

Table 5 – Frequency of unmet needs and other CANE ratings (interviewers' perspective): differences between baseline and follow-up (12 months)

Need domains	Baseline		Follow-up		*p*-value[a]
	Unmet needs	No needs/ Met needs	Unmet needs	No needs/ Met needs	
People with Dementia, n (%)					
Accommodation	-	54 (100.0)	1 (1.9)	53 (98.1)	1.000
Looking after home	-	53 (100.0)	1 (1.9)	52 (98.1)	1.000
Food	1 (1.9)	52 (98.1)	1 (1.9)	52 (98.1)	1.000
Self-care	-	53 (100.0)	-	53 (100.0)	1.000
Caring for another person	1 (1.9)	53 (98.1)	2 (3.7)	52 (96.3)	1.000
Daytime activities	9 (16.7)	45 (83.3)	9 (16.7)	45 (83.3)	1.000
Memory	2 (3.8)	51 (96.2)	6 (11.3)	47 (88.7)	0.289
Eyesight/hearing/communication	1 (2.0)	50 (98.0)	2 (3.9)	49 (96.1)	1.000
Mobility	1 (1.9)	52 (98.1)	4 (7.5)	49 (92.5)	0.250
Continence	2 (6.1)	46 (93.9)	-	53 (100.0)	0.250
Physical health	1 (1.9)	52 (98.1)	3 (5.7)	51 (94.3)	0.500
Medicines/drugs	2 (4.0)	48 (96.0)	5 (10.0)	45 (90.0)	0.453
Psychotic symptoms	1 (2.0)	50 (98.0)	-	51 (100.0)	1.000
Psychological distress	11 (22.9)	37 (77.1)	9 (18.8)	39 (81.3)	0.791
Information	2 (4.3)	45 (95.7)	4 (4.3)	45 (95.7)	1.000
Deliberate self-Harm	2 (3.8)	50 (96.2)	-	52 (100.0)	0.500
Accidental self-Harm	4 (8.0)	46 (92.0)	1 (2.0)	49 (98.0)	0.250
Abuse/neglect	1 (2.0)	49 (98.0)	-	50 (100.0)	1.000
Behavior	1 (2.0)	50 (98.0)	4 (7.8)	47 (92.2)	0.375
Alcohol	-	52 (100.0)	-	52 (100.0)	1.000
Company	13 (25.5)	38 (74.5)	7 (13.7)	44 (86.3)	0.180
Intimate relationships	2 (3.8)	50 (96.2)	3 (5.8)	49 (94.2)	1.000
Money	-	52 (100.0)	-	52 (100.0)	1.000
Benefits	2 (5.4)	35 (94.6)	1 (2.7)	36 (97.3)	1.000
Carers, n (%)					
Information	7 (13.7)	44 (86.3)	14 (27.5)	37 (72.5)	0.118
Psychological distress	23 (45.1)	28 (54.9)	12 (23.5)	39 (76.5)	**0.007**

[a] McNemar test

results lend themselves to different interpretations, and it may be that some people with dementia underrated their own unmet needs due to denial or anosognosia. Nevertheless, and somehow unexpectedly, their carers also reported significantly lower levels of total unmet needs at follow-up.

At item/domain level, these people with dementia already displayed a picture of complex biopsychosocial unmet needs at baseline, mainly regarding 'company', 'distress' and 'daily activities'. At follow-up, these remained the three most frequent unmet needs and the overall pattern did not differ significantly, even though 'company' and 'distress' unmet needs decreased slightly. On the contrary, in line with the clinical and functional changes in the sample over time, the number of 'memory', 'medicines', 'mobility' and 'behavior' unmet needs slightly increased.

Notwithstanding, these changes were not accompanied by significant modifications in formal services' use: only four participants started to use them, definitely less than expected (one of the inclusion criteria was some degree of expectation that the person would require formal support within 12 months). At least partly, more use of informal care may have contributed to this, namely on account of extended supervision time.

Notably, these primary carers reported higher levels of contribution in care provision at follow-up, more than half stating a contribution higher than 80%. In accordance,

Table 6 – Formal and informal care utilization: differences between baseline and follow-up (12 months)

	Baseline	Follow-up	*p*-value
Formal care[a]			
No formal care utilization, n (%)	34 (53.1)	30 (46.9)	0.388[c]
Formal care utilization, n (%)	20 (45.5)	24 (54.5)	
Nursing services at home, n	1	1	
Home care, n	0	1	
Home-delivery meal services, n	2	3	
Day care, n	0	1	
Transports (healthcare-related), n	0	1	
Other (e.g., housekeeper), n	13	15	
Unspecified, n	4	2	
Informal care[a]			
Time spent by carers, minutes/day (mean, SD)			
Activities of daily living	12.3 (17.4)	7.9 (12.0)	0.106[d]
Instrumental activities of daily living	11.8 (14.7)	14.8 (15.6)	0.229[d]
Supervision	7.0 (11.5)	15.2 (14.6)	**0.001**[d]
Total	29.4 (25.2)	37.9 (21.3)	0.066[d]
Other informal carer involved, n (%)			0.810[e]
0	12 (24.0)	11 (22.0)	
1	18 (36.0)	14 (28.0)	
2	10 (20.)	15 (30.0)	
3	4 (8.0)	8 (16.0)	
4 or more	6 (12.0)	2 (4.0)	
Level of contribution in care provision[b], n (%)			**0.004**[e]
21% - 40%	1 (2.0)	0 (0.0)	
41% - 60%	3 (6.0)	2 (4.0)	
61% - 80%	16 (32.0)	6 (12.0)	
81% - 100%	30 (60.0)	42 (84.0)	

[a] Over the past 30 days;
[b] Assessment of the level of contribution of the main carer, i.e., the one that was interviewed (among all involved informal carers);
[c] McNemar test;
[d] Paired samples *T*-test;
[e] Wilcoxon test

although effect sizes were low, carers' perseverance time (their estimate of how long they can continue in this way if the situation remains unchanged) tended to decrease (p = 0.045), approaching the low levels reported in other studies[33] while their depressive symptoms tended to increase (p = 0.030). Nevertheless, stability was almost the rule concerning other carer-related measures, namely quality of life, burden of care and 'information' unmet needs. Carers' 'psychological distress' unmet needs were even significantly lower at follow-up: although almost half of carers had this type of unmet need at baseline, this decreased to less than a quarter at follow-up. Such a finding remains consistent with higher involvement in caregiving over time, reflecting that more needs are being met by formal and/or informal support and not a decrease in overall needs.

The analysis of other outcome measures for people with dementia also yielded interesting results. QOL-AD ratings remained stable overall, regardless of being self or proxy-reported. In the longitudinal analysis of the EU-Actifcare large sample, carer's proxy-ratings were significantly lower than self-ratings at all timepoints for the QOL-AD, just like for the ICECAP-O (measuring capability, a construct closely related to quality of life); proxy-ratings declined over time, but self-ratings remained stable. It was concluded that quality of life ratings in dementia must be interpreted with caution and in the context of each caregiving relationship.[34,35] In the present analysis, restricted to the Portuguese subsample, the usual pattern of significantly worse

proxy reports by carers or other informants[22,36] was not observed. A recent review suggested there may be stronger agreement on more observable quality-of-life domains e.g., physical health and mobility, than with, for example, anxiety/depression, emotional well-being[36] but perhaps this tendency is mitigated when proxies are repeatedly reminded to respond from the person's perspective.[37] Other measures related with quality of life, either generic (EQ-5D, ICECAP-O) or disease-specific (DEMQOL), were also considered for EU-Actifcare reports, where cross-validating quality-of-life tools in dementia was also a (secondary) aim. Analyzing the small subsample of the present study, we only reported QOL-AD results, the disease-specific measure with more in-depth documentation of validity and test-retest reliability in Portugal.

The quality of the relationship between persons with dementia and their carers also remained stable, regardless of who rated it (person with dementia or carer). After all, relationship quality obviously contributes to quality-of-life appraisals.

On the whole, our results support previous suggestions that deterioration in quality of life is not inevitable throughout the dementia journey. King et al used other quality-of-life measures (EQ-5D-3L and DEMQOL, both self and proxy-rated) reporting overall stability over one year except for proxy-ratings of the EQ-5D-3L, which declined.[35] They argued that, depending on which measure is used, the observed changes may be associated with different factors.[35] However, given our small numbers we did not undertake multivariable analyses.

These findings in Portugal must be contextualized in the larger EU-Actifcare cohort study. We previously highlighted that, in comparison with other countries' participants at baseline, Portuguese patient-carer dyads more often shared the same household, mirroring North-South differences in Europe concerning caregiving.[13] Portuguese participants displayed lower education levels and carers specifically reported lower sense of coherence and more depressive symptoms. However, their sense of coherence scores did not deviate much from findings in similar samples; and their mean levels of depressive symptoms (falling within the 'normal' to 'possible case' range, per international cut-offs) would not represent clinical depression in most cases.

Our study also illustrates the importance of dementia needs assessment,[19] underlining once more the prevalence of psychosocial unmet needs. In a recent Chilean study, for instance, the most frequent unmet needs were again 'daily activities' (39.2%), 'company' (36.1%), and 'memory' (34.9%).[38] Coming back to the role of formal support, the EU-Actifcare results on access and use of services align with recent literature documenting limited receipt of support services among people with mild-moderate dementia[39] and inequalities in care structures, including dementia-specific services, throughout Europe.[40] Overall, we should more systematically consider users and carers' views and priorities, as in value-based healthcare.[41]

Another aspect has to do with the interpretation of the scores of the psychosocial measures in our sample, a matter which is not always easy. For instance, QOL-AD ratings were higher than in the Portuguese validation study,[22] but this was partly conducted in long-term care. Regarding the absolute values of caregiving-related outcomes, we found no other analyses with, for example, the PAI, RSS or LOC measures (Table 1) in Portugal; a Portuguese study reported higher LSNS-6 scores in older people who were not necessarily carers.[42] Regarding studies in other countries, the LSNS-6, PAI and RSS scores we report fell within the usual range for similar populations,[43-45] but these carers seemingly displayed a higher locus of control.[45]

It must also be noted that our study was conducted prior to the COVID-19 pandemic: Portuguese research began to unravel the additional impact of such challenges for these vulnerable populations.[46]

Limitations

Our results must be cautiously interpreted. They are not generalizable, not even to the subgroup of community-dwellers with mild or moderate dementia in Portugal. First, our small convenience sample at baseline (66 dyads) was recruited to serve the purposes of the large EU-Actifcare cohort study. Inclusion criteria were deliberately restrictive; for instance, participants could not rely on significant formal care but would be expected to do so after the one-year follow-up.[12,13] Notwithstanding, the sample was diversified regarding region and context of recruitment (healthcare levels, social services in charge). Despite a certain deviation towards higher education, the sample typicity at baseline was somehow ensured. Second, our analyzable sample was further reduced to 54 dyads, as 12 were lost to follow-up. In seven cases, attrition came from carers' exhaustion or the person's institutionalization: the results could have been different if we had been able to assess them at follow-up. However, we found no significant differences between the analyzable sample and the remaining dyads at baseline.

Although this was an observational study, it may be that some participants found the comprehensive, extended assessment process reassuring and supportive in itself, arguably influencing subjective measurements related to, for example, needs or social support. On the other hand, the use of multiple researchers to collect data potentially introduces variation in measurements,[38] and this other source of bias was surely minimized here.

Finally, a one-year follow-up period may be too short to

grasp the complexity of the evolution of dementia, possibly contributing to the stability of many outcomes.

Is this it? Implications of the study

Despite the limitations of the study, we believe our results to be rather important, nonetheless. First, over one year of progressing dementia, these dyads did not worsen most outcomes significantly, including unmet needs, quality of life, or most carers' measures (except depressive symptoms and perseverance time). Therefore, it is often possible to preserve quality of life, even if transiently, and even before launching specific psychosocial interventions.

Second, although their levels remained stable overall, unmet needs did exist at baseline and/or follow-up. The fact that people with dementia have many and complex biopsychosocial needs is also uncontentious in Portugal.[20] Most rely on family carers with their own needs, displaying objective and subjective burden and psychological distress.[47,48] In this context, the responses of health and social services are still grossly inadequate,[9] which leads us to a third point.

By assessing clinical-functional and social characteristics, perceived needs, and access to and use of formal services over one year, this study highlights the importance of interventions targeting specific needs, which frequently change over short periods of time. While the evidence base for interventions to enhance timely access and appropriate use of community services remains limited,[49] they could reduce the unmet needs of people with dementia and their families along with other negative outcomes such as carers' burden and psychological morbidity.

Fourth, many participants were recruited from primary care. The SPICE five-item assessment (focusing on senses, physical ability, incontinence, cognition, and emotional distress domains) was derived from the 24-item CANE specifically for primary care users and, later, tested in Portugal as well.[50] Although some of the most-rated unmet needs in the present study would not be screened by SPICE, it tackles 'cognition' and 'psychological distress', and perhaps combining it with the two CANE carer items could prove cost-effective in such populations.

Finally, important research gaps should be acknowledged. Future studies should consider longer follow-up periods and larger samples. They should also include people with mild-to-moderate dementia who did not even reach the appropriate clinical services, which frequently happens in Portugal. Assessment bias may be decreased by combining qualitative and quantitative methods, as we did in other EU-Actifcare studies and plan to do regarding ongoing analyses of the Portuguese subsample.

CONCLUSION

This was a longitudinal, observational, and comprehensive analysis of the Portuguese cohort that integrated the larger EU-Actifcare project on community-dwelling people with mild to moderate dementia.

We found a decline in patients' cognitive and functional measures and a slight increase in neuropsychiatric symptoms; this was associated with relatively little additional input from formal services, with the main carer spending more time providing supervision for the person with dementia and taking on greater overall responsibility for care. The significant increase in depressive symptoms may be interpreted as an early sign of role-captivity for these main carers. While the relative stability of quality of life may also be seen in a positive light, our results pertain to a small, albeit typical, convenience sample with some attrition, and arguably longer follow-up periods are needed in this field.

Above all, at our 12-month follow-up, we still found relevant unmet needs in specific areas; these were mainly 'psychological distress', 'daytime activities' and 'company' for people with dementia, and 'information' and 'psychological distress' for their carers. This calls for timely interventions that may be tailored to person-centered assessments of need.

ACKNOWLEDGMENTS

The Actifcare consortium was coordinated by Frans Verhey and Marjolein de Vugt (Maastricht University) and included, besides the authors of this paper: Claire Wolfs, Ron Handels, Liselot Kerpershoek (Maastricht University, The Netherlands); Gabriele Meyer, Astrid Stephan, Anja Bieber, Anja Broda (Martin Luther University Halle-Wittenberg, Germany); Hannah Jelley (Bangor University, United Kingdom); Anders Wimo, Anders Sköldunger, Britt-Marie Sjölund (Karolinska Institutet, Sweden); Knut Engedal, Geir Selbaek, Mona Michelet, Janne Rosvik, Siren Eriksen (Vestfold Hospital Trust/ Oslo University Norway); Kate Irving, Louise Hopper, Rachael Joyce (Dublin City University, Ireland); Orazio Zanetti, Daniel M. Portolani (IRCCS Centro S. Giovanni di Dio - Fatebenefratelli, Italy).

The Portuguese Actifcare Workgroup included, besides the authors of this paper: Alexandra Fernandes, Ana Sá Machado, Bernardo Barahona Corrêa, Helena Bárrios, Joana Grave, João Guimarães and Manuel Caldas de Almeida.

We wish to thank all participants in the study, and clinical services involved (ACES Alentejo Central, Centro de Saúde de Mora, USF Fernão Ferro mais, USF Marginal, Hospital Egas Moniz/CHLO, Hospital do Mar – Luz Saúde), Alzheimer Portugal, Associação de Beneficência Popular de Gouveia and Santa Casa da Misericórdia de Mora.

AUTHOR CONTRIBUTIONS

MGP: Contributed to the design of the EU-Actifcare study. Principal investigator of the Actifcare project in

Portugal. Planned the present study analyses. Drafted the manuscript.

MJM: Contributed to the design of the EU-Actifcare study. Coordinated and conducted the fieldwork in Portugal. Planned and conducted the present study analyses. Drafted the manuscript.

RFA: Planned and conducted the present study analyses. Drafted the manuscript.

AV, CB, LA, TAR: Closely collaborated in the Actifcare study planification and implementation in Portugal, and in fieldwork. Provided relevant contributions to the manuscript.

BW: Designed and coordinated the EU-Actifcare cohort study. Provided relevant contributions to the manuscript.

MdV, FV: Coordinators of the EU-Actifcare consortium. Designed the EU-Actifcare cohort study. Provided relevant contributions to the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors declare that no competing interests exist.

FUNDING SOURCES

The Actifcare project in Portugal had support from Fundação para a Ciência e a Tecnologia (FCT-JPND-HC-0001/2012), under the JPND (EU Joint Programme – Neurodegenerative Disease Research) initiative (JPND/2013/2).

This secondary analysis was funded by Fundação Ciência e Tecnologia, I.P. national support through CHRC (UIDP/04923/2020).

REFERENCES

1. GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health. 2022;7:e105-5.
2. Prince M, Wimo A, Guerchet M, Ali G, Wu YT, Prina M. World Alzheimer report 2015: the global impact of dementia. London: Alzheimer's Disease International; 2015.
3. Jönsson L, Tate A, Frisell O, Wimo A. The costs of dementia in Europe: An updated review and meta-analysis. Pharmacoeconomics. 2023;41:59-75.
4. Pires CL, Duarte N, Paúl C, Ribeiro O. Custos associados à prestação informal de cuidados a pessoas com demência. Acta Med Port. 2020;33:559-67.
5. Gonçalves-Pereira M, Verdelho A, Prina M, Marques MJ, Xavier M. How many people live with dementia in Portugal? A discussion paper of national estimates. P J Public Health. 2021;39:58-67.
6. Costa J, Borges M, Encarnação R, Firmino H, Gonçalves-Pereira M, Lindeza P, et al. Custo e carga da doença de Alzheimer nos idosos em Portugal. Sinapse. 2021;21:201-11.
7. Portugal. Office of Assistant Secretary of State and Health. Dispatch no. 5988/2018 - Estratégia da Saúde na Área das Demências. Diário da República, II Série, no. 116 (2018/06/19).
8. Balsinha C, Iliffe S, Dias S, Freitas A, Barreiros FF, Gonçalves-Pereira M. Dementia and primary care teams: obstacles to the implementation of Portugal's Dementia strategy. Prim Health Care Res Dev. 2022;23:e10.
9. Gonçalves-Pereira M, Leuschner A. Portugal. In: Burns A, Robert P, editors. Dementia care: international perspectives. Oxford: Oxford University Press; 2019:219-30.
10. Werner P, Mittelman MS, Goldstein D, Heinik J. Family stigma and caregiver burden in Alzheimer's disease. Gerontologist. 2012;52:89-97.
11. Stephan A, Bieber A, Hopper L, Joyce R, Irving K, Zanetti O, et al. Barriers and facilitators to the access to and use of formal dementia care: findings of a focus group study with people with dementia, informal carers and health and social care professionals in eight European countries. BMC Geriatr. 2018;18:131.
12. Kerpershoek L, de Vugt M, Wolfs C, Jelley H, Orrell M, Woods B, et al. Access to timely formal dementia care in Europe: protocol of the Actifcare (ACcess to Timely Formal Care) study. BMC Health Serv Res. 2016;16:423.
13. Gonçalves-Pereira M, Marques MJ, Balsinha C, Fernandes A, Machado A, Verdelho A, et al. Necessidades de cuidados e recurso aos serviços na demência: avaliação inicial da coorte Portuguesa no Estudo Actifcare. Acta Med Port. 2019;32:355-67.
14. American Psychiatric Association. DSM-IV-TR: manual de diagnóstico e estatística das perturbações mentais. 4ª ed. Lisboa: Climepsi Editores; 2002.
15. Morris JC. The clinical dementia rating (CDR): Current version and scoring rules. Neurology. 1993;43:2412-4.
16. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-98.
17. Reynolds T, Thornicroft G, Abas M, Woods B, Hoe J, Leese M, et al. Camberwell Assessment of Need for the Elderly (CANE). Br J Psychiatry. 2000;176:444-52.
18. Wimo A, Gustavsson A, Jonsson L, Winblad B, Hsu MA, Gannon B. Application of resource utilization in dementia (RUD) instrument in a global setting. Alzheimers Dement. 2013;9:429-35.
19. Miranda-Castillo C, Woods B, Orrell M. The needs of people with dementia living at home from user, caregiver and professional perspectives: a cross-sectional survey. BMC Health Serv Res. 2013;13:43.
20. Fernandes L, Gonçalves-Pereira M, Leuschner A, Martins S, Sobral M, Azevedo L, et al. Validation study of the Camberwell Assessment of Need for the Elderly (CANE) in Portugal. Int Psychogeriatr. 2009;21:94.
21. Logsdon RG, Gibbons LE, McCurry SM, Teri L. Assessing quality of life in older adults with cognitive impairment. Psychosom Med. 2002;64:510-9.
22. Bárrios H, Verdelho A, Narciso S, Gonçalves-Pereira M, Logsdon R, de Mendonça A. Quality of life in patients with cognitive impairment: validation of the Quality of Life–Alzheimer's Disease scale in Portugal. Int Psychogeriatr. 2013;25:1085-96.
23. Kaufer DI, Cummings JL, Ketchel P, Smith V, MacMillan A, Shelley T, et al. Validation of the NPI-Q, a brief clinical form of the neuropsychiatric inventory. J Neuropsychiatry Clin Neurosci. 2000;12:233-9.
24. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994;47:1245-51.
25. Lawton M, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. Nurs Res. 1969;19:278.
26. Brouwer WB, van Exel NJ, van Gorp B, Redekop WK. The CarerQol instrument: a new instrument to measure care-related quality of life of informal caregivers for use in economic evaluations. Qual Life Res.

2006;15:1005-21.
27. Voormolen DC, van Exel J, Brouwer W, Sköldunger A, Gonçalves-Pereira M, Irving K, et al. A validation study of the CarerQol instrument in informal caregivers of people with dementia from eight European countries. Qual Life Res. 2021;30:577-88.
28. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361-70.
29. Greene JG, Smith R, Gardiner M, Timbury GC. Measuring behavioural disturbance of elderly demented patients in the community and its effects on relatives: a factor analytic study. Age Ageing. 1982;11:121-6.
30. Kraijo H, Brouwer W, de Leeuw R, Schrijvers G, van Exel J. The perseverance time of informal carers of dementia patients: validation of a new measure to initiate transition of care at home to nursing home care. J Alzheimers Dis. 2014;40:631-42.
31. Hancock GA, Reynolds T, Woods B, Thornicroft G, Orrell M. The needs of older people with mental health problems according to the user, the carer, and the staff. Int J Geriatr Psychiatry. 2003;18:803-11.
32. Orrell M, Hancock GA, Liyanage KC, Woods B, Challis D, Hoe J. The needs of people with dementia in care homes: the perspectives of users, staff and family caregivers. Int Psychogeriatr. 2008;20:941-51.
33. Richters A, Melis RJ, van Exel NJ, Olde Rikkert MG, van der Marck MA. Perseverance time of informal caregivers for people with dementia: construct validity, responsiveness and predictive validity. Alzheimers Res Ther. 2017;9:26.
34. O'Shea E, Hopper L, Marques M, Gonçalves-Pereira M, Woods, B, Jelley H, et al. A comparison of self and proxy quality of life ratings for people with dementia and their carers: a European prospective cohort study. Aging Ment Health. 2020;24:162-70.
35. King D, Farina N, Burgon C, Feeney Y, Berwald S, Bustard E, et al. Factors associated with change over time in quality of life of people with dementia: longitudinal analyses from the MODEM cohort study. BMC Geriatr. 2022;22:469.
36. Hutchinson C, Worley A, Khadka J, Milte R, Cleland J, Ratcliffe J. Do we agree or disagree? A systematic review of the application of preference-based instruments in self and proxy reporting of quality of life in older people. Soc Sci Med. 2022;305:115046.6
37. Hutchinson C, Whitehurst DG, Crocker M, Lay K, Engel L, Ratcliffe J. Measuring quality of life in residential aged care using the EQ-5D-5L: a cross-sectional study on the impact of cognition level and proxy perspective on interrater agreement. Health Soc Care Community. 2023;2023:1-11.
38. Tapia Muñoz T, Slachevsky A, León-Campos MO, Madrid M, Caqueo-Urízar A, Rohde GC, et al. Predictors of unmet needs in Chilean older people with dementia: a cross-sectional study. BMC Geriatr. 2019;19:106.
39. Horik JO, Collins R, Martyr A, Henderson C, Jones RW, Knapp M, et al. Limited receipt of support services among people with mild-to-moderate dementia: Findings from the IDEAL cohort. Int J Geriatr Psychiatry. 2022;37:10.1002/gps.5688.8
40. Schmachtenberg T. Structures for the care of people with dementia: a European comparison. BMC Health Serv Res. 2022;22:1372.
41. Jessen F, Georges J, Wortmann M, Benham-Hermetz S. What matters to patients with Alzheimer's disease and their care partners? Implications for understanding the value of future interventions. J Prev Alzheimers Dis. 2022;9:550-5.
42. Ribeiro O, Teixeira L, Duarte N, Azevedo MJ, Araújo L, Barbosa S, et al. Versão Portuguesa da escala breve de redes sociais de Lubben (LSNS-6). Kairós-Gerontol. 2012;15:217-34..
43. Lubben J, Blozik E, Gillmann G, Iliffe S, von Renteln Kruse W, Beck JC, et al. Performance of an abbreviated version of the Lubben social network scale among three European community-dwelling older adult populations. Gerontologist. 2006;46:503-13.
44. Ulstein I, Wyller TB, Engedal K. The relative stress scale, a useful instrument to identify various aspects of carer burden in dementia? Int J Geriatr Psychiatry. 2007;22:61-7.
45. Bruvik FK, Ulstein ID, Ranhoff AH, Engedal K. The effect of coping on the burden in family carers of persons with dementia. Aging Ment Health. 2013;17:973-8.
46. Borges-Machado F, Barros D, Ribeiro Ó, Carvalho J. The effects of COVID-19 home confinement in dementia care: physical and cognitive decline, severe neuropsychiatric symptoms and increased caregiving burden. Am J Alzheimer's Dis. 2020;35:153331752097672.
47. Cheng ST. Dementia caregiver burden: a research update and critical analysis. Curr Psychiatry Rep. 2017;19:64.
48. Gonçalves-Pereira M, Carmo I, Silva JA, Papoila AL, Mateos R, Zarit SH. Caregiving experiences and knowledge about dementia in Portuguese clinical outpatient settings. Int Psychogeriatrics. 2010;22:270-80.
49. Røsvik J, Michelet M, Engedal K, Bieber A, Broda A, Gonçalves-Pereira M, et al. Interventions to enhance access to and utilization of formal community care services for home dwelling persons with dementia and their informal carers. A scoping review. Aging Ment Health. 2020;24:200-11.
50. Balsinha C, Marques MJ, Gonçalves-Pereira M. A brief assessment unravels unmet needs of older people in primary care: a mixed-methods evaluation of the SPICE tool in Portugal. Prim Health Care Res Dev. 2018;19:637-43.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

EDITORIAL
PERSPECTIVA
ARTIGO ORIGINAL
PROTOCOLOS
PUBLICAÇÕES CURTAS
ARTIGO DE REVISÃO
CASO CLÍNICO
IMAGENS MÉDICAS
NORMAS ORIENTAÇÃO
CARTAS

Validation of the Bipolar Recovery Questionnaire for the Portuguese Population: Recovery and Predictors in People with Bipolar Disorder

Validação do Questionário de Recuperação Bipolar para a População Portuguesa: Recuperação e Preditores em Pessoas com Perturbação Bipolar

Julieta AZEVEDO✉[1,2,3], Diogo CARREIRAS[1,4], Raquel GUIOMAR[1], Maria João MARTINS[1,2,5], António MACEDO[2,6,7], Paula CASTILHO[1]
Acta Med Port 2024 May;37(5):368-378 ▪ https://doi.org/10.20344/amp.20790

ABSTRACT

Introduction: The paradigm in mental health care is progressively moving towards a recovery-focused perspective. Thus, there is a need for validated instruments to measure recovery in bipolar disorder (BD). The Bipolar Recovery Questionnaire (BRQ) is the most used instrument to assess it. The aim of this study was to translate and perform a cross-cultural adaptation of the BRQ to European Portuguese (PT-PT) and to explore further associations of recovery with sociodemographic and emotional regulation, as well as recovery predictors to inform future research and clinical practice.

Methods: The BRQ was forward-translated and back-translated until a consensus version was found, and a test-retest design was used to assess temporal stability. Participants were recruited in public hospitals and organizations supporting people with BD, either referred by their psychiatrists or psychologists or through self-referral. Eighty-eight individuals diagnosed with BD were recruited to complete a battery of Portuguese-validated self-report questionnaires to assess recovery (BRQ), clinical mood symptoms (Hospital Anxiety and Depression Scale), affect (Positive and Negative Affect Scale), well-being (brief Quality of Life for Bipolar Disorder; Satisfaction with Life Scale) and emotion regulation (Difficulties in Emotion Regulation Scale).

Results: The BRQ showed excellent internal consistency with a Cronbach alpha of 0.92, and test-retest exhibited good reliability (r = 0.88). Construct validity was confirmed through/by positive and moderate correlations with quality of life (QoL; r = 0.58) and positive affect (r = 0.52), and negative moderate correlations with depression (r = -0.64), and negative affect (r = -0.55). Both satisfaction with life (β = 0.38, p = 0.010) and recovery (β = 0.34, p = 0.022) impacted quality of life, supporting the BRQ's incremental validity. Depressive symptoms and emotion dysregulation accounted for 51% of its variance.

Conclusion: The BRQ is a valid and reliable instrument to measure recovery in people with BD in the Portuguese population and is suitable for both clinical and research contexts.

Keywords: Bipolar Disorder; Psychometrics; Recovery of Function; Reproducibility of Results; Surveys and Questionnaires; Translations

RESUMO

Introdução: O paradigma da saúde mental está a evoluir progressivamente para uma perspetiva centrada na recuperação. Assim, são necessários instrumentos validados para medir a recuperação na perturbação bipolar (PB). O Questionário de Recuperação Bipolar (BRQ) é o instrumento mais utilizado para avaliar este construto. O objetivo deste estudo foi traduzir e realizar uma adaptação transcultural do BRQ para o português europeu (PT-PT), explorar associações adicionais da recuperação com características sociodemográficas e regulação emocional, e investigar preditores de recuperação para contribuir para estudos e práticas clínicas futuras.

Métodos: Foi feita a tradução do BRQ para português e retroversão, chegando-se a uma versão consensual entre os tradutores, e um desenho teste-reteste foi usado para avaliar a estabilidade temporal do instrumento. Os participantes foram recrutados em hospitais públicos e organizações de apoio a pessoas com PB pelos seus psiquiatras, psicólogos ou por autorreferenciação. Oitenta e oito pessoas com diagnóstico de PB preencheram uma bateria de questionários de autorresposta para avaliar a recuperação (BRQ), sintomas clínicos de humor (Escala Hospitalar de Ansiedade e Depressão), afeto (Escala de Afeto Positivo e Negativo), bem-estar (Qualidade de Vida Breve para Perturbação Bipolar; Escala de Satisfação com a Vida) e regulação emocional (Escala de Dificuldades na Regulação Emocional).

Resultados: O BRQ apresentou uma excelente consistência interna, com um alfa de Cronbach de 0,92, e o teste-reteste apresentou uma boa fiabilidade (r = 0,88). A validade do constructo foi confirmada através das correlações positivas e moderadas com a qualidade de vida (r = 0,58) e afeto positivo (r = 0,52), e correlações negativas moderadas com a depressão (r = -0,64) e o afeto negativo (r = -0,55). Tanto a satisfação com a vida (β = 0,38, p = 0,010) como a recuperação (β = 0,34, p = 0,022) tiveram impacto na qualidade de vida, apoiando a validade incremental do BRQ. Os sintomas depressivos e a desregulação emocional foram responsáveis por 51% da sua variância.

Conclusão: O BRQ é um instrumento válido e fiável para medir a recuperação em pessoas com PB na população portuguesa, sendo adequado para contextos clínicos e de investigação.

Palavras-chave: Inquéritos e Questionários; Perturbação Bipolar; Psicometria; Qualidade de Vida; Recuperação de Função Fisiológica; Reprodutibilidade dos Testes; Traduções

INTRODUCTION

Bipolar disorder (BD) is characterized by fluctuations in mood states and energy that vary in frequency and severity, affecting around 2.4% of the global population.[1] This poses substantial challenges for individuals, their families, and

1. Center for Research in Neuropsychology and Cognitive and Behavioral Intervention (CINEICC). Faculdade de Psicologia e de Ciências da Educação. Universidade de Coimbra. Coimbra. Portugal.
2. Institute of Psychological Medicine (IPM). Faculdade de Medicina. Universidade de Coimbra. Coimbra. Portugal.
3. School of Psychology and Sport Science. Bangor University. Bangor. United Kingdom.
4. Instituto Superior Miguel Torga. Coimbra. Portugal.
5. Serviços Médicos Universitários. Universidade de Coimbra. Coimbra. Portugal.
6. Coimbra Institute for Biomedical Imaging and Translational Research (CIBIT). Coimbra. Portugal.
7. Centro Hospitalar e Universitário de Coimbra (CHUC). Coimbra. Portugal.

✉ **Autor correspondente:** Julieta Azevedo. julietazevedo@gmail.com

Recebido/*Received*: 09/10/2023 - **Aceite/*Accepted*:** 11/03/2024 - **Publicado *Online*/*Published Online*:** 15/04/2024 - **Publicado/*Published*:** 02/05/2024

healthcare systems worldwide due to its chronic and recurrent nature,[2] and BD has been associated with functional and cognitive impairment and a reduction in quality of life.[3,4] Traditionally, the primary goal of treatment has revolved around reducing symptoms and preventing relapses, with the aim of achieving symptomatic remission and functional stability.[5,6] However, a growing body of evidence suggests that this symptom-centered approach may not fully address the complexities and holistic needs of individuals living with BD[7] and people with BD have shown their dissatisfaction with this model, exhibiting interest in taking control of their lives rather than returning to the elusive state of the premorbid level of functioning.[8] According to Merikangas *et al*,[1] BD is responsible for the loss of more disability-adjusted life-years than all forms of cancer or major neurologic conditions, which has a marked effect on the overall quality of life (QoL) of both patients and their families.[9]

Consequently, mental health is witnessing a paradigm shift towards embracing a personal recovery-focused model, which encompasses pursuing a satisfying and meaningful life, even when clinical symptomatology is present.[10,11] This concept has become increasingly important and is seen as a desired outcome for mental health care programs in severe mental disorders, specifically for BD.[8] Recovery is described as a personal journey of coping with mental illness, which involves a series of subjective experiences and, therefore, is based on the person's empowerment, self-directedness and perception of competence to deal with their difficulties.[12] Hence, considering the significant impact that BD has on various aspects of daily life (i.e., work productivity, interpersonal relationships, etc.), achieving recovery is essential and it should focus on fostering resilience, enhancing self-management skills, and promoting quality of life and well-being and improving inter-episodic residual symptoms to enhance global functioning.[13] Thornton and Lucas[14] made an effort to clarify the model of recovery, by showing an integrative view, where the goal of recovery is determined through the conception of a life to be valued and hoped for by the subject concerned, and not a normative and standardized view of recovery for all.

According to a recent systematic review of personal recovery instruments in BD,[8] there are only two recovery-focused scales specifically validated for BD: the Questionnaire of Personal Recovery (QPR) and the Bipolar Recovery Questionnaire (BRQ). The QPR was initially a 22-item questionnaire with two subscales (intrapersonal and interpersonal recovery) developed from service users' accounts of recovery from psychosis, recruited in the National Health Service (United Kingdom).[15] This questionnaire was then reduced to a one-factor solution with 15 items,[16] with a sample of 335 participants with a schizophrenia spectrum diagnosis, demonstrating adequate internal consistency (α = 0.93) and test-retest reliability (r = 0.70). The QPR was later applied to a wider sample with different mental health disorders, including 61 participants with BD,[17] and its validity to use with BD was confirmed by Kraiss and collaborators,[18] with a sample of 102 people diagnosed with BD, even though there were no reported adaptations to the questionnaire. The QPR is answered on a 5-point Likert scale, ranging from 0 (disagree strongly) to 4 (agree strongly), with higher scores indicating more personal recovery.

The second, the BRQ,[19] is a 36-item questionnaire, and its items were generated based on a review of the literature and an earlier qualitative study with people with BD, which explored personal definitions, experiences, and accounts of recovery. Its psychometric properties were assessed in a study with 60 participants, the majority with a diagnosis of bipolar disorder I (87%) and the remainder with bipolar disorder II (13%). The study reported that BRQ had a good to excellent consistency (α = 0.875) and excellent test-retest reliability (α = 0.866; p < 0.001).[19] The BRQ has been used widely to measure recovery improvements in BD after undergoing treatment, with all the intervention studies reported in the aforementioned systematic review using the BRQ.[8] So far, this is still the only instrument specifically constructed for people with BD. It asks individuals to rate their level of agreement with each of the 36 items in the previous week, going from 0 (strongly disagree) to 100 [strongly agree; on a 100 mm visual analogue scale (VAS)]. Due to having a small sample size (n = 60), the authors did not perform a factor analysis of the BRQ and recommended using it as a single-factor scale.

As far as we know, there is no instrument available in European Portuguese (PT-PT) to measure recovery in people with BD, which further contributes to a lack of data on this topic, particularly in middle and low-income countries.

The aim of this study was to translate and validate BRQ to PT-PT, analyze its psychometric properties, and explore recovery predictors that can inform research and clinical practice.

METHODS

Ethics and study design

This research is part of a broader project that aims to improve the assessment and intervention for people in the bipolar spectrum (ref.: SFRH/BD/130116/2017). The project was approved by the Faculty of Psychology and Educational Sciences of the University of Coimbra Ethics Committee and received further approval from the hospitals and organizations involved in the study [i.e., Coimbra Hospital and University Centre, Leiria Hospital Centre, West Hospital Centre, Association for the Support of Depressive and Bipolar Patients (ADEB)].

This was a two-phase study where 1) the full process of

translation and cross-cultural adaptation of the BRQ from English to PT-PT was performed following recommendations for psychological tests, and 2) we carried out an observational, prospective validation study, including patients with bipolar disorder, that assessed the psychometric properties of the PT-PT version of the BRQ and explored BD recovery predictors. A comprehensive analysis was conducted, including descriptive statistics of the items, qualitative feedback on the items, evaluation of construct and incremental validity, examination of Cronbach's alpha, and a test-retest analysis (with data collected in a second visit, six weeks after the baseline). Participants gave written informed consent, data confidentiality was assured, and clear instructions were provided about the General Data Protection Regulations (GDPR).

Bipolar Recovery Questionnaire translation and cross-cultural adaptation

Permission to translate and validate the BRQ from English to PT-PT was granted by Lancaster University, which states that this instrument is free to use and translate. The forward translation to Portuguese was conducted by three independent Portuguese native speakers fluent in English (two clinical psychologists and one psychiatrist and researcher), following the guidelines that encourage at least two independent translators.[20] The two versions were compared, and the discrepancies were discussed between the translators and the research team, and a consensus was reached. A back-translation was then made from the agreed version by two different members of the research team who did not take part in the previous discussion, and this was compared with the original version, which was deemed similar. Finally, the last version was discussed with experienced psychiatrists (n = 3) and psychologists (n = 2) in dealing with people with BD, inquiring them about its clarity, language adequacy and comprehensibility. Additionally, five patients with this disorder were asked to fill in the questionnaire in a one-to-one in person session, and asked questions according to the principles of cognitive interviewing to assess translated questionnaires (i.e., common standardized questions regarding clarity, adequacy, language and type of response of the questionnaire, and allowing for flexibility and additional questions to clarify any identified problems). The feedback was positive, with all the participants considering it clear, coherent, and overall easy to comprehend, reporting the visual analogic scale (from 0 - 100) in particular as a strong point, and easy to understand. The BRQ scale for psychometric investigation asks participants to rate their level of agreement (on a visual analogue scale), in the last week, with 36 items assessing their sense of recovery (same as the original) going from 0 to 100 (with labels across the VAS: 0 - 'strongly disagree', 25 - 'disagree', 75 - 'agree' and 100 - 'strongly agree'), with the total score varying from 0 to 3600. The BRQ asks participants to report their agreement with sentences such as "I struggle to make sense of the experiences I have had".

The total BRQ score is calculated by summing individual scores of all items of which 12 are reverse scored. Higher BRQ total scores indicate higher self-rated sense of recovery.

Procedures and inclusion/exclusion criteria

Recruitment took place in three public hospitals via clinician referrals, the ADEB and through online advertisement and flyer distribution in outpatient services (allowing self-referral) and took place between December 2019 and January 2021.The study was presented to all the healthcare professionals at the clinical sites and the ADEB, the inclusion and exclusion criteria were explained, and they were asked to refer patients. Additionally, the ADEB disseminated our study in their newsletter and contributed with referrals. All patients included in this study were outpatients when they filled in the questionnaires, even though the referral and initial contact could be established while they were inpatients.

After being informed about the study's aims and providing written informed consent, all participants were invited to attend a clinical interview assessment to confirm the diagnosis, which could occur in person or online. This study was initially conceptualized to be mainly recruited in person. However, there was a six-month interruption of the in-person recruitment due to COVID-19 restrictions, which led to assessments and questionnaires moving mainly online. When participants could not attend the clinical interview (in person or online in a video call), they would still be included in the study as long as they had a well-established diagnosis made by their psychiatrist (for more than two years). To corroborate the diagnosis, these participants had to fill out an additional screening tool, the Mood Disorder Questionnaire (MDQ; n = 10) and meet the threshold for BD suggested by the authors.[21] All participants answered sociodemographic questions and a battery of self-report questionnaires, which were sent either online (using the Lime Survey platform; https://limesurvey.fpce.uc.pt/) or provided in paper format (ratio 70:30, respectively). Participants who responded in paper format were all recruited before the COVID-19 restrictions.

The inclusion criteria consisted of having a diagnosis of bipolar and related disorders, being aged between 18 and 65, and being a Portuguese-speaking individual. Exclusion criteria included acute manic episode, substance-induced bipolar or related disorder, psychotic symptoms during the interview, and significant cognitive deterioration (described by the clinician or identified during the clinical interview).

Measures

Clinician rated

The Clinical Interview for Bipolar Disorders (CIBD)[22] is a Portuguese semi-structured comprehensive assessment tool for BD and related disorders appropriate for the diagnosis of bipolar disorders and assessment of current mood episodes in adults based on the DSM-5-TR criteria.

Self-reported questionnaires

All the instruments used in this section have been validated for the Portuguese population.

The Mood Disorder Questionnaire (MDQ)[21,23] is a 15-item self-reported screening instrument that can be used to identify individuals who are most likely to have bipolar disorder. The internal reliability for the MDQ was strong in the original study (Cronbach's alpha = 0.88), and an acceptable reliability was found in the Portuguese version (α = 0.76).

The Brief Quality of Life in Bipolar Disorder – short version (Brief QoL.BD)[24,25] is a self-reported quality of life measure for people with BD, comprising 12 items assessed on a standard five-point Likert response scale (strongly disagree – strongly agree). Each item measures a domain of quality of life (physical, sleep, mood, cognitive, leisure, social, spirituality, finances, household, self-esteem, independence, and identity). The reliability of the Portuguese version was good, with an alpha of 0.89. The measure QoL.BD was used to assess construct and incremental validity.

The Positive and Negative Affect Scale (PANAS)[26,27] is a self-reported questionnaire divided into two subscales: PANAS-PA and PANAS-NA (positive and negative affect, respectively). The reliability of the Portuguese version (αNA = 0.89 and αPA = 0.86) was identical to the original version (αNA = 0.87 and αPA = 0.88). It is used for construct validity.

The Hospital Anxiety and Depression Scale (HADS)[28,29] assesses emotional changes in a hospital setting, with two subscales: HADS-ANX and HADS-DEP (anxiety and depression, respectively). The Portuguese version achieved values of α = 0.76 for anxiety subscale and α = 0.80 for depression.

Satisfaction With Life Scale (SWLS)[30,31] measures subjective well-being through five items, measured on a seven-point Likert-type scale. The original scale showed an α = 0.87 and the Portuguese version an α = 0.89. This questionnaire was used for incremental validity.

The Difficulties in Emotional Regulation Scales (DERS)[32,33] is a self-reported questionnaire that assesses difficulties in emotion regulation, providing a total score and six subscales: nonacceptance of emotional responses, difficulty engaging in goal-directed behavior, impulse control difficulties, lack of emotional awareness, limited access to emotion regulation strategies, and lack of emotional clarity. The 36 items are rated on a five-point Likert scale ranging between 1 (almost never) and 5 (almost always). The Portuguese version of the scale presents excellent reliability (α = 0.92).

Data analyses and psychometric validation

Statistical analyses were done using the SPSS software version 22 (Statistical Package for the Social Sciences: IBM Corp.). Normality of data was tested with the Kolmogorov-Smirnov test and examining the skewness (Sk) and kurtosis (Ku) values (normality assumed for Sk < 3 and Ku < 8; Kline, 2005)[34] and no violations were found. Outliers were examined considering the boxplot diagram, and one outlier was removed. Missing data were handled using mean-score imputation (missings < 1%) to evaluate reliability and construct validity. Cronbach's alpha coefficient was calculated as the measure of internal reliability with an acceptable reference value of 0.70, good from 0.80 to 0.89, and excellent above 0.90.[35]

The construct validity was evaluated via Pearson's correlations, considering the correlation coefficients as weak from 0.10 to 0.39, moderate from 0.40 to 0.69, and strong above 0.70.[36] A subsample was used for this analysis, which included the participants that had filled in all the entire battery of tests. We correlated the BRQ with Brief QoL.BD (quality of life), PANAS (positive and negative affect) and HADS (depression) for convergent validity. For incremental validity, a regression model used the BRQ as dependent variable, and the SWLS (satisfaction with life) and Brief QoL.BD (quality of life) as independent variables.

To explore the association between the BRQ and sociodemographic and clinical variables, we needed to recode the work situation variable into two groups: working (employed) and not working (unemployed and on medical leave).

The BRQ predictors were explored through several multiple regression analyses (performed sequentially) to assess the variance explained by psychological distress symptoms (anxiety and depressive symptoms - HADS), positive and negative affect (PANAS) and difficulties in regulating emotions (DERS). Assumptions were verified, and homoscedasticity was assessed by visual inspection of a plot of studentized residuals *versus* unstandardized predicted values. The multicollinearity assumption was tested using Variance Inflation Factor (VIF) values, with VIF > 10 considered problematic.[37] When assessing multicollinearity, anxiety violated this assumption and was thus removed from the model. The final multiple regression model included the significant predictors that respected the assumptions for multiple regression and significantly predicted the outcome variable.

Participants

The participants were 88 people with a disorder from the

BD spectrum, of which 59 were women (67%), and 29 were men (33%). The age of participants ranged between 20 and 65 years (M = 43.74 ± 11.17). Most participants were employed (64.7%) and 13.6% were on medical leave. Fifty-two participants (59.1%) had a diagnosis of bipolar disorder I, 25 were diagnosed with bipolar disorder II (28.4%), one was diagnosed with other specified bipolar and related disorders (1.1%), and 10 were diagnosed with bipolar without having their type specified (11.4%). A full description of participant demographics and clinical features is reported in Table 1.

RESULTS

Descriptive statistics

The mean, standard deviation, item-total correlation and alpha if item deleted are presented for all BRQ items in Table 2.

Reliability and temporal stability

The BRQ showed excellent reliability, with Cronbach's alpha of 0.92 for the total score. To examine test-retest reliability, 31 participants agreed to complete the BRQ a second time (six weeks later). The test-retest correlation suggested good reliability (r = 0.88, p < 0.001).

Construct validity

Convergent validity was explored through Pearson's correlations displayed in Table 3, with the BRQ showing a negative moderate correlation with depression and negative affect and a positive moderate correlation with positive affect and quality of life.

Incremental validity

A hierarchical regression predicting quality of life was

Table 1 – Sample characteristics (n = 88)

	Sex (n)		**Total** (n / %)	
Diagnosis	♀	♂	Total	%
Bipolar I Disorder	36	16	52	59.1
Bipolar II Disorder	15	10	25	28.4
Other Specified Bipolar and Related Disorder	1	0	1	1.1
Diagnosed with Bipolar Disorder[1]	7	3	10	11.4
	n		%	
Ongoing treatment				
Psychiatric	80		90.9	
Psychological intervention	35		39.8	
Civil status				
Single	36		40.9	
Married / Nonmarital partnership	35		39.8	
Divorced / Separated	17		19.3	
Living area				
Urban	59		67.0	
Rural	29		33.0	
Work situation				
Student	7		7.9	
Employed (and working)	37		42.0	
On medical leave	12		13.6	
Retired	7		7.9	
Unemployed	16		18.2	
Other	9		10.2	
	Mean		**SD**	
Age of onset	24.2		8.23	
Years of education	14.54		3.57	
Age	43.74		11.17	

n: frequency; %: percentage; ♀: women; ♂: men; SD: standard deviation
1: Participant diagnosed and referred by their psychiatrist without specifying the type – filled out self-reported questionnaires

Table 2 – Item properties of the Bipolar Recovery Questionnaire (n = 88)

Item	Mean	SD	Correlation item-total	α if item deleted
1. I struggle to make sense of the experiences I have had*	49.55	26.99	0.416	0.917
2. I have the resources to effectively manage my health	62.94	24.20	0.492	0.916
3. I am content with who I am as a person	52.47	28.25	0.727	0.913
4. I have little control over my mood*	48.98	29.63	0.340	0.918
5. I avoid taking on challenges in life that matter to me*	53.23	25.85	0.475	0.916
6. I see recovery as a lifelong process	73.70	21.60	0.222	0.919
7. I think (...) compared with when they first occurred	74.58	20.03	0.297	0.918
8. I can access the help I need in order to stay well	69.35	25.98	0.504	0.916
9. My experiences have made me the person I am today	76.43	22.82	0.483	0.916
10. I recognise when (...) that aren't good for my well-being	66.18	24.87	0.571	0.915
11. I am able to engage (...) personally meaningful to me	54.70	26.60	0.625	0.914
12. Recovery means (...) my mental health problems*	63.39	27.59	0.066	0.922
13. I am unsure (...) of the experiences I have had*	44.73	27.96	0.374	0.918
14. I feel in control of the things that happen in my life	47.83	24.06	0.606	0.915
15. I am productive in the things in life I engage in	60.33	26.00	0.618	0.914
16. I depend on others to maintain my own well-being*	45.95	27.81	0.407	0.917
17. I feel confident (...) in the things in life that interest me	53.44	25.56	0.712	0.913
18. I can have mood experiences and still get on with my life	61.75	22.73	0.507	0.916
19. I can see where (...) I have had have come from	64.97	22.49	0.452	0.916
20. I am able to decide (...) to maintain my well-being	68.59	21.85	0.483	0.916
21. I get little personal satisfaction (...) I am involved in*	51.33	26.62	0.542	0.915
22. I have the knowledge (...) for my mental health	74.64	20.21	0.532	0.916
23. I am unhappy with the person I have become*	57.91	29.68	0.600	0.914
24. I sometimes let my mood (...) important tasks to do*	36.56	23.33	0.354	0.918
25. The high standards I set (...) fluctuations in my mood	51.77	26.48	0.370	0.918
26. I play a central role in maintaining my own well being	77.66	19.40	0.480	0.916
27. I have the ability to achieve my goals in life	58.24	26.63	0.737	0.913
28. My ability to make (...) my friends and family	62.59	30.06	0.419	0.917
29. I find it hard to engage (...) that are valuable to me*	45.94	27.64	0.554	0.915
30. I can still be in recovery (...) mood episodes in the future	73.72	17.78	0.486	0.916
31. Understanding where (...) from help me manage them	78.47	16.83	0.405	0.917
32. I have little control over the (...) decisions in my life*	63.41	25.16	0.639	0.914
33. I am able to engage (...) that are valuable to wider society	55.72	27.07	0.540	0.915
34. The knowledge I have (...) me to look after myself	71.64	21.26	0.589	0.915
35. The activities I do make a difference to others	58.88	25.08	0.458	0.916
36. Being in recovery (...) well in every aspect of my life*	56.63	28.07	-0.047	0.923

M: mean; SD: standard deviation [*M*/SD are from a visual analogue scale (VAS) varying from 0: strongly disagree to 100: strongly agree]; α: Cronbach's alpha
*: reversed items

conducted to examine how much the BRQ added to the information provided by existing variables (satisfaction with life and positive affect) in assessing quality of life. In the first step, satisfaction with life and positive affect were entered as predictors. This model was significant, explaining 51% of the quality of life's variance ($F_{(2, 41)} = 23.09$, $p < 0.001$). In a second step, recovery was also entered as a predictor and the F change was significant, attaining a model that

Table 3 – Pearson's correlations between variables (n = 60)

	1	2	3	4	5
1. Recovery (BRQ)	1	-	-	-	-
2. Depression (HADS-DEP)	-0.64**	1	-	-	-
3. Positive affect (PANAS-PA)	0.52**	-0.70**	1	-	-
4. Negative affect (PANAS-NA)	-0.55**	0.60**	-0.48**	1	-
5. Quality of life (Brief QoL-BD)	0.58**	-0.67**	0.57**	-0.54**	1

**: $p < 0.01$
HADS: Hospital Anxiety and Depression Scale; PANAS: Positive and Negative Affect Scale; Brief QoL-BD: Brief Quality of Life in Bipolar Disorder – short version; BRQ: Bipolar Recovery Questionnaire; DERS: Difficulties in Emotional Regulation Scale

explained 56% of quality of life ($F_{(3, 40)} = 19.02$, $p < 0.001$). In this final model, positive affect did not have a significant predictive effect ($\beta = 0.17$, $p = 0.211$). In contrast, satisfaction with life ($\beta = 0.38$, $p = 0.010$) and recovery ($\beta = 0.34$, $p = 0.022$) impacted quality of life, suggesting the incremental value of the BRQ.

Association with sociodemographic variables and other clinical outcomes

The BRQ presented non-significant correlations with age ($r = -0.14$, $p = 0.201$), years of education ($r = 0.02$, $p = 0.887$) and age of onset ($r = -0.02$, $p = 0.845$). Moreover, no differences in the BRQ ($t_{(85)} = -1.724$, $p = 0.088$) were found between male ($M = 2266.38$, $SD = 435.83$) and female ($M = 2096.17$, $SD = 433.09$) participants and civil status ($F_{(84, 2)} = 2.302$, $p = 0.351$). Regarding the work situation, two groups were defined as working (employed) and not working (unemployed and on medical leave), and differences were not found ($t_{(68)} = 1.661$, $p = 0.101$). Participants with current psychological treatment ($M = 2068.25$, $SD = 409.10$) were found to have marginally lower non-significant BRQ scores ($t_{(75)} = 2.176$, $p = 0.053$) than participants with no current psychological treatment ($M = 2283.48$, $SD = 450.23$).

Furthermore, regarding clinical outcomes, the BRQ showed negative moderate correlations with depression ($r = -0.64$), and difficulties in regulating emotions ($r = -0.68$). All correlations were statistically significant ($p < 0.001$). The correlations between the BRQ and DERS subscales were all significant and negative, with r ranging between -0.33 and -0.63 ($p < 0.001$; Table 4).

Predictors of recovery in bipolar disorder

Multiple linear regression was performed to explore the predictors of the BRQ, including positive and negative affect, depressive symptoms and difficulties regulating emotions. A final model established that depressive symptoms ($\beta = -0.374$, $p = < 0.001$) and difficulties in regulating emotions ($\beta = -0.484$, $p = < 0.001$) were significant predictors of recovery, accounting for 54.7% of the BRQ's variance ($F_{(2, 44)} = 28.747$, $p = 0.003$).

DISCUSSION

Traditionally, treatment success assessment focuses primarily on symptom reduction and relapse prevention.[11] More recently, greater attention has been given to the recovery perspective regarding functionality, life satisfaction and quality regardless of the presence or absence of psychopathological symptoms.[8,38] The PT-PT adaptation and validation of the BRQ intended to fill an existing gap in the assessment of recovery in BD in Portugal. In the current study, the BRQ presented good psychometric properties, indicating excellent internal consistency and good test-retest reliability. These results concur with previous research on the original version of the BRQ, which also showed good internal consistency and reliability over time.[19] Some particularly low item-total correlations were found for items 12 and 36, which raises questions about their relevance for the overall measure of recovery. However, both items were kept due to their qualitative importance regarding recovery perception, covering beliefs about recovery [the final version of the questionnaire is available as an Appendix (Appendix 1:

Table 4 – Correlations between BRQ and DERS subscales (n = 64)

DERS subscales	BRQ
Non-acceptance of emotional responses	-0.57**
Difficulty engaging in goal-directed behaviour	-0.42**
Impulse control difficulties	-0.52**
Lack of emotional awareness	-0.33**
Limited access to emotion regulation strategies	-0.63**
Lack of emotional clarity	-0.53**

**: $p < 0.01$
BRQ: Bipolar Recovery Questionnaire; DERS: Difficulties in Emotion Regulation Scale

https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/20790/15391)]. Jones *et al*[19] meticulously improved the BRQ, refining it based on feedback from clinical staff, researchers, and service users. In the current investigation, the BRQ also received positive feedback regarding clarity and usability from both participants and clinicians.

The correlation results suggested that recovery was associated with fewer depressive symptoms and negative affect and increased positive affect and quality of life in the expected direction. These results support construct validity and concur with previous research that reported negative associations between recovery and psychopathological symptoms[39,40] and positive associations with quality of life.[3] The BRQ's correlations with positive affect and both quality and satisfaction with life are consistent with the conceptual vision of recovery as a process that promotes a rich and fulfilling life, even in the presence of symptoms.[8] These results are consistent with the importance of recovery in mental health care programs, as suggested by a recent systematic review.[41]

The incremental validity analysis showed that the BRQ significantly enhanced the hierarchical regression model's capacity to explain the quality-of-life variance, adding 5% explanatory power to the previous predictors (life satisfaction and positive affect). This result suggests that focusing on the individual perceptions of recovery and potentially fostering more adaptive ways to cope with the disorder significantly impacts the quality of life in BD. This further supports the idea that targeting symptom reduction is not enough to increase the quality of life of people with BD, as suggested by a systematic literature review,[42] and that strategies that might increase and facilitate their recovery are fundamental. Furthermore, studies found significant quality of life impairments even when the participants were clinically euthymic,[4] as well as difficulties in regulating and accessing emotion regulation strategies, suggesting their inclusion in adjunct psychological treatment.[43]

Considering the lack of sociodemographic information regarding people with BD in Portugal, this study additionally explored the association between sociodemographic factors and recovery to inform future research and clinical work. The results suggested no significant associations between age, years of education and recovery. However, previous studies found different results.[44,45] A possible explanation might be related to the differences in the sample characteristics and cultural differences, which might lead to distinct results. Future studies with a larger Portuguese population can help clarify if these differences prevail. Moreover, there were no significant differences between sex in recovery scores. While previous studies have suggested that BD presentation might differ between genders, mentioning men's higher risk of a comorbid substance abuse disorder and women presenting higher rates of mania episode-related hospitalisations,[46] there is no indication that the patient's gender impacts overall recovery or treatment response.[47]

The recovery levels of people with and without current psychological treatment seemed similar, albeit with a propensity for individuals undergoing treatment to display slightly lower scores. This might reflect that people seeking psychological treatment are the ones facing greater challenges and obstacles in their journey towards recovery. In this study, we did not control for the modality, duration, and frequency of the psychological interventions, hindering further interpretation of this result. Therefore, future studies should collect information on the presence/absence of psychological interventions and carefully study or control their impact on the overall results.

Additionally, the current study explored the associations of psychopathological and clinical outcomes with recovery. This study also shed light on the impact of emotional regulation and affect-related constructs (i.e., dysregulation, positive and negative affect) in the recovery of people with BD, pointing to the importance of emotional regulation in people's perception and confidence in the recovery process (BRQ). The two subscales of the DERS that had the strongest associations with recovery were "limited access to emotional regulation strategies" and "non-acceptance of emotional responses", which is in line with previous studies that confirmed the association between emotion regulation and recovery.[39,48] These associations underline the importance of emotion regulation strategies and acceptance of emotions for recovery. These outcomes may inform potential targets for future clinical intervention studies that are aimed at increasing recovery, suggesting that interventions focusing on cultivating openness and acceptance of emotions and the ability to regulate them may be helpful in achieving it. These findings are in agreement with recent research about the potential benefits of mindfulness-based interventions for BD,[49,50] which can increase the acceptance of emotions and mood regulation, and preliminary results also point to emotion regulation improvements through dialectical behavior therapy for BD.[48,51]

Adding to the research on recovery predictors in BD, our multiple regression results suggest that depressive symptoms and difficulties in regulating emotions portray significant predictors of this construct, accounting for half of its variance. These results align with previous research, which demonstrated the negative impact of depressive symptoms on recovery and overall well-being in BD.[52] Similarly, the effect of difficulties in emotion regulation in BD has been extensively reported,[53-55] with fewer studies exploring the association with recovery.[39] A recent pilot study showed preliminary data on the impact of emotional regulation training

on improving recovery in people with BD, but more robust studies are necessary to draw generalizable conclusions.[48]

While our study contributes valuable insights into the assessment and validation of the BRQ for Portuguese, some limitations are worth mentioning. Firstly, it was not possible to perform a factorial analysis due to the small sample size, considering this is an extensive questionnaire (36 items). A clinical sample of people with BD is hard to collect, particularly in a small country like Portugal. Thus, even if we used a minimum standard for a confirmatory factor analysis of five people per questionnaire,[56] we would need a minimum sample of 180 patients. Secondly, the sample was small to explore differences between participants who responded online and in paper format. Additionally, two items within the BRQ exhibited notably low correlations with the overall score, casting doubt on their psychometric quality.

Future research with larger sample sizes should explore these findings and perform factorial analysis to confirm the one-factor structure, potentially leading to the refinement or elimination of items to enhance the scale's psychometric properties. Despite these considerations, this study stands as a crucial initial step towards psychometric support for the Portuguese version of the BRQ and was able to surpass the original study's sample size. Without a Portuguese version of the scale, the concept of recovery in BD would continue to be unexplored in Portugal.

Another limitation of the current study relies on the exclusive use of self-reported questionnaires to measure recovery, which might lead to response bias due to comprehensibility limitations or social desirability. Future studies should include multiple informants and have, for example, clinician-rated recovery measures.

CONCLUSION

In conclusion, this study represents a valuable contribution to the psychometric properties of the BRQ for BD in different samples and countries, making it available in Portuguese, a language that, as far as we know, has no available measures to assess recovery in BD. Furthermore, it contributes to the recovery field, providing new insights into the construct predictors and associated sociodemographic and clinical outcomes. Future studies should aim to assess recovery perceptions within BD and actively address recovery as a desirable and attainable therapeutic goal in clinical studies.

ACKNOWLEDGEMENTS

We want to thank all the mental health professionals, hospitals, organizations, and participants who participated in our studies.

AUTHOR CONTRIBUTIONS

JA: Study design, data collection and analysis, writing and critical review of the manuscript.

DC, RG: Data analysis, writing and critical review of the manuscript.

MJM: Writing and critical review of the manuscript.

AM, PC: Critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

The research was financially supported by the Fundação para a Ciência e Tecnologia (FCT) in the form of an individual doctorate scholarship for the first author JA (reference number: SFRH/BD/130116/2017) and an individual doctorate scholarship of the co-author RG (Reference number: SFRH/BD/5099/2020). The funder played no role in the study design, collection, analysis or interpretation of data or preparation of this manuscript.

REFERENCES

1. Merikangas KR, Jin R, He JP, Kessler RC, Lee S, Sampson NA, et al. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. Arch Gen Psychiatry. 2011;68:241-51.
2. Treuer T, Tohen M. Predicting the course and outcome of bipolar disorder: a review. Eur Psychiatry. 2010;25:328-33.
3. Echezarraga A, Calvete E, González-Pinto AM, Las Hayas C. Resilience dimensions and mental health outcomes in bipolar disorder in a follow-up study. Stress Heal. 2018;34:115-26.
4. Bonnin CD, Reinares M, Martinez-Aran A, Jimenez E, Sanchez-Moreno J, Sole B, et al. Improving functioning, quality of life, and well-being in patients with bipolar disorder. Int J Neuropsychopharmacol. 2019;22:467-77.
5. Andersson P, Tistad M, Eriksson Å, Enebrink P, Sturidsson K. Implementation and evaluation of illness management and recovery (IMR) in mandated forensic psychiatric care – study protocol for a multicenter cluster randomized trial. Contemp Clin Trials Commun. 2022;27:100907.
6. Nestsiarovich A, Hurwitz NG, Nelson SJ, Crisanti AS, Kerner B, Kuntz MJ, et al. Systemic challenges in bipolar disorder management: a patient-centered approach. Bipolar Disord. 2017;19:676-88.
7. Yildiz A, Ruiz P, Nemeroff CB, editors. The bipolar book: history, neurobiology, and treatment. New York: Oxford University Press; 2015.

8. Chirio-Espitalier M, Schreck B, Duval M, Hardouin JB, Moret L, Bronnec MG. Exploring the personal recovery construct in bipolar disorders: definition, usage and measurement. a systematic review. Front Psychiatry . 2022;13:876761.
9. Ogilvie AD, Morant N, Goodwin GM. The burden on informal caregivers of people with bipolar disorder. Bipolar Disord. 2005;7:25-32.
10. Frost BG, Tirupati S, Johnston S, Turrell M, Lewin TJ, Sly KA, et al. An integrated recovery-oriented model (IRM) for mental health services: evolution and challenges. BMC Psychiatry. 2017;17:1-17.
11. Jacob K. Recovery model of mental illness: a complementary approach to psychiatric care. Indian J Psychol Med. 2015;37:117-9.
12. Carpiniello B, Vita A, Mencacci C, editors. Recovery and major mental disorders. Cham: Springer International Publishing; 2022.
13. Fico G, Anmella G, Murru A, Vieta E. Predictors of clinical recovery in bipolar disorders. In: Carpiniello B, Vita A, Mencacci C, editors. Recovery and major mental disorders . Cham: Springer International Publishing; 2022. p. 155-72.
14. Thornton T, Lucas P. On the very idea of a recovery model for mental health. J Med Ethics. 2011;37:24-8.
15. Neil ST, Killbride M, Pitt L, Nothard S, Welford M, Sellwood W, et al. The questionnaire about the process of recovery (QPR): a measurement tool developed in collaboration with service users. Psychosis. 2009;1:145-55.
16. Law H, Neil ST, Dunn G, Morrison AP. Psychometric properties of the questionnaire about the process of recovery (QPR). Schizophr Res. 2014;156:184-9.
17. Williams J, Leamy M, Pesola F, Bird V, Le Boutillier C, Slade M. Psychometric evaluation of the questionnaire about the process of recovery (QPR). Br J Psychiatry. 2015;207:551-5.
18. Kraiss JT, Ten Klooster PM, Chrispijn M, Stevens AW, Kupka RW, Bohlmeijer ET. Measuring personal recovery in people with bipolar disorder and exploring its relationship with well-being and social role participation. Clin Psychol Psychother. 2019;26:540-9.
19. Jones S, Mulligan LD, Higginson S, Dunn G, Morrison AP. The bipolar recovery questionnaire: psychometric properties of a quantitative measure of recovery experiences in bipolar disorder. J Affect Disord. 2013;147:34-43.
20. Fenn J, Tan CS, George S. Development, validation and translation of psychological tests. B J Psych Adv. 2020;26:306-15.
21. Hirschfeld RM. The mood disorder questionnaire: a simple, patient-rated screening instrument for bipolar disorder. Prim Care Companion J Clin Psychiatry. 2002;4:9-11.
22. Azevedo J, Castilho P, Carreiras D, Martins MJ, Carvalho CB, Cherpe S, et al. Development of the clinical interview for bipolar disorder (CIBD) – rational and experts' panel evaluation. J Neurol Neurol Sci Disord. 2023;9:45-54.
23. Castelo MS, Carvalho ER, Gerhard ES, Costa CM, Ferreira ED, Carvalho AF. Validação da versão em português do questionário de transtornos do humor em uma população de pacientes psiquiátricos. Braz J Psychiatry. 2010;32:424-8.
24. Michalak EE, Murray G, Collaborative RESearch Team to Study Psychosocial Issues in Bipolar Disorder (CREST.BD). Development of the QoL.BD: a disorder-specific scale to assess quality of life in bipolar disorder. Bipolar Disord. 2010;12:727-40.
25. Azevedo J, Roque M, Carreiras D, Castilho P, Macedo A. Quality of life in bipolar disorder: portuguese validation of the brief QoL.BD questionnaire. J Psychiatry Ment Disord. 2023;8:1-7.
26. Galinha IC, Pais-Ribeiro J. Contribuição para o estudo da versão portuguesa da positive and negative affect schedule (PANAS): II – estudo psicométrico. Análise Psiclógica. 2005;2:219-27.
27. Watson D, Clark L, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol. 1988;54:1063-70.
28. Zigmond AS, Snaith RP, Snaith PR. The hospital anxiety and depression scale. Acta Psychiatr Scand.1983;67:361-70.
29. Pais-Ribeiro J, Silva I, Ferreira T, Martins A, Meneses R, Baltar M. Validation study of a portuguese version of the hospital anxiety and depression scale. Psychol Health Med. 2007;12:225-37.
30. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. J Pers Assess. 1985;49:71-5.
31. Laranjeira CA. Preliminary validation study of the portuguese version of the satisfaction with life scale. Psychol Heal Med. 2009;14:220-6.
32. Coutinho J, Ribeiro E, Ferreirinha R, Dias P. Versão portuguesa da escala de dificuldades de regulação emocional e sua relação com sintomas psicopatológicos. Rev Psiquiatr Clin. 2010;37:145-51.
33. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopathol Behav Assess. 2004;26:41-54.
34. Kline RB. Principles and practice of structural equation modeling. New York: Guilford Press; 2005.
35. Peterson RA. A meta-analysis of cronbach's coefficient alpha. J Consum Res. 1994;21:381-91.
36. Dancey C, Reidy J. Statistics without maths for psychology. 7th ed. London: Pearson Education; 2017.
37. Field A, Miles J, Field Z. Discovering statistics using SPSS. Sage. 2013;81:169-70.
38. Todd NJ, Jones SH, Lobban FA. "Recovery" in bipolar disorder: how can service users be supported through a self-management intervention? A qualitative focus group study. J Ment Heal. 2012;21:114-26.
39. Kraiss JT, ten Klooster PM, Frye E, Kupka RW, Bohlmeijer ET. Exploring factors associated with personal recovery in bipolar disorder. Psychol Psychother. 2021;94:667-85.
40. Weintraub MJ, Schneck CD, Walshaw PD, Chang KD, Sullivan AE, Singh MK, et al. Longitudinal trajectories of mood symptoms and global functioning in youth at high risk for bipolar disorder. J Affect Disord. 2020;277:394-401.
41. Hancock J, Perich T. Personal recovery in psychological interventions for bipolar disorder: a systematic review. Aust Psychol. 2022;57:215-25.
42. Michalak EE, Yatham LN, Lam RW. Quality of life in bipolar disorder: a review of the literature. Health Qual Life Outcomes. 2005;3:72.
43. Becerra R, Cruise K, Murray G, Bassett D, Harms C, Allan A, et al. Emotion regulation in bipolar disorder: are emotion regulation abilities less compromised in euthymic bipolar disorder than unipolar depressive or anxiety disorders? Open J Psychiatry. 2013;3:1-7.
44. Wingo AP, Baldessarini RJ, Holtzheimer PE, Harvey PD. Factors associated with functional recovery in bipolar disorder patients. Bipolar Disord. 2010;12:319-26.x
45. Peters A, Sylvia LG, da Silva Magalhães PV, Miklowitz DJ, Frank E, Otto MW, et al. Age at onset, course of illness and response to psychotherapy in bipolar disorder: results from the systematic treatment enhancement program for bipolar disorder (STEP-BD). Psychol Med. 2014;44:3455-67.
46. Hendrick V, Altshuler LL, Gitlin MJ, Hammen C. Gender and bipolar illness. J Clin Psychiatry. 2000;61:7623.
47. Arnold LM. Gender differences in bipolar disorder. Psychiatr Clin North Am. 2003;26:595-620.
48. Wright K, Dodd AL, Warren FC, Medina-Lara A, Dunn B, Harvey J, et al. Psychological therapy for mood instability within bipolar spectrum disorder: a randomised, controlled feasibility trial of a dialectical behaviour therapy-informed approach (the ThrIVe-B programme). Int J Bipolar Disord. 2021;9:20.
49. Bojic S, Becerra R. Mindfulness-based treatment for bipolar disorder: a systematic review of the literature. Eur J Psychol. 2017;13:573-98.
50. Lovas DA, Schuman-Olivier Z. Mindfulness-based cognitive therapy for bipolar disorder: a systematic review. J Affect Disord. 2018;240:247-61.
51. Eisner L, Eddie D, Harley R, Jacobo M, Nierenberg AA, Deckersbach T. Dialectical behavior therapy group skills training for bipolar disorder. Behav Ther. 2017;48:557-66.
52. Salvatore P, Tohen M, Khalsa HM, Baethge C, Tondo L, Baldessarini RJ. Longitudinal research on bipolar disorders. Epidemiol Psychiatr Sci. 2007;16:109-17.
53. Miola A, Cattarinussi G, Antiga G, Caiolo S, Solmi M, Sambataro F. Difficulties in emotion regulation in bipolar disorder: a systematic review and meta-analysis. J Affect Disord. 2022;302:352-60.
54. van Rheenen TE, Murray G, Rossell SL. Emotion regulation in bipolar disorder: profile and utility in predicting trait mania and depression propensity. Psychiatry Res. 2015;225:425-32.
55. Kurtz M, Mohring P, Förster K, Bauer M, Kanske P. Deficits in explicit emotion regulation in bipolar disorder: a systematic review. Int J bipolar

Disord. 2021;9:15.
56. Hatcher L. A step-by-step approach to using the SAS system for factor analysis and structural equation modeling. North Carolina: SAS Institute, Inc.; 1994.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Disforia de Género: Conceitos, Diagnóstico e Abordagem Clínica

Gender Dysphoria: Concepts, Diagnosis and Clinical Management

Carolina ALVES RODRIGUES[1], Miriam MARGUILHO✉[1], Bárbara FERREIRA[1], Sandra NASCIMENTO[1], Miguel NASCIMENTO[1], Sónia CARDOSO[1], Mariana SILVA[2], Ana Cristina PABLO[1], Catarina SOARES[1], Carlos FERNANDES[1], Marco GONÇALVES[1]
Acta Med Port 2024 May;37(5):379-385 ▪ https://doi.org/10.20344/amp.21057

RESUMO

A disforia de género é definida como uma condição em que existe sofrimento mental associado à incongruência entre o género experienciado pela pessoa e o sexo que lhe foi atribuído à nascença. O género como conceito e a disforia de género como condição com necessidade de intervenção multidisciplinar têm evoluído tão rapidamente quanto a sua visibilidade na sociedade, tornando premente a necessidade de promover a literacia e a formação de todos os profissionais de saúde nesta área. Este artigo de revisão pretende contribuir para o esclarecimento informado e baseado em evidência científica acerca das pessoas com disforia de género e sua abordagem clínica, contribuindo para uma prática segura, inclusiva e livre de discriminação no que concerne aos seus cuidados de saúde.
Palavras-chave: Disforia de género/diagnóstico; Disforia de género/tratamento

ABSTRACT

Gender dysphoria is defined as a condition characterized by mental suffering associated with the incongruence between one's experienced gender and their birth-assigned sex. Gender as a construct and gender dysphoria as a condition in need of multidisciplinary intervention have developed as swiftly as their visibility in society, making it mandatory to promote the literacy and education of all healthcare professionals in this area. This article aims to review information based on scientific evidence on people with gender dysphoria and its clinical approach, while contributing to a safe, inclusive, and non-discriminatory practice of healthcare.
Keywords: Gender Dysphoria/diagnosis; Gender Dysphoria/therapy

INTRODUÇÃO

A palavra 'género', com origem no francês *gendre* (atualmente *genre*), significa "tipo, categoria, divisão".[1] De uma forma geral, assume-se que o género corresponde ao sexo, mas isso nem sempre se verifica. Existem pessoas que desde fases precoces ou em fases posteriores da sua vida, sentem uma discordância entre o sexo que lhes foi atribuído à nascença e a sua identidade de género. Esta discordância, associada a sofrimento mental, poderá corresponder ao diagnóstico de disforia de género (DG).[2,3]

Este artigo pretende fazer uma breve nota histórica sobre a evolução da definição de género, um esclarecimento da terminologia atual e restantes conceitos essenciais no âmbito da prática da sexologia clínica. Após a análise dos dados epidemiológicos referentes à prevalência atual da DG e dos sintomas tipicamente associados a esta condição, terminaremos com a abordagem das mais recentes recomendações no que concerne o diagnóstico e intervenção na DG. Alertamos que esta leitura não dispensa, contudo, a consulta de bibliografia especializada para um conhecimento mais aprofundado da matéria.

NOTA HISTÓRICA EM SEXOLOGIA

O termo 'género' foi usado pela primeira vez em Sexologia pelo psicólogo John Money, em 1955, na sua obra "*Hermaphroditism, gender and precocity in hyperadrenocorticism: psychologic*".[4] O conceito foi, assim, difundido, acabando por ser adotado pelas escolas feministas como forma de distinguir o socialmente construído do definido biologicamente.

O termo 'transexualidade', cunhado por Magnus Hirschfeld em 1923,[5] surgiu pela primeira vez na 9.ª edição da "Classificação Internacional de Doenças" em 1975 (CID-9)[6] e, de seguida, na 3.ª edição do "Manual de Diagnóstico e Estatística das Perturbações Mentais" (DSM III)[7], em 1980. Quase duas décadas depois, o termo foi substituído pelo diagnóstico de perturbação de identidade de género (DSM IV).[8] Já em 2013, aquando da publicação do DSM-5, e apesar de cumprir os mesmos critérios, a denominação da condição passa a DG, mantendo-se sobretudo o foco no sofrimento relacionado com a discordância entre o género experienciado e o sexo atribuído à nascença.[9] Esta alteração teve como principal objetivo frisar que o diagnóstico se deve focar na disforia em si, e não na identidade de género da pessoa. Esta última não representa uma doença e não carece de qualquer tipo de intervenção, sendo definida apenas pelo próprio e de acordo com a sua autodeterminação.

Nos anos 40, Henry Benjamin foi pioneiro no acompanhamento de pessoas com discordância entre o sexo atribuído à nascença e o sentimento de pertença a uma

1. Consulta de Sexologia. Hospital Júlio de Matos. Unidade Local de Saúde São José. Lisboa. Portugal.
2. Serviço de Psiquiatria de Ligação. Hospital São José. Unidade Local de Saúde São José. Lisboa. Portugal.
✉ **Autor correspondente:** Miriam Marguilho. miriamgmarguilho@campus.ul.pt
Recebido/*Received*: 04/12/2023 - **Aceite/*Accepted*:** 04/03/2024 - **Publicado *Online*/*Published Online*:** 03/04/2024 - **Publicado/*Published*:** 02/05/2024

identidade de género.[10] A partir do seu trabalho nasceu a Associação Internacional de Disforia de Género Harry Benjamin,[11] atualmente denominada Associação Mundial de Profissionais de Saúde Transgénero [World Professional Association for Transgender Health (WPATH)], que continua a ser a associação de referência mundial na área, publicando periodicamente as suas normas de intervenção nesta população. Em 2022 foi publicada a 8.ª edição,[12] consultável no *site* da associação.

A permanência da DG nos manuais de doença mental continua a ser controversa. A discussão desenvolve-se à volta de que o uso do diagnóstico perpetua ideia de que a identidade dita transgénero é uma perturbação mental e dos que apoiam a permanência do diagnóstico como forma de facilitar o acesso aos cuidados de saúde necessários e o aprofundar da investigação e de tratamentos eficazes.[13,14]

Na sua última versão, a CID-11[15] substituiu o diagnóstico de 'transexualidade' por 'incongruência de género'

Tabela 1 – Glossário[12,16-18]

Sexo atribuído à nascença	Refere-se à identificação da pessoa como masculina, feminina ou intersexo, com base em características físicas. O sexo atribuído à nascença é frequentemente baseado na aparência dos genitais externos.
Género	Dependendo do contexto, o género pode ser uma referência à identidade de género, expressão de género e/ou ao papel de género, incluindo as expectativas culturalmente associadas a pessoas a quem foi atribuído o sexo feminino ou masculino à nascença. Para além de mulher e homem (que podem ser cisgénero ou transgénero), existem identidades transgénero, não-binárias, *queer*, agénero, com fluidez de género; muitos outros géneros são reconhecidos em todo o mundo.
Cisgénero	Refere-se a pessoas cuja identidade de género corresponde ao que lhes foi atribuído à nascença.
Transgénero	Descreve pessoas cujas identidades de género e/ou expressões de género não são congruentes com as tipicamente expectáveis consoante o género que lhes foi atribuído à nascença.
Intersexo	Refere-se a pessoas que nascem com características sexuais ou reprodutivas que não encaixam nas definições binárias de feminino ou de masculino.
Não-binário	Refere-se a identidades de género que se posicionam fora do binário de género clássico. Pessoas não-binárias podem identificar-se como parcialmente homem ou parcialmente mulher; identificar-se por vezes como mulher e outras vezes como homem; identificar-se com um género diferente de homem ou mulher; ou como não tendo qualquer género.
Identidade de género	Refere-se ao significado profundo, interno e intrínseco do género da própria pessoa.
Expressão de género	Refere-se à forma como a pessoa age ou expressa o seu género no dia a dia e dentro do contexto da sua cultura e sociedade. A expressão de género através da aparência física pode incluir vestuário, penteado, acessórios, cosméticos, intervenções hormonais e cirúrgicas, bem como maneirismos, discurso, padrões comportamentais e nomes. A expressão de género de uma pessoa pode ou não ser congruente com a sua identidade de género.
Papéis de género	Construções específicas de uma cultura e sociedade, definidos pelas características femininas e masculinas que a sociedade atribui a mulheres e a homens.
Não conformidade de género	Descreve um indivíduo cuja identidade, papéis ou expressão de género não são típicos para indivíduos a quem foi atribuído determinado género à nascença.
Disforia	Estado emocional desorganizado e complexo caracterizado por um conjunto de sintomas, entre eles a irritabilidade, descontentamento e ressentimento interpessoal.
Disforia de género	Descreve um estado de sofrimento ou desconforto que surge quando a identidade de género da pessoa difere do que é fisicamente ou socialmente associado ao género que lhe foi atribuído à nascença. É também um termo diagnóstico presente no DSM-5, denotando a incongruência entre o género atribuído à nascença e o género vivenciado pela pessoa, quando esta é acompanhada de sofrimento. Nem todas as pessoas transgénero nem com diversidade de género sofrem de disforia de género.
Orientação sexual	Refere-se à identidade sexual, atrações e comportamentos da pessoa em relação a outros, com base no seu género ou características sexuais e nos dos seus parceiros. A orientação sexual e a identidade de género são termos distintos e independentes.
Transfobia	Refere-se a atitudes, crenças e ações negativas relacionadas com a população transgénero e com diversidade de género como um grupo. A transfobia pode manifestar-se através de políticas e práticas discriminatórias a nível estrutural ou a níveis específicos e pessoais. A transfobia pode ser internalizada, quando pessoas transgénero ou com diversidade de género aceitam e refletem tais preconceitos sobre si próprias ou outras pessoas transgénero ou com diversidade de género. Podendo ser resultado de ignorância não intencional, os seus efeitos nunca são benignos.

(IG), transferindo-o do capítulo das doenças mentais e comportamentais para o capítulo das condições relacionadas com a saúde sexual, afastando-o assim do crivo da perturbação mental.

A diversidade na identidade de género e a sua expressão ao longo da vida, que não estão estereotipicamente associadas ao sexo atribuído à nascença, são um fenómeno humano culturalmente diverso, mutável e comum, que não deve ser visto como negativo ou patológico.

TERMINOLOGIA

Importa definir e clarificar alguns conceitos básicos relacionados com esta temática e que vão sendo referidos ao longo do artigo. Alertamos que a Tabela 1 não é exaustiva, pois não engloba toda a diversidade de identidades autodeterminadas.

EPIDEMIOLOGIA[19]

Segundo um estudo levado a cabo em 2017,[19] a prevalência da DG situa-se entre 0,5% e 1,3% entre crianças, adolescentes e adultos. Estes números podem variar de acordo com a tipologia de estudos e com a região geográfica, com taxas mais elevadas na Europa Ocidental e América e inferiores em países como o Japão. Segundo a DSM-5,[9] a prevalência de DG em indivíduos adultos do sexo masculino varia entre 0,005% e 0,014% e entre 0,002% e 0,003% em adultos do sexo feminino.

ABORDAGEM DIAGNÓSTICA

A WPATH recomenda que o diagnóstico seja estabelecido por um profissional de saúde mental com formação específica e experiência prática com pessoas com diversidade de género que necessitem do acesso a intervenções afirmativas de género, médicas ou cirúrgicas, no sentido de diminuir o sofrimento associado.[12] O diagnóstico de DG implica a presença dos critérios de diagnóstico das classificações DSM-5[9] ou CID-11 (incongruência de género)[15] – ver Tabelas 2 e 3.

Tabela 2 – Critérios de diagnóstico de disforia de género segundo o DSM-5[9]

A. Uma marcada incongruência entre o género experienciado/expresso e o género atribuído, com uma duração de pelo menos seis meses, manifestada por pelo menos dois dos seguintes:
1. Uma marcada incongruência entre o género experienciado/expresso e as características sexuais primárias e/ou secundárias (ou, em jovens adolescentes, as características sexuais secundárias esperadas).
2. Um forte desejo de se libertar das suas características sexuais primárias e/ou secundárias devido a uma marcada incongruência entre o género experienciado/expresso (ou, em jovens adolescentes, a um desejo de prevenir o desenvolvimento das características sexuais secundárias esperadas).
3. Um forte desejo pelas características sexuais primárias e/ou secundárias do outro género.
4. Um forte desejo de ser do outro género (ou de algum género alternativo diferente do género atribuído).
5. Um forte desejo de ser tratado como se fosse do outro género (ou de algum género alternativo diferente do género atribuído).
6. Uma forte convicção de que tem os sentimentos e reações típicos de outro género (ou de algum género alternativo diferente do género atribuído).
B. A condição associa-se a mal-estar clinicamente significativo ou défice social, ocupacional ou noutras áreas importantes do funcionamento.

Tabela 3 – Critérios de diagnóstico de incongruência de género segundo o CID-11[15]

Incongruência de género na adolescência ou adultícia
É caracterizada pela incongruência marcada e persistente entre o género experienciado de um indivíduo e o sexo que lhe foi atribuído, a qual envolve muitas vezes o desejo de 'transitar', no sentido de viver e de ser aceite como uma pessoa do género experienciado, através de tratamento hormonal, cirúrgico ou outros serviços de saúde, com o objetivo de alinhar o corpo do indivíduo, tanto quanto desejado e dentro dos possíveis, com o género experienciado.
O diagnóstico não pode ser atribuído previamente ao início da puberdade.
A presença singular de comportamentos e preferências de não conformidade de género não são critérios para o diagnóstico.
Incongruência de género na infância
É caracterizada pela incongruência marcada entre o género experienciado/expresso e o sexo atribuído na criança pré-púbere. Inclui um forte desejo de ser de um género diferente do sexo que lhe foi atribuído; uma forte rejeição da sua própria anatomia sexual ou características sexuais secundárias antecipadas e/ou um forte desejo pelas características sexuais primárias e/ou secundárias antecipadas do outro género; e brincadeiras de faz de conta, brinquedos, jogos ou atividades que são típicas do género experienciado.
A incongruência de género deve persistir por pelo menos dois anos.
A presença singular de comportamentos e preferências de não conformidade de género não são critérios para o diagnóstico.

CARACTERÍSTICAS DO DIAGNÓSTICO

As pessoas com DG apresentam uma marcada discordância entre o sexo que lhes foi atribuído à nascença e a sua identidade de género. No entanto, para o estabelecimento do diagnóstico é fundamental haver evidência de mal-estar relativamente a esta discordância, a maior parte das vezes manifestado por um elevado desconforto com o seu sexo biológico, nomeadamente a presença das características sexuais primárias ou secundárias, ou papéis sociais de género.

Em 2020 foi realizada uma revisão sistemática[20] que teve como objetivo a síntese da literatura qualitativa existente relativamente à fenomenologia da DG em adultos. Foram identificadas quatro dimensões do sofrimento: 1) relativo à discordância entre o sexo atribuído e o género vivenciado; 2) interação entre o género atribuído, a identidade de género e a sociedade; 3) consequências negativas da identidade de género e 4) processamento interno da rejeição e transfobia.

SOFRIMENTO RELATIVO À DISCORDÂNCIA ENTRE O GÉNERO ATRIBUÍDO E O GÉNERO VIVENCIADO

Refere-se à vivência de sentimentos negativos relacionados com a discordância entre a identidade de género do próprio e o seu corpo, gerando conflito interno, confusão e sentimentos de negação relacionados com a sua identidade de género, disforia direcionada a determinadas características corporais da pessoa e sentimentos de desconexão.[21,22]

A disforia é descrita como sentimentos de inquietação, ódio e repulsa pelo próprio corpo, sendo os genitais e as características sexuais secundárias tais como a presença/ausência do pelo facial e corporal geralmente o foco, com várias tentativas de supressão dos mesmos.[20,23] O sofrimento também pode estar associado ao medo do futuro, e este à sensação de impotência e de perda do controlo, e ansiedade relativa à tomada de decisões de vida importantes relacionadas com a sua identidade e afirmação de género.[24] Estas circunstâncias podem estar associadas à elevada prevalência de psicopatologia em pessoas com DG, incluindo depressão e comportamentos suicidas.[25-28]

INTERAÇÃO ENTRE O GÉNERO ATRIBUÍDO, A IDENTIDADE DE GÉNERO E A SOCIEDADE

Esta dimensão reconhece a natureza social da identidade de género. Algumas normas e expectativas históricas e culturais são atribuídas a um determinado comportamento e expressão desse mesmo género, cuja interpretação social leva à assunção da identidade de género mais provável da pessoa.[20] No entanto, são dimensões distintas e independentes. Quando são assumidas de forma automática, com base em normas e expectativas, podem levar à vivência de um sofrimento profundo, pelo medo associado a uma interpretação errada sobre a identidade de género da pessoa.[29] Desta forma, a interação social é muitas vezes identificada como um fator precipitante de disforia, pela expectativa de rejeição associada à sua identidade de género.[20]

CONSEQUÊNCIAS NEGATIVAS DA IDENTIDADE DE GÉNERO

Os indivíduos com disforia de género sentem-se muitas vezes isolados da sociedade e das suas comunidades, havendo referência a uma dificuldade na aceitação de pessoas que não se conformam com as tradicionais normas de género. É reportada uma diminuição do sentido de pertença à comunidade, invisibilidade, falta de validação e solidão.[30]

PROCESSAMENTO INTERNO DA REJEIÇÃO E TRANSFOBIA

A experiência da rejeição cria um estado de hipervigilância pelo receio de ser vítima de discriminação ou violência, que o próprio relaciona com o facto de ser transgénero, estando associado ao aumento da perceção do perigo e ao medo compreensível de sair da sua própria casa.[31] Estes receios expõem os indivíduos a elevados níveis de ansiedade e ativação psicológica.[20] Paralelamente, as narrativas externas e negativas acerca das pessoas transgénero podem levar ao desenvolvimento de sentimentos de vergonha e desencadear aquilo que é definido como a transfobia internalizada.[32] A consciência deste estigma social associado à sua identidade de género, quando internalizado pelo próprio, pode levar à vivência de sentimentos de ódio, confusão e vergonha.[20,32]

DIAGNÓSTICO DIFERENCIAL

O diagnóstico de DG em adultos é facilitado quando as primeiras manifestações da disforia surgem durante a infância, com exacerbação do sofrimento após as mudanças da puberdade e persistência do mesmo durante a vida adulta.

O profissional de saúde mental deve definir um plano de avaliação, seguimento e cuidados adaptados e ritmados de acordo com as necessidades do próprio. As pessoas com quadros clínicos agudos comórbidos devem ter a assistência devida, com restabelecimento da sua capacidade de autodeterminação e tomada de decisão em relação aos cuidados clínicos desejados, caso estas tenham sido perturbadas. Nas pessoas com um quadro claro e definido de DG é antiético e contra os direitos humanos, incluindo de saúde, adiar as intervenções indicadas.

A Tabela 4 inclui um resumo dos principais diagnósticos diferenciais aquando da avaliação de uma pessoa com história de DG.

Tabela 4 – Diagnóstico diferencial da disforia de género[33]

Não conformidade com os papéis de género	Pode ser diferenciada com base no grau de sofrimento associado e questionando se o indivíduo se identifica ou não com o género que lhe foi atribuído à nascença.
Perturbação dismórfica corporal	Nesta perturbação o indivíduo geralmente perceciona uma parte do seu corpo como gravemente deformada, desejando a sua remoção ou alteração, enquanto na DG as alterações desejadas têm origem na discordância entre as características anatómicas presentes e a identidade de género com que o indivíduo se identifica. Podem ser comórbidos.
Perturbação de travestismo	Refere-se a indivíduos para quem o comportamento de travestismo provoca excitação sexual e causa mal-estar e/ou outros défices, sem nunca questionar o género que lhes foi atribuído à nascença. Podem ser comórbidos.
Esquizofrenia e outras perturbações psicóticas	Os delírios relacionados com o género estão presentes em até 20% dos doentes com perturbações psicóticas – a sua diferenciação da DG é geralmente facilitada pelas diferenças no seu conteúdo, bem como pela presença circunscrita às descompensações da doença de base e pela ausência dos restantes critérios da DG. Podem ser comórbidos.

ABORDAGEM CLÍNICA

A WPATH disponibiliza normas de orientação clínica que permitem guiar a abordagem dos profissionais de saúde no âmbito dos cuidados afirmativos de género.[12] A versão mais recente, publicada em 2022, define que estes cuidados, denominados de autoafirmação de género, devem ser preferencialmente multidisciplinares e em equipas especializadas, tendo como objetivo primordial acompanhar e facilitar o acesso de pessoas com DG a intervenções seguras e eficazes que permitam auxiliar o processo de autoafirmação de género da pessoa e contribuir para a sua saúde global.[12] São definidos como princípios gerais destes cuidados o respeito pela diversidade de identidades e expressões de género, pela autonomia e autodeterminação, bem como a luta contra a discriminação e o estigma associados à diversidade de género.[12]

A comunicação reveste-se de especial importância neste âmbito, tendo o potencial de funcionar como facilitador ou como barreira no acesso a cuidados de saúde competentes e inclusivos.[34,35] É considerada boa prática clínica perguntar à pessoa qual o nome e pronomes escolhidos e ser consistente na sua utilização, bem como esclarecer o significado subjetivo dos termos utilizados para definir e autodeterminar a identidade de género.[34]

A afirmação de género pode ser conceptualizada como o conjunto de dimensões sociais, psicológicas, médicas e legais que contribuem para a apoiar e afirmar a identidade de género da pessoa, quando discordante do sexo que lhe foi atribuído à nascença.[36] A afirmação de género é individual, autodeterminada e não existem etapas específicas 'mandatórias', sendo as necessidades adaptadas à medida de cada pessoa, da sua identidade e variabilidade na expressão de género.[33]

A dimensão social (também designada como transição social) engloba modificações na apresentação externa ou forma de se relacionar com os outros (amigos, família) que melhor refletem a identidade de género da pessoa. Incluem a escolha de nomes e pronomes preferidos, alteração da identificação legal no registo civil, modificações no vestuário e no comportamento.[36] Em Portugal, à semelhança do que acontece noutros países, a mudança legal de género é independente dos cuidados de saúde. Desde 2018, a Lei n.º 38/2018 de 7 de agosto estabelece o direito à autodeterminação da identidade de género e expressão de género, possibilitando que qualquer pessoa de nacionalidade portuguesa e maior de idade possa requerer mudança de género e de nome próprio no registo civil, sem necessidade de apresentar relatório com menção de diagnóstico.[37]

INTERVENÇÕES MÉDICAS E CIRÚRGICAS

Algumas pessoas com DG desejam e beneficiam de intervenções médicas afirmativas de género, que englobam cuidados diferenciados em áreas específicas, nomeadamente terapia hormonal e intervenções cirúrgicas.[38] A evidência científica demonstra que o grau em que a aparência das pessoas transgénero está de acordo com sua identidade de género, segundo a vivência subjetiva e a experiência individual, é o melhor preditor de qualidade de vida e *outcomes* de saúde mental após as intervenções médicas afirmativas de género.[20] Numa revisão sistemática realizada em 2010, demonstrou-se que após a realização das intervenções médicas, 80% das pessoas com DG relatavam melhoria significativa da disforia, 78% descreveram melhoria significativa nos sintomas psicológicos, 80% relataram melhoria na qualidade de vida e 72% denotaram melhoria na sua função sexual.[39] Com base em 11 estudos longitudinais, Dhejne *et al* reportaram níveis de psicopatologia e de perturbações psiquiátricas após intervenções afirmativas de género sobreponíveis aos da população em geral.[40] Nem todas as pessoas com DG pretendem submeter-se a estas intervenções, sendo essencial informar e esclarecer, bem como avaliar critérios clínicos de elegibilidade para as mes-

mas.[33,41] Previamente ao início de intervenções médicas é fundamental abordar o tema da fertilidade e preservação de gâmetas, pelo efeito potencialmente irreversível na fertilidade.[12,42]

A intervenção hormonal consiste na administração segura e eficaz de hormonas como a testosterona, no caso da terapêutica de afirmação de género masculinizante, ou estrogénio e anti androgénios – ciproterona, espironolactona e agonistas da hormona libertadora de gonadotrofinas (GnRH) –, no caso da terapêutica de afirmação de género feminizante. O objetivo será a supressão da secreção de hormonas sexuais determinadas ao nascimento, que se manifestam a partir da puberdade e induzem os níveis hormonais adequados ao sexo pretendido.[42] As mudanças induzidas de feminização ou masculinização do corpo são necessárias e desejadas por muitas pessoas (mas não todas) com DG para o alívio da disforia decorrente da discordância entre determinadas características corporais e a identidade de género.[12,42] Num estudo prospetivo, Heylens *et al* demonstraram que após o início de terapia hormonal, o nível de sofrimento psicológico, medido através da escala *Symptom Checklist 90* (SCL-90), era equivalente ao grupo de controlo da população geral.[42]

As intervenções cirúrgicas afirmativas de género englobam uma variedade de procedimentos que têm como objetivo modificar aspetos corporais de forma a torná-los congruentes com a identidade de género. A título de exemplo: cirurgia mamária (aumento ou redução), cirurgia maxilo-facial, cirurgia ao aparelho vocal e cirurgia génito-urinária.[12] Em Portugal, o Serviço Nacional de Saúde (SNS) assegura a realização de cirurgia genital de afirmação de género na Unidade Reconstrutiva Génito-Urinária e Sexual (URGUS) do Centro Hospitalar e Universitário de Coimbra, desde novembro de 2011; e no Centro Hospitalar Universitário de Santo António (CHUdSA), desde dezembro de 2022 (dados fornecidos pela assessoria de comunicação do gabinete do Ministro da Saúde). O Centro Hospitalar Lisboa Central iniciou a realização de cirurgia mamária de afirmação de género em novembro de 2023.

CONCLUSÃO

O debate à volta do género continuará a evoluir, assim como a terminologia e as necessidades das pessoas que procuram cuidados médicos por questões ligadas ao género. O género é, cada vez mais, conceptualizado à luz da diversidade e não dos binómios feminino-masculino e mulher/homem, até então prevalentes, revestindo de especial complexidade a avaliação e interpretação da informação nesta área, que caminha no sentido da despatologização da não-conformidade/incongruência de género. Ainda assim, o diagnóstico de DG continua presente nas classificações diagnósticas, tendo evoluído para IG na versão mais recente da CID – a CID-11. Assim, este artigo pretende alertar para a importância de conhecer os principais termos presentes na literatura científica, de fazer um diagnóstico correto, nos casos em que esteja presente sofrimento – aplicando os critérios atuais de DG ou de IG –, e encaminhar para cuidados afirmativos de género, quando essa for a vontade da pessoa. É importante reforçar ainda que cada percurso é individual e autodeterminado, não existindo etapas expectáveis ou obrigatórias durante o processo de afirmação de género. O papel do clínico é, assim, comunicar de forma empática, informada e inclusiva, identificar as necessidades individuais da pessoa e oferecer cuidados médicos adequados ou encaminhar para equipas especializadas e multidisciplinares. O impacto do acesso atempado a cuidados de saúde afirmativos de género é bem conhecido, reduzindo de forma significativa os níveis de sofrimento psicológico e melhorando a qualidade de vida.

CONTRIBUTO DOS AUTORES

CAR, MG, SC, MGS: Redação e revisão crítica do manuscrito.

BF, SN, MN, ACP, CS, CF, MG: Revisão crítica do manuscrito.

Os autores aprovaram a versão final a ser publicada.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Appendix I: Indo-European roots. The American Heritage Dictionary of the English Language. 4th ed. Boston: Houghton Mifflin Company; 2000.
2. Crocq MA. How gender dysphoria and incongruence became medical diagnoses – a historical review. Dialogues Clin Neurosci. 2021;1:44-51.
3. Beek TF, Cohen-Kettenis PT, Kreukels BP. Gender incongruence/gender dysphoria and its classification history. Int Rev Psychiatry. 2015;1369-627.
4. Money J. Hermaphroditism, gender and precocity in hyperadrenocorticism: psychologic findings. Bull John Hopkins Hosp. 1955;96:253-64.
5. Drescher J. Gender dysphoria and disorders of sex development. Progress in care and knowledge. Chapter 7. Gender identity diagnoses: history and controversies. New York: Springer Science; 2013.
6. World Health Organization. International statistical classification of diseases and related health problems. 9th ed. Genebra: WHO; 1977.
7. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd ed. Washington: APA; 1980.
8. American Psychiatric Association. Diagnostic and statistical classification of diseases and related health problems. 4th ed. Washington: APA; 1994.
9. American Psychiatric Association. Diagnostic and statistical classification

of diseases and related health problems. 5th ed. Washington: APA; 2013.
10. Schaefer LC, Wheeler CW. Harry Benjamin's first ten cases (1938-1953): a clinical historical note. Arch Sex Behav. 1995;24:73-93.
11. Cohen-Kettenis PT, Gooren LJ. Transsexualismo: a review of etiology, diagnosis and treatment. J Psychosom Res. 1999;46:315-33.
12. Coleman E, Radix AE, Bouman WP, Brown GR, de Vries AL, Deutsch MB, et al. Standards of care for the health of transgender and gender diverse people, Version 8. Int. J Transgend Health. 2022;23:S1-259.
13. Drescher J. Controversies in gender diagnoses. LGBT Health. 2014;1:10-4.
14. Drescher J. Queer diagnoses: parallels and contrasts in the history of homosexuality, gender variance, and the diagnostic and statistical manual (DSM). Arch Sex Behav. 2010;39:427-60.
15. World Health Organization. International statistical classification of diseases and related health problems. 11th ed. Genebra: WHO; 2019.
16. Bem SL. Gender schema theory: a cognitive account of sex typing. Psychol Rev. 1981;88:354-64.
17. Guss C, Shumer D, Katz-Wise SL. Transgender and gender nonconforming adolescent care: psychosocial and medical considerations. Curr Opin Pediatr. 2015;26:421-6.
18. Moretti P, Bachetti MC, Sciarma T, Tortorella A. Dysphoria as a psychiatric syndrome: a preliminary study for a new transnosographic dimensional approach. Psychiatr Danub. 2018;30:582-7.
19. Zucker KJ. Epidemiology of gender dysphoria and transgender identity. Sexual Health. 2017;14:404-11.
20. Cooper K, Russell A, Mandy W, Butler C. The phenomenology of gender dysphoria in adults: A systematic review and meta-synthesis. Clin Psychol Rev. 2020;80:101875.
21. Goodrich KM. Lived experiences of college-age transsexual individuals. J Coll Couns. 2012;15:215-32.
22. Mullen G, Moane G. A qualitative exploration of transgender identity affirmation at the personal, interpersonal, and sociocultural level. Int J Transgend. 2013;14:140-54.
23. Giovanardi G, Morales P, Mirabella M, Fortunato A, Chianura L, Speranza AM, et al. Transition memories: experiences of trans adult women with hormone therapy and their beliefs on the usage of hormone blockers to suppress puberty. J Endocrinol Invest. 2019;1-10.
24. Applegarth G, Nuttal J. The lived experience of transgender people of talking therapies. Int J Transgend. 2016;17:66-72.
25. Baams L, Beek T, Hille H, Zevenbergen FC, Bos HM. Gender nonconformity, perceived stigmatization, and psychological well-being in Dutch sexual minority youth and young adults. A mediation analysis. Arch Sex Behav. 2013;42:765-73.
26. Bockting W, Miner MH, Romine R, Hamilton A, Coleman E. Stigma, mental health, and resilience in an online sample of the US transgender population. Am J Public Health. 2013;103:943-51.
27. Connolly MD, Zervos MJ, Barone CJ, Johnson CC, Joseph CL. The mental health of transgender youth: advances in understanding. J Adolesc Health. 2016;59:489-95.
28. Puckett JA, Maroney MR, Wadsworth LP, Mustanki B, Newcomb ME. Coping and discrimination: The insidious effects of gender minority stigma on depression and anxiety in transgender individuals. J Clin Psychol. 2019;76:176-94.
29. Rood BA, Maroney MR, Puckett JA, Berman AK, Reisner SL, Pantalone DW. Identity concealment in transgender adults: a qualitative assessment of minority stress and gender affirmation. Am J Orthopsychiat. 2017;18:704-13.
30. Smith AJ, Hallum-Montes R, Nevin K, Zenker R, Sutherland B, Reagor S, et al. Determinants of transgender individuals' well-being, mental health and suicidality in a rural state. Rural Ment Health. 2018;42:116-32.
31. Rood BA, Reisner SL, Surace FI, Puckett JA, Maroney MR, Pantalone DW. Expecting rejection: understanding the minority stress experiences of transgender and gender-nonconforming individuals. Transgend Health. 2016;1:151-64.
32. Scandurra C, Vitelli R, Maldonato NM, Valerio P, Bochicchio V. A qualitative study on minority stress subjectively experienced by transgender and gender nonconforming people in Italy. Sexologies. 2019;28:61-71.
33. Byne W, Karasic DH, Coleman E, Eyler AE, Kidd JD, Meyer-Bahlburg HF, et al. Gender dysphoria in adults: an overview and primer for psychiatrists. Transgend Health. 2018;3:57-A3.
34. Walter PB, Amets SS, Joz M, Adam S, Joshua DS, Madeline BD, et al. Language and trans health. Int J Transgend. 2017;18:1-6.
35. Rodrigues J, Lemos C, Figueiredo Z. Discriminação e barreiras ao acesso ao serviço nacional de saúde percecionados por pessoas trans. Rev Port Psiquiatria Saúde Mental. 2020;6:98-108.
36. Rothblum ED. The Oxford handbook of sexual and gender minority mental health. Oxford: Oxford University Press; 2020.
37. Portugal. Decreto-Lei n.º38/2018. Diário da República, I Série, n.º 151 (2018/08/07). p.3922-4.
38. Lew-Starowicz, M, Giraldi A, Krüger TH. Psychiatry and sexual medicine: a comprehensive guide for clinical practitioners. Hannover: Springer International Publishing; 2021.
39. Murad MH, Elamin MB, Garcia MZ, Mullan RJ, Murad A, Erwin PJ, et al. Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes. Clin Endocrinol. 2010;72:214-31.
40. Dhejne C, Van VR, Heylens G, Arcelus J. Mental health and gender dysphoria: a review of the literature. Int Rev Psychiatry. 2016;28:44-57.
41. Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, et al. Endocrine treatment of gender- dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2017;102:3869-903.
42. Heylens G, Verroken C, De Cock S, T'Sjoen G, Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with agender identity disorder. J Sex Med. 2014;11:19-26.
43. Direção-Geral da Saúde, Administração Central do Sistema de Saúde. Circular Normativa Conjunta. URGUS – Unidade do SNS para o acompanhamento de utentes no processo de reatribuição sexual. Lisboa: DGS; 2017.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Coping with Gender Dysphoria in a Rural Environment during Adolescence

Manifestações da Disforia de Género no Adolescente em Ambiente Rural

Ana Luísa RIBEIRO✉[1], Carlos MAGALHÃES VIEIRA[1], Marta PIRES RIBEIRO[1], Justino GONÇALVES[2], Paulo RIBEIRO[3]
Acta Med Port 2024 May;37(5):386-390 ▪ https://doi.org/10.20344/amp.19731

ABSTRACT

Gender dysphoria is socially more visible and discussed today, but still underdiagnosed. It refers to distress and/or impaired function caused by inconsistency between the sex assigned at birth and gender identification. Clinical manifestations are variable. Lack of training and investment in gender issues make the diagnosis and management in primary care complex, particularly in conservative and isolated communities, with poor access to information and specialized health services. We describe the diagnosis of gender dysphoria and use of a patient centered multidisciplinary and family approach in a 12-year-old rural born adolescent, assigned female at birth. Our aim is to raise awareness of early symptoms and signs of gender dysphoria and problems faced by transgender people and their families during childhood, leading to gender dysphoria, and we hope our successful approach might improve healthcare provision for these patients, particularly in rural areas.

Keywords: Adolescent; Gender Dysphoria; Gender Identity; Rural Population

RESUMO

A disforia de género adquiriu recentemente maior visibilidade social e mais espaço de debate público, mas permanece subdiagnosticada. Refere-se a um sofrimento e/ou impacto na funcionalidade, causados pela incongruência entre o sexo designado no nascimento e a identidade de género. As manifestações clínicas são variáveis. A falta de formação e investimento em questões de género dificultam o diagnostico e a abordagem em cuidados de saúde primários, particularmente em comunidades rurais, onde é mais complicado aceder a cuidados especializados e informação. Descrevemos o diagnóstico e a utilização de uma abordagem multidisciplinar, centrada no paciente e família, num adolescente de 12 anos, designado do sexo feminino ao nascimento, com identidade de género masculina. Pretende-se dar a conhecer sinais, sintomas e problemas enfrentados por alguns indivíduos transgénero na infância e respetivas famílias, que podem favorecer disforia de género, esperando que a abordagem utilizada contribua para melhorar os cuidados de saúde a estes utentes, nomeadamente em áreas rurais.

Palavras-chave: Adolescente; Disforia de Género; Identidade de Género; População Rural

INTRODUCTION

Gender dysphoria (GD) is defined by the Diagnostic and Statistical Manual of Mental Disorders 5 Text Revision™ (DSM-5 TR™) as a marked, persistent incongruence between one's experienced/expressed gender and the sex assigned at birth (at least six months) that leads to discomfort, significant distress, and/or impaired functioning.[1]

Puberty is related to a major body transformation, including the development of secondary sexual characteristics, which may worsen the child's discomfort and trigger GD. During adolescence, this can manifest in poor socialization, anxiety, depression, suicidal thoughts, and high-risk behaviors (e.g., illicit drug use, unprotected sexual activity).[2]

Screening and identification of early signs of GD is crucial to a child's or adolescent's wellbeing, but a lack of training makes management of GD in primary care complex and challenging, especially in more traditional, rural areas.[3]

We describe the diagnosis of GD and the implementation of a patient-centered multidisciplinary and family approach in a transgender adolescent, to enlighten early manifestations of GD and difficulties faced by trans people, but also by other elements of the lesbian, gay, bisexual, transgender, queer or questioning, intersex, asexual, and plus (LGBTQIA+) community, their families and primary care professionals from a rural environment.

CASE DESCRIPTION

AL (fictitious name) is a 12-year-old adolescent assigned female at birth, with no relevant past medical history, studying at the local school with good performance, currently in 8th grade. Being the youngest child of six, from a low-medium socioeconomic background and a rural nuclear family, AL's family history included moderate alcohol consumption (father) and previous major depressive disorder (mother – from 1995 to 2000 related to conflict in peer relationships). The relationship amongst family members was described as close and positive, especially with the mother and the oldest sister, who left the house to study abroad, but it was described as conflicting with the father. The genogram and family relationships are represented in Fig. 1.

The patient presented to a routine yearly primary health care checkup, accompanied by his mother. On examination, there was an evident evasive attitude, manifested by poor investment in speaking, yes or no answers only when questioned, and no effort to elaborate the conversation.

1. Medicina Geral e Familiar. Unidade Local de Saúde de Trás-os-Montes e Alto Douro. Chaves. Portugal.
2. Serviço de Psiquiatria da Infância e Adolescência. Unidade Local de Saúde de Trás-os-Montes e Alto Douro. Vila Real. Portugal.
3. Psicologia Clínica. Unidade Local de Saúde de Trás-os-Montes e Alto Douro. Vila Real. Portugal.
✉ **Autor correspondente:** Ana Luísa Ribeiro. analuisapiresribeiro@gmail.com
Recebido/*Received*: 05/02/2023 - **Aceite/*Accepted*:** 14/08/2023 - **Publicado *Online*/*Published Online*:** 22/01/2024 - **Publicado/*Published*:** 02/05/2024

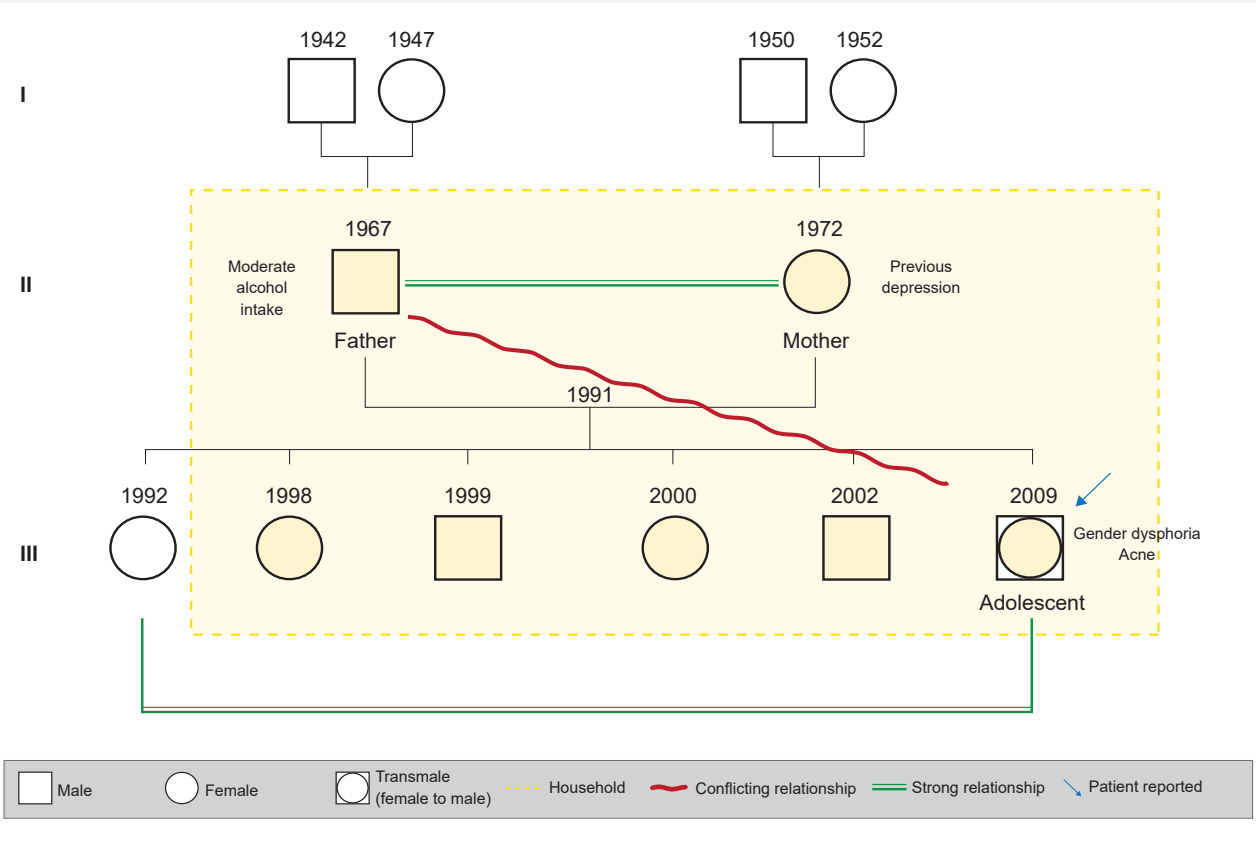


Figure 1 – Genogram and Mitchel Psychofigure in September 2021

The patient was dressed in loose-fitting sports clothing, and when body parts were exposed to perform blood pressure and abdominal examination, multiple patterned scars and some fresh superficial wounds on the forearms and abdomen were evident and appeared to be self-inflicted. It was also possible to ascertain the presence of hirsutism, vulgar facial-dorsal acne and overweight. The mother expressed concerns regarding an isolated episode of alcohol ingestion and a suicidal attempt with pills that, according to the patient, was not planned and occurred following a relationship breakdown with a 19-year-old girl whom the patient had met online, described as the first amorous experience. Both episodes were not disclosed beyond the mother and the child, and no healthcare professionals had been involved. The mother mentioned the child was struggling with anxiety, lack of sleep, poor socialization with peers/family and increased appetite. She also recalled that, as early as 2 years old, AL used to preferably play with the brother's toys instead of the sister's stereotyped 'girly' games, not appreciating dresses, skirts and pink clothes.

We started our approach by assessing the youth's concerns and sources of anxiety, related to being perceived as a girl by others, excessive weight, and acne. We also identified the presence of panic attacks at school as an active problem. A referral was made to the psychiatry department, and the case was discussed with a community psychologist, a nutritionist, and the school health team. Routine child visits were scheduled every two weeks. Laboratory and imaging work-up, including endocrine panel and pelvic suprapubic ultrasound were performed due to virilization signs but the results were unremarkable.

The cause of the scars and the motivation for the suicide attempt were only disclosed by the adolescent during the second medical appointment. The patient stated feeling uncomfortable with breast growth and menstrual bleeding and did not wish to achieve a masculine or female body image, even though he preferred to be addressed by a male name, currently used by the team. The patient also felt very disturbed by comments from colleagues about his appearance (e.g., "You will never be a real man") and constant disagreements with the father, who used to treat the adolescent as 'daddy's girl' before puberty began and the dynamic shifted into one of conflict and distance.

During the first three visits the patient seemed very

keen to cooperate. Contrasting with this pleasing behavior towards healthcare professionals, the patient became more depressed at home, revealed irritable mood, insomnia and school grades/performance decreased. At this point the patient was assessed by the local child and adolescent psychiatry department in the context of GD, where the diagnosis was confirmed, and sertraline 25 mg and quetiapine 50 mg were prescribed. A referral was also made by the primary care team to two centers for sexology and sexuality, one at a time, as requested by the mother and AL, in order to overcome breast growth and the development of female characteristics. Both centers declined the referral due to the lack of capacity to respond in reasonable time to patients outside their catchment area and also because AL was already followed by the local child and adolescent psychiatrist, who would be expected to be the one to actually make the referral if deemed necessary, according to one of the centers.

Acne, hirsutism and weight improved with lifestyle modifications and directed therapy (laser and topical treatment), but not mental wellbeing. Even with regular medical appointments, supportive psychotherapy, pharmacological therapy, and the attempt by the community school health team and school board members to promote an inclusive educational environment, the patient felt hopeless, suffering with social judgement and comments at school and beyond, and showed impaired concentration.

According to the mother, the patient continued to enroll in high-risk behaviors (alcohol and cannabis consumption), and the most serious incident culminated with his admission in a comatose state to the local emergency department during school hours due to binge ingestion of alcohol. AL was found alone and covered with ground dirt in an isolated area outside the school by the firefighters who were routinely patrolling the area. On admission, AL presented a blood alcohol content of 3.1 g/L and panel drug testing was negative. There were no signs of non-consensual sexual activity. After regaining consciousness, the adolescent regretted the episode and admitted to having skipped school, drinking alcohol, and smoking cannabinoids with older friends that day, who also reported feeling very ashamed.

That episode was a turning point. The father, previously described by both the mother and the patient as a rigid and conservative person, was called to participate. He revealed not being upset but rather confused and guilty with the severity of the situation. He seemed to realize the suffering his child was dealing with. A judicial complaint concerning the individuals who sold beverages to the minor was filed and the school was also involved. However, stigma towards the adolescent intensified since, living in a small city, the episode of emergency admission spread to the school community and other parents.

A care and safety plan was negotiated with both the parents and the patient. Some aspects that the adolescent thought to be helpful during the therapeutic process included transitioning to a new school in an urban area, parental support and acceptance of AL's gender expression and choices, and enrolling in pleasurable activities, like football and skating (unavailable in the previous area). The patient committed to sharing concerns with parents or healthcare professionals rather than colleagues or online, to avoid high-risk behaviors and to improve overall school performance. AL's parents and siblings made an effort to remain flexible with his choices, and parental assertiveness was maintained regarding rules and limits on core matters such as drugs and alcohol consumption, setting age-appropriate boundaries for social media use, and establishing limits on when and where the child can go out and with whom they should spend time.

As primary care clinicians, we became not only a source of support for both the patient and his family members, but also a resource in terms of information and guidance. Parental psychological support was also provided. During our approach, the assumption of a sick role was not encouraged, and positive reinforcement of achievements was provided.

One year later, the patient started art lessons at a new school. The depressive symptoms and cognitions (attention, learning and memory) improved. His social and academic skills improved, and AL stated that being addressed to by his preferred social name by teachers and colleagues added a sense of belonging. Parental support and reconnection with father translated in regaining the feeling of protection and love. Due to progressive development of secondary sexual characteristics, AL agreed to be referred to a pediatric endocrinology specialist. To our knowledge, he is not engaged in any sexual or romantic relationship. AL is currently observed every three months, alternating between the family physician, psychiatry and psychologist, and is weaning sertraline and quetiapine. Until the date of article acceptance, no referral was made to the sexology center by the child and adolescent psychiatrist.

The timeline of relevant events is summarized on Table 1.

DISCUSSION

Children with cross-gender identification are at risk of GD. Role playing during childhood and adolescence is not considered unusual, but some individuals might still be confused about their gender identity beyond puberty.[4,5] Even though watchful waiting and careful observation are reasonable approaches to GD during childhood, withholding medical intervention may do more harm than good.[2]

Family physicians are in a privileged position to identify

Table 1 – Timeline of relevant events

Timeline of relevant events	
2009	Birth of AL.
2011	From age 2, the mother recalls AL playing with the brother's toys instead of sister's 'girly' games, and not appreciating dresses, skirts or pink clothes.
2019/2020	Social withdrawal began due to the COVID-19 pandemic confinement and oldest sister leaving home to study abroad. Puberty began (menarche by the end of the year), reported anxiety related to female body and conflicts with the father.
7/2021	First amorous experience with a 19-year-old girl.
8/2021	Relationship breakup and beginning of self-mutilation and alcohol consumption. Symptoms of poor concentration, sleep disturbance and irritability. Panic attacks at school. First episode of suicide attempt with pills.
9/2021	Routine checkup 12-13 years old, started regular follow up (15 - 30 days) with family doctor, psychology, nutrition and school health team. Opened up with the family doctor about gender questioning on second appointment.
10/2021	First appointment with child and adolescent psychiatry department, started quetiapine and sertraline. School performance declined.
01/2022	Abandoned psychiatry follow-up, stating not feeling understood or improving. Referred to a center for sexology and sexual health by the family doctor, which alleged lack of resources for patients outside the catchment area and did not accept the referral.
04/2022	Rescheduled a second appointment with previous child and adolescent psychiatry department which confirmed the diagnosis of gender dysphoria. Sense of hopelessness. Suffers with social judgement and comments at school and beyond. Continued to engage in high-risk behaviors (alcohol and tobacco abuse).
05/2022	Admitted, unconscious, to the local emergency department from binge ingestion of alcohol and cannabinoids during school hours. Involvement of the father, negotiation and setting of a care and safety plan. Cessation of consumptions. New referral by the family doctor to a different center of sexology and sexual health, which did not accept the referral as AL was already being followed by a psychiatrist at the local hospital.
06/2022	Episode of binge drinking and consumptions spreading to school community and other parents, intensifying the stigma towards AL. Continued implementation of the care plan.
09/2022	Transition to a new urban school and enrollment in pleasurable activities. Started to sense acceptance by peers, family and school members. Improvement of depressive symptoms and cognitions. Gave two interviews to the local university to share the experience of being transgender.

gender diversity and maladaptive coping mechanisms and to promote healthy and positive outcomes due to their proximity with families and communities and continuity of care throughout the life cycle.[6] During childhood, these individuals may frequently prefer clothing, hairstyles, toys, activities, and playmates that are stereotypically considered more appropriate for the opposite sex, reflecting an innate preference of the child.[5,7] During this stage, particularly after the ages of five to six, their primary source of distress is related to their inability to be perceived by others as their authentic gender, which may result in mood or behavior problems. Gender dysphoria may intensify or emerge as they begin to understand the consistency of the designated gender, for example, through the development of genitalia. The desire for genitals that correspond with gender identity is a distinguished characteristic of GD (designated males may try to hide or even cut off their penises, and designated females may ask for a penis from their parents).[2,5,8] Consistent, persistent, and insistent gender-diverse behaviors and expression in prepubertal children appear to be associated with continued GD after puberty.[2,8,9] With the appearance of secondary sexual characteristics, the feeling that internal gender identity does not match their genitals might be enhanced and therefore aggravate distress, which may become overwhelming, leading to isolation, anxiety, depression, suicidality, and dangerous behavior (e.g., illicit drug use, unprotected sexual activity).[5] Therefore, early identification of children who are struggling with gender identity may help to prevent adverse mental and/or physical health consequences.

We have learned that, in these situations, a multidisciplinary and multi-dimensional family approach is recommended.[3,10] The treatment of GD in adults involves psychotherapy, hormonal treatment, and surgical treatment. Parental engagement, education, and coaching is key when approaching children with GD by increasing acceptance of gender fluidity and facilitating harmony between the child and their environment. Working with the school community is also important.[3]

The case described revealed that the lack of information, community discrimination, social isolation, and segregation during childhood may have a serious impact on mental health. This article also points to the fact already described in the literature that transgender adolescents in rural communities are at risk of drug use and self-harm, of being rejected by family and exploited or abused by adults during sexual initiation. Uncontrolled social media use and a lack of dialogue between family members seem to worsen the problem.

The literature suggests there are disparities in terms of information and mental health access in rural areas due to geographical barriers (transportation, time to travel, accommodation costs), financial difficulties, and education opportunities. The evidence also supports that schools in rural areas present significantly less exposure and access to other transgender adolescents, resources, and support groups, which means there is a tendency for lower levels of community belongingness.[11] An inclusive, comprehensive, patient-and family-centered intervention involving local health resources, school, and all household members contributed to a positive outcome.[3]

To the best of our knowledge, there are very few reports of GD in Portuguese adolescents. We have described our first case of GD diagnosis and management, a challenging case marked by advances and setbacks, requiring new skills and tools not provided during medical education, to keep up with gender lexicon and indiscriminatory supportive solutions (how to address a transgender patient, surveillance specificities and healthcare resources). As for the difficulties faced, the authors recommend that future efforts must be made to guarantee equal access to mental, sexology, and sexual health services, regardless of the patient's location, and that any barriers to the contact between primary care and secondary care services must fade. A validated questionnaire to screen gender dysphoria and a form to expedite the referral would have been very helpful to our clinical practice, given the limited resources available. Beyond medical practice, it is also essential to invest in the training of healthcare and education professionals and to promote the inclusion and wellbeing of gender minorities.

AUTHOR CONTRIBUTIONS

ALR: Study design, writing and critical review of the manuscript.

CMV, MPR: Writing and critical review of the manuscript.

JG, PR: Study design, writing, critical review and approval of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PARENTAL AND PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington DC; APA: 2022.
2. Forcier M, Olson-Kennedy J. Gender development and clinical presentation of gender diversity in children and adolescents. [cited 2022 Oct 13]. Available from: https://www.uptodate.com/contents/gender-development-and-clinical-presentation-of-gender-diversity-in-children-and-adolescents.
3. Malpas J. Between pink and blue: a multi-dimensional family approach to gender nonconforming children and their families. Fam Process. 2011;4:453-70.
4. National Health Service. Gender dysphoria. 2020. [cited 2022 Oct 13]. Available from: https://www.nhs.uk/conditions/gender-dysphoria/.
5. Kaltiala-Heino R, Bergman H, Tyolajarvi M, Frisén L. Gender dysphoria in adolescence: current perspectives. Adolesc Health Med Ther. 2018;9:31-41.
6. Olson J, Forbes C, Belzer M. Management of the transgender adolescent. Arch Pediatr Adolesc Med. 2011;165:171-6.
7. Fridell SR, Owen-Anderson A, Johnson LL, Bradley SJ, Zucker KJ. The playmate and play style preferences structured interview: a comparison of children with gender identity disorder and controls. Arch Sex Behav. 2006;35:729-37.
8. Wallien MS, Cohen-Kattenis PT. Psychosexual outcome of gender-dysphoric children. J Am Acad Child Adolesc Psychiatry. 2008;47:1413-23.
9. Steensma TD, McGuire JK, Kreukels BP, Beekman AJ, Cohen-Kettenis PT. Factors associated with desistence and persistence of childhood gender dysphoria: a quantitative follow-up study. J Am Acad Child Adolesc Psychiatry. 2013;52:582-90.
10. Prasad G, Aparna B. A case report of gender dysphoria with morbid jealousy in a natal female. Indian J Psychol Med. 2017;39:800-2.
11. Anderson H. Rural transgender and gender-nonconforming individuals' experiences with social media during adolescence. Minneapolis; Walden University: 2019.

ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Bikini Contact Dermatitis Due to Mercaptobenzothiazole

Dermatite de Contacto a Biquíni Secundária ao Mercaptobenzotiazol

Carolina FIGUEIREDO✉[1], Francisca CUNHA[2], Margarida GONÇALO[1]
Acta Med Port 2024 May;37(5):391-392 ▪ https://doi.org/10.20344/amp.20492

Keywords: Dermatitis, Allergic Contact/etiology; Latex Hypersensitivity/etiology; Textiles/adverse effects; Thiazoles/adverse effects
Palavras-chave: Dermatite de Contacto Alérgica/etiologia; Hipersensibilidade ao Látex/etiologia; Têxteis/efeitos adversos; Tiazóis/efeitos adversos

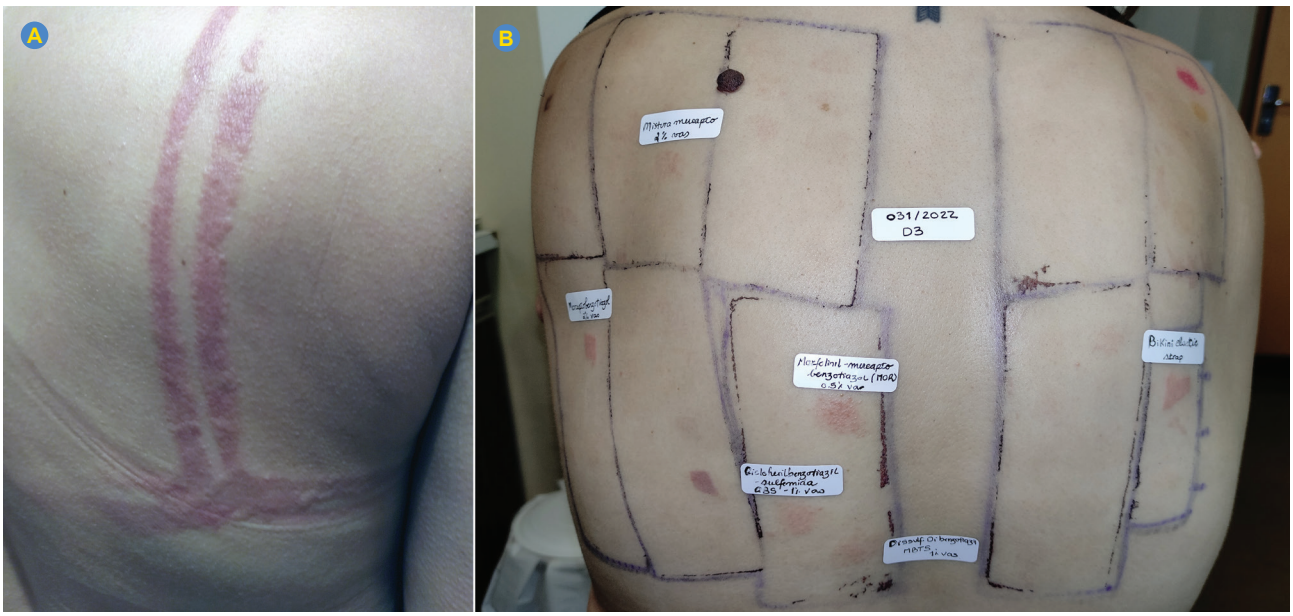


Figure 1 – Linear erythematous and edematous plaques distributed along the contact area with the rubber bands of the bikini straps (A); Patch test results on day three. Positive reactions were found to mercaptobenzothiazole 2.0% pet (+), mercapto mix 2% pet (+), N-cyclohexyl-2-benzothiazolesulfenamide 1% pet (+), 2-(4-morpholinylmercapto)benzothiazole 0.5% pet (+), dibenzothiazyl disulfide 1% pet (+) and bikini rubber straps 'as is' (+). The patient was advised to minimize exposure to rubber products (B).

A 30-year-old woman with no history of allergies or atopy presented with pruritic linear erythematous plaques distributed along the area of the bikini straps after wearing a wet bikini for several hours (Fig. 1A). Since allergic contact dermatitis (ACD) was suspected, patch testing was performed with the European Baseline Series, textile and rubber additives series and the dry bikini 'as is'. Positive reactions were found to the bikini straps 'as is' and to several rubber additives including Mercapto mix (+) and 2-Mercaptobenzothiazole 2.0% pet (+) (Fig. 1B), confirming the diagnosis of ACD. Textile contact dermatitis is a common condition caused by different allergens and irritants.[1] Mercaptobenzothiazole, an additive used in rubber products, is a frequent cause of hand and foot dermatitis by footwear and gloves.[1] However, ACD to rubber components in clothing is rarer.[2]

In this case, the allergic reaction only occurred with a wet swimsuit, pointing to the role of water in dissolving the mercaptobenzothiazole molecules from the rubber straps.

AUTHOR CONTRIBUTIONS

CF: Data collection and writing of the manuscript.
FC: Writing of the manuscript.
MG: Critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

1. Departamento de Dermatologia. Centro Hospitalar e Universitário de Coimbra. Coimbra. Portugal.
2. Departamento de Imunoalergologia. Centro Hospitalar e Universitário de Coimbra. Coimbra. Portugal.
✉ **Autor correspondente:** Carolina Figueiredo. ana.cda.figueiredo@gmail.com
Recebido/*Received*: 02/08/2023 - **Aceite/*Accepted*:** 17/11/2023 - **Publicado *Online*/*Published Online*:** 22/03/2024 - **Publicado/*Published*:** 02/05/2024

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Lisi P, Stingeni L, Cristaudo A, Foti C, Pigatto P, Gola M, et al. Clinical and epidemiological features of textile contact dermatitis: an Italian multicentre study. Contact Dermatitis. 2014;70:344-50.
2. Jung P, Sesztak-Greinecker G, Wantke F, Gotz M, Jarisch R, Hemmer W, et al. Bikini dermatitis due to mercaptobenzothiazole. Contact Dermatitis. 2006;54:345-6.

Médicos de Família e Nutricionistas nos Centros de Saúde, Comentário a "Hábitos Alimentares das Pessoas com Diabetes Mellitus Tipo 2 em Portugal: Um Estudo Transversal"

Family Physicians and Nutritionists in Health Centers, Commentary on "Eating Habits of People with Type 2 Diabetes Mellitus in Portugal: A Cross-Sectional Study"

Palavras-chave: Comportamento Alimentar; Diabetes Mellitus Tipo 2; Ingestão de Alimentos; Portugal
Keywords: Diabetes Mellitus, Type 2; Eating; Feeding Behavior; Portugal

Caro Editor,

No artigo "Hábitos Alimentares das Pessoas com Diabetes Mellitus Tipo 2 em Portugal: Um Estudo Transversal"[1] publicado em janeiro do corrente ano na Acta Médica Portuguesa, Rodriguez *et al* observaram que apenas pouco mais de um terço dos doentes com diabetes estudados (36,2%, n amostra = 550) obtiveram um *score* considerado saudável no *UK Diabetes and Diet Questionnaire*. Os autores constataram ainda que a maioria consumia pão diariamente, mas limitava o consumo de açucares.[1]

Estes resultados são preocupantes e sugerem uma potencial deterioração da dieta dos doentes com diabetes seguidos nos Cuidados de Saúde Primários, já que em 2009 partilhei no *Second Virtual Congress of General Practice and Family Medicine* (na altura organizado pelo *virtual GP/FM working group* da Associação Portuguesa de Medicina Geral e Familiar) dados sobre os hábitos alimentares de uma amostra de doentes com diabetes tipo 2 (n = 56) de um centro de saúde, com a maioria a realizar uma alimentação aproximadamente correta. À semelhança do estudo de Rodriguez *et al*[1] o pão era o hidrato de carbono mais ingerido. Contudo, o total consumido era inferior à dose diária recomendada. Carne/peixe (200 g/dia) foram as principais fontes de proteínas. Sopas, legumes, saladas e frutas eram ingeridos diariamente pela maioria da amostra. Além disso, a maioria evitava a ingestão de produtos ricos em óleos/gorduras, bem como doces e bebidas alcoólicas. Ainda nesta amostra, 95% afirmou estar informado pelo seu médico de família ou enfermeiro sobre as mudanças a realizar no seu estilo de vida.

Apesar de os dados destes dois estudos não serem diretamente comparáveis, pelas suas diferenças metodológicas, levantam-se importantes questões. Será que a amostra de Rodriguez *et al*[1] estava igualmente informada sobre as alterações no estilo de vida através da consulta médica/de enfermagem de diabetes nos respetivos centros de saúde? É conhecido o impacto benéfico da educação em saúde em indivíduos com diabetes para a adesão à dieta adequada e no controlo dos níveis de glicemia.[2] Será que no período entre os estudos se verificou uma redução da capacidade das equipas de família de melhor educarem os doentes com diabetes por si acompanhados? As recomendações internacionais aconselham a referenciação dos doentes com diabetes para educação nutricional individualizada e dirigida à diabetes no momento do diagnóstico e depois conforme as necessidades.[3] No presente momento, como médicos de família, com que facilidade conseguiríamos implementar estas recomendações nas nossas unidades funcionais? Saliento que já em 2022 a Ordem dos Nutricionistas reconhecia a marcada carência de nutricionistas nos antigos agrupamentos de centros de saúde.[4]

Apelo, assim, para que nas recém-criadas unidades locais de saúde (ULS) seja completamente executado (e até superado) o despacho n.º 6556/2018 do Secretário de Estado Adjunto e da Saúde de 2018 que implementa serviços de nutrição nas instituições do Serviço Nacional de Saúde,[5] para a tão necessária e desejada articulação e cooperação entre médicos de família e nutricionistas, sob a ótica da integração de cuidados e colaboração em equipa, atributos deste novo modelo organizativo.

CONFLITOS DE INTERESSE

O autor declara não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Rodriguez BC, Rosendo I, Coelho TI, Mendes PD, Rodrigues GS, Francisco AF, et al. Eating habits of people with type 2 diabetes mellitus in Portugal: a cross-sectional study. Acta Med Port. 2024;37:27-35.
2. Gvozdanović Z, Farčić N, Placento H, Lovrić R, Dujmić Ž, Jurić A, et al. Diet education as a success factor of glycemia regulation in diabetes patients: a prospective study. Int J Environ Res Public Health. 2019;16:4003.
3. Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KH, MacLeod J, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care. 2019;42:731-54.
4. Ordem dos Nutricionistas. Integração de nutricionistas no Serviço Nacional de Saúde. Ordem dos Nutricionistas: Observatório da Profissão; 2022. [consultado 2024 jan 13]. Disponível em: https://www.ordemdosnutricionistas.pt/documentos/observatorio/2022/SNS/Integracao_Nutricionistas_SNS_ON_V4.pdf.
5. Portugal. Despacho n.º 6556/2018, Saúde – Gabinete do Secretário de Estado Adjunto e da Saúde. Diário da República, II Série, n.º 127 (2018/07/04). p. 18560-1.

Filipe PRAZERES✉[1,2]
1. Unidade de Saúde Familiar Beira Ria. Gafanha da Nazaré. Portugal.
2. Faculdade de Ciências da Saúde. Universidade da Beira Interior. Covilhã. Portugal.
✉ **Autor correspondente:** Filipe Prazeres. filipeprazeresmd@gmail.com
Recebido/*Received*: 13/01/2024 - **Aceite/*Accepted*:** 09/02/2024 - **Publicado *Online*/*Published Online*:** 25/03/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21218

Fazer Mais e Melhor Relativamente ao Consumo de Álcool em Portugal Implica uma Mudança Social

To Do More and Better Regarding Portugal's Alcohol Consumption, a Social Change Is Needed

Palavras-chave: Consumo de Álcool; Prevenção Primária, Política Pública
Keywords: Alcohol Drinking; Primary Prevention; Public Policy

Caro Editor,

Na edição de junho de 2022 da vossa revista foi publicada uma carta ao editor intitulada "Consumo de Álcool em Portugal: Precisamos de Fazer Mais",[1] na qual se aborda o controlo do consumo de álcool no nosso país. Congratulamos o autor por enfatizar a importância de medidas de prevenção primária postas em prática no âmbito do aconselhamento simples nos cuidados de saúde primários (CSP) como estratégias fundamentais.

A utilização de instrumentos de rastreio, seguidos de aconselhamento simples, intervenção breve ou referenciação para cuidados especializados consoante a gravidade dos problemas associados ao consumo de álcool é uma ação precoce e custo-efetiva, principalmente no contexto dos CSP.[2] Todavia, em Portugal, a sua adoção ainda não foi sistematizada e introduzida na rotina dos profissionais, existindo apenas alguns casos experimentais e de boas práticas.

Salientamos que a abordagem efetiva dos problemas ligados ao álcool obriga à consideração e inclusão de políticas públicas no âmbito da prevenção primordial, visando proteger a saúde e o bem-estar da população exposta às bebidas alcoólicas. Medidas como o aumento de impostos e taxas e restrições à disponibilidade, acesso e *marketing* dos produtos são necessárias.[3] Apesar de estas medidas serem recomendadas pela Organização Mundial de Saúde (OMS) e por peritos internacionais e adotadas por inúmeros países, os governos e instituições nacionais têm demonstrado resistência à sua implementação e vulnerabilidade à influência económica, *playbook* e *lobby* da indústria do álcool.[4]

Uma vez que parece não existir um consumo de álcool seguro para a saúde, o seu consumo não deve ser recomendado.[5] Há décadas que é reconhecido como carcinogénico, associando-se a sete tipos de cancro, incluindo o cancro de mama. A nível populacional contribui para o aumento do risco de desenvolvimento das principais doenças crónicas não transmissíveis, assim como para o aumento do risco de suicídio, violência e criminalidade, atingindo mais incisivamente populações desfavorecidas e promovendo maior disparidade social e económica.[3]

A potenciação do rastreio, aconselhamento, referenciação e tratamento, tal como o treino dos profissionais é uma das prioridades do atual Plano de Ação Europeu para o Álcool, integrando a iniciativa SAFER da OMS. No entanto, mais importante ainda é reivindicar medidas políticas de mudança social. Um exemplo é o debate sobre a rotulagem e advertências em bebidas alcoólicas, que ocorre nas instâncias da União Europeia e tem recebido oposição no cenário político português, um direito à informação do consumidor que deve ser apoiado e concretizado pelas entidades de saúde pública.

Então o que fazer relativamente ao consumo de álcool em Portugal? Precisamos, realmente, de fazer mais e melhor.

CONTRIBUTO DOS AUTORES

Todos os autores contribuíram de igual forma para o desenho, implementação e elaboração do artigo.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Santos Coelho F. Consumo de álcool em Portugal: precisamos de fazer mais. Acta Med Port. 2022;35:504-14.
2. Angus C, Thomas C, Anderson P, Meier P, Brennan A. Estimating the cost-effectiveness of brief interventions for heavy drinking in primary health care across Europe. Eur J Public Health. 2017;27:345-51.
3. Babor TF, Casswell S, Graham K, Huckle T, Livingston M, Rehm J, et al. Alcohol: no ordinary commodity summary of the third edition. Addiction. 2022;117:3024-36.
4. Paixão MM, Mialon M. Help or hindrance? The alcohol industry and alcohol control in Portugal. Int J Environ Res Public Health. 2019;18:4554.
5. Anderson BO, Berdzuli N, Ilbawi A, Kestel D, Kluge, HP, Krech, R, et al. Health and cancer risks associated with low levels of alcohol consumption. Lancet Public Health. 2023;8:e6-7.

Francisca PULIDO VALENTE✉[1], Hilson CUNHA[2]
1. Unidade de Saúde Pública da Amadora. Unidade Local de Saúde Amadora Sintra. Amadora. Portugal.
2. Departamento de Medicina. Faculdade de Ciências da Saúde. Universidade da Beira Interior. Covilhã. Portugal.
✉ **Autor correspondente:** Francisca Pulido Valente. franciscavalente@campus.ul.pt
Recebido/*Received*: 14/12/2023 - **Aceite/*Accepted*:** 22/02/2024 - **Publicado *Online*/*Published Online*:** 27/03/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21100

Polymyalgia Rheumatica After COVID-19 Vaccination: Data from the EudraVigilance Database

Polimialgia Reumática Após Vacinação Contra COVID-19: Dados da Base EudraVigilance

Keywords: Adverse Drug Reaction Reporting Systems; COVID-19 Vaccines; Drug Monitoring; Pharmacovigilance; Polymyalgia Rheumatica
Palavras-chave: Farmacovigilância; Monitorização de Fármacos; Polimialgia Reumática; Vacinas Contra COVID-19; Sistemas de Notificação de Reações Adversas de Fármacos

Dear Editor,

Recently, the novel coronavirus (COVID-19) pandemic led to the rapid development of vaccines. Potential side effects have been notified on global pharmacovigilance databases, such as EudraVigilance, which contains reports of suspected adverse reaction (SAR) for drugs authorized in the European Union. These reports are generated by national competent authorities [such as Autoridade Nacional do Medicamento e Produtos de Saúde (INFARMED), the Portuguese medicines agency], marketing authorization holders, and sponsors of clinical trials. The Individual Case Safety Reports (ICSR) can be signaled by healthcare or non-healthcare professionals. Although incapable of establishing causality, the reporting of SAR can detect emerging safety signals concerning a specific drug, prompting further investigation.

Polymyalgia rheumatica (PMR) is an inflammatory disease characterized by pain and stiffness in the shoulder and pelvic girdle of older individuals. Although its cause remains unknown, environmental triggers, such as vaccination, might play a role.[1] It has been postulated that molecular mimicry and certain vaccine adjuvants might induce autoimmune syndromes after vaccination.[2] Indeed, reports of suspected cases of PMR following COVID-19 vaccination have been recently published.[3]

We aimed to identify suspected cases of PMR following COVID-19 vaccination, using data from the public version of EudraVigilance. We retrieved all ICSR signaled by healthcare professionals within the European Economic Area, containing a SAR of PMR between January 1, 2021, to May 1, 2023, attributed to COVID-19 vaccines approved by the European Medicines Agency. A detailed analysis of each ICSR was carried out to eliminate potential duplicates or cases of aggravated preexisting PMR. We performed a descriptive analysis of the available data, including sociodemographic variables, severity, and outcome of SAR.

During this period, of the 1 426 786 reports in EudraVigilance concerning SAR associated with COVID-19 vaccines, 433 (0.03%) included suspected PMR and met our inclusion criteria (Table 1). Most cases concerned women (n = 227; 52.4%) and individuals within an age range of 65 - 85 years (n = 273; 63.0%). mRNA vaccines were more frequently involved (n = 359; 82.9%) than viral vector-based vaccines. At least one criterion of seriousness was reported in 363 cases (83.8%), such as medically important conditions and hospitalization.

In conclusion, we found, through the use of the EudraVigilance database, a small number of PMR cases following COVID-19 vaccination, in comparison with the magnitude of other SAR. Although these findings are somewhat reassuring, COVID-19 vaccines will probably remain under close pharmacovigilance scrutiny over the next few years, and new potential adverse events might be encountered. The possibility of a causal effect between COVID-19 vaccines and the development of PMR is still poorly understood, requiring further data for clarification.

AUTHOR CONTRIBUTIONS

CPO: Study design, data collection and analysis, writing of the manuscript.

SFA, CV, ARP, AB: Study design, critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Falsetti P, Conticini E, Acciai C, Baldi C, Bardelli M, Gentileschi S, et al. Polymyalgia rheumatica following infective triggers or vaccinations: a different subset of disease? Reumatologia. 2020;58:76-80.
2. Chen Y, Xu Z, Wang P, Li XM, Shuai ZW, Ye DQ, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. Immunology. 2022;165:386-401.
3. Ottaviani S, Juge PA, Forien M, Ebstein E, Palazzo E, Dieudé P. Polymyalgia rheumatica following COVID-19 vaccination: a case-series of ten patients. Joint Bone Spine. 2022;89:105334.

Table 1 – Characteristics of individual case safety reports in the EudraVigilance database, containing a suspected adverse reaction of polymyalgia rheumatica from January 1, 2021 to May 1, 2023, attributed to COVID-19 vaccines approved by the European Medicines Agency.

Characteristic	n (%)
Year of Reporting	
- 2021	186 (43.0)
- 2022	203 (46.9)
- 2023[a]	44 (10.2)
COVID-19 vaccine type	
- mRNA vaccine	359 (82.9)
- Viral vector vaccine	74 (17.1)
Sex	
- Female	227 (52.4)
- Male	203 (46.9)
- Not specified	3 (0.7)
Age range	
- 18 to 64 years	119 (27.5)
- 65 to 85 years	273 (63.0)
- Older than 85 years	26 (6.0)
- Not specified	15 (3.5)
Suspected adverse reaction considered serious	363 (83.8)
Seriousness criteria[b]	
- Resulting in medically important conditions	259 (59.8)
- Requiring or prolonging hospitalization	80 (18.5)
- Resulting in disability/incapacity	42 (9.7)
- Resulting in death	1 (0.2)
Reaction outcome at time of report	
- Not recovered	194 (44.8)
- Recovering	154 (35.6)
- Recovered	29 (6.7)
- Recovered with sequelae	11 (2.5)
- Fatal	1 (0.2)
- Unknown	44 (10.2)
Suspected drug	
- Only COVID-19 vaccine	421 (97.2)
- Other suspected drug	12 (2.8)

[a]: Until May 1, 2023
[b]: Each case might meet more than one criterion

Cláudia PINTO OLIVEIRA✉[1,2], Sofia FERREIRA AZEVEDO[1,2], Carolina VILAFANHA[1,2], Ana Rita PRATA[1,2], Anabela BARCELOS[1,2]

1. Rheumatology Department. Centro Hospitalar do Baixo Vouga. Aveiro. Portugal.
2. Centro Académico Clínico Egas Moniz Health Alliance. Universidade de Aveiro. Aveiro. Portugal.

✉ **Autor correspondente:** Cláudia Pinto Oliveira. 71800@chbv.min-saude.pt

Recebido/*Received*: 11/12/2023 - **Aceite/*Accepted*:** 22/02/2024 - **Publicado *Online*/*Published Online*:** 12/04/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.20952

Anterior Cervical Cystic Lymphangioma in an Adult Patient

Linfangioma Cístico Cervical Anterior no Adulto

Keywords: Head and Neck Neoplasms; Lymphangioma, Cystic
Palavras-chave: Linfangioma Quístico; Neoplasias de Cabeça e Pescoço

Cystic lymphangioma (CL) is a rare benign tumour, located most frequently in the posterior cervical triangle.[1] Approximately 90% of these lesions are diagnosed before the age of two, and only a small number of cases are reported in adults.[1,2] Most patients are asymptomatic, although compressive symptoms, such as dysphagia, difficulty in breathing or hoarseness may occur.[1] Diagnosis is based on clinical findings, imaging methods and biopsy.[1,3] Surgery is the treatment of choice.[1,3]

A 50-year-old female presented with a large anterior cervical cystic mass, which we assumed to be a thyroglossal duct cyst (TDC), based on clinical and imaging findings. On objective examination, the patient presented an anterior cervical mass, mobile with swallowing and protrusion of the tongue. The cervical computed tomography (CT) revealed a large, homogeneous cystic lesion, 7.5 cm in highest diameter, centered in the anterior cervical region (Fig. 1). Up to this point of the investigation, the gathered information pointed to TDC as the likely diagnosis. The biopsy was inconclusive. Intraoperatively, the lesion we found was, surprisingly, highly suggestive of a CL, with no path being identified that could represent a thyroglossal duct (Fig. 2). The lesion was excised, and the postoperative period was uneventful. The histological examination confirmed the diagnosis. At six-month follow-up, the patient remained asymptomatic, with no evidence of recurrence. In this case, the uncommon location of the CL led to a probable preoperative diagnosis of TDC. Therefore, although CL is a rare entity in adults, it should be included in the differential diagnosis of a neck mass, even in atypical locations.

PREVIOUS AWARDS AND PRESENTATIONS

This work was presented as a poster and selected for presentation at the *33.º Encontro de Cirurgia - Cirurgia Geral Gaia*, in October 2023, in Vila Nova de Gaia, Porto.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

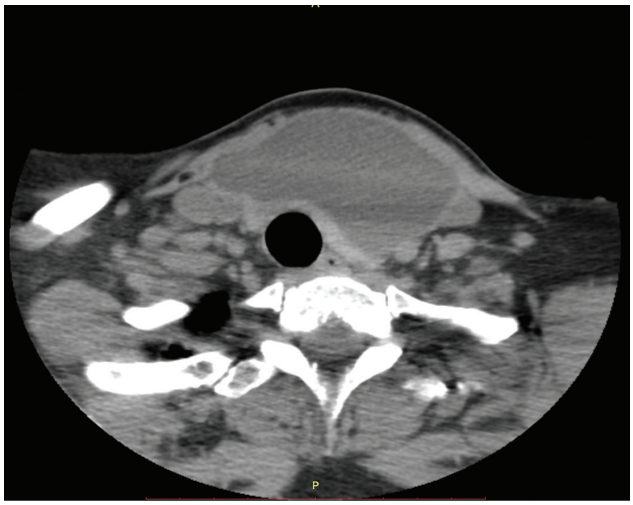


Figure 1 – Cervical CT scan demonstrating a large, homogeneous cystic lesion in the anterior cervical region, 7.5 cm in in highest diameter

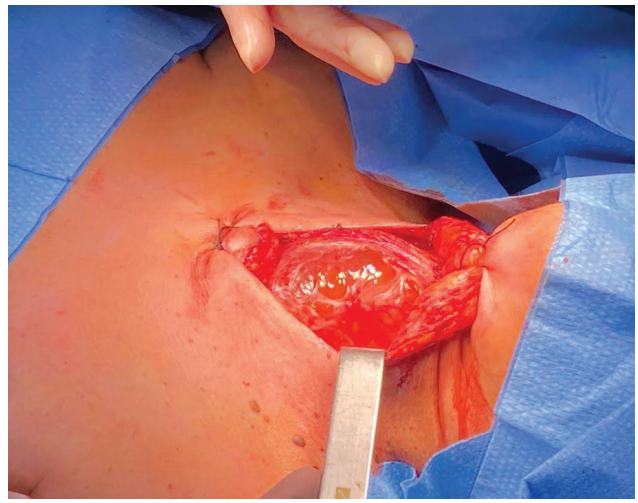


Figure 2 – Intra-operative identification of a lesion suggestive of cystic lymphangioma, with no path being identified that could represent a thyroglossal duct

REFERENCES

1. Tzortzis AS, Maniatakos VP, Tsintzos S, Tzortzis G. Cervical cystic lymphangioma in an adult patient. a case report of a rare entity. Acta Medica. 2021;64:224-6.
2. Wang J, Yang Y, Guo J, Yao Y, Dong L, Mou Y, et al. Cervical lymphangioma in adults: a report of seven cases and review of the literature. Laryngoscope Investig Otolaryngol. 2022;7:751-6.
3. Kaira V, Kaira P, Agarawal T. Cervical cystic lymphangiomas in adults: a case series of a rare entity with literature review. Head Neck Pathol. 2021;15:503-8.

Bárbara NETO CASTRO✉[1], Daniel MARTINS[1], David Afonso JOÃO[2], Susana GRAÇA[1], Manuel OLIVEIRA[1]

1. General Surgery Department. Centro Hospitalar Vila Nova de Gaia/Espinho. Vila Nova de Gaia. Portugal.
2. Department of Pathology. Centro Hospitalar de Vila Nova de Gaia/Espinho. Vila Nova de Gaia. Portugal.

✉ **Autor correspondente:** Bárbara Neto Castro. barbara91castro@gmail.com

Recebido/*Received*: 16/11/2023 - **Aceite/*Accepted*:** 22/02/2024 - **Publicado *Online*/*Published Online*:** 19/04/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.20960

Hamman's Sign: Rediscovering Cardiac Auscultation Through a Pneumomediastinum

Sinal de Hamman: Redescobrindo a Auscultação Cardíaca Através de um Pneumomediastino

Keywords: Chest Pain/diagnosis; Heart Auscultation; Mediastinal Emphysema/diagnosis
Palavras-chave: Auscultação Cardíaca/diagnóstico; Dor no Peito; Enfisema Mediastínico/diagnóstico

Pneumomediastinum and pericarditis are distinct etiologies of chest pain with unique mechanisms and specific treatments, but they can exhibit overlapping characteristics.

A 19-year-old male with well-controlled asthma and anti-hydroxy-3-methylglutaryl-co-enzyme A reductase (anti-HMGCR) inflammatory myopathy (IM) under corticosteroids, immunoglobulins and methotrexate, presented with three-day retrosternal pleuritic pain, triggered by a Valsalva maneuver during exercise at the gym. The patient had had an upper respiratory tract infection in the previous month. His physical examination was normal, except for a crackling noise noticed on the left border of the sternum, interpreted as a pericardial rub. The electrocardiogram (ECG) showed sinus rhythm with slight PR depression of the inferior leads and early repolarization pattern (Fig. 1). Serial troponins were negative. A transthoracic echocardiogram was unremarkable. A chest X-ray revealed a pneumomediastinum (Fig. 2). A computed tomography (CT) scan excluded complications. Given the absence of trauma, drug consumption, and any signs suggestive of Boerhaave syndrome (spontaneous rupture of the esophagus), a spontaneous origin was considered. The patient was successfully managed conservatively with mild analgesia and close clinical monitoring and was discharged on the ninth day of admission.

Spontaneous pneumomediastinum has a higher prevalence rate among male adolescents with asthma. It typically manifests with sudden pleuritic chest pain, associated with conditions that increase intrathoracic pressure. Physical exercise has previously been described as a trigger for pneumomediastinum and a history of an upper respiratory tract infection has also been linked to this condition. Pneumomediastinum has been reported in inflammatory myopathies.[1] Although there are no reported cases in patients with anti-HMGCR IM, the patient presented with a mild active disease, which made the authors question the inflammatory status as a risk factor.

Pneumomediastinum may present with a normal physical examination, but the presence of subcutaneous emphysema and mediastinal crunching sound on auscultation (Hamman's sign) is highly suspicious, despite being easily mistaken with other pre-cordial sounds. There are other reports where Hamman's sign on auscultation was misinterpreted as a pericardial rub leading to the false assumption of acute pericarditis.[2-4] Pericardial rubs result from the inflammation of the pericardium producing a 'scratchy' sound best heard within the left third intercostal space, leaning forward, after forced expiration. On the other hand, Hammam's sign results from the dissected air during systole, producing a 'crunching' and 'crackling' noise that is synchronous with the heartbeat.[5] It is noteworthy that within the medical literature, the term 'Hamman's sign/syndrome' may be used to denote both the radiological findings and the clinical syndrome associated with spontaneous pneumomediastinum.

Another complicating factor in the diagnosis is the presence of ECG changes: the slight depression of the inferior PR segment further strengthened the suspicion of pericarditis.

In conclusion, the diagnosis of pneumomediastinum can be challenging. This case emphasizes a frequently forgotten but revealing finding on physical examination: the

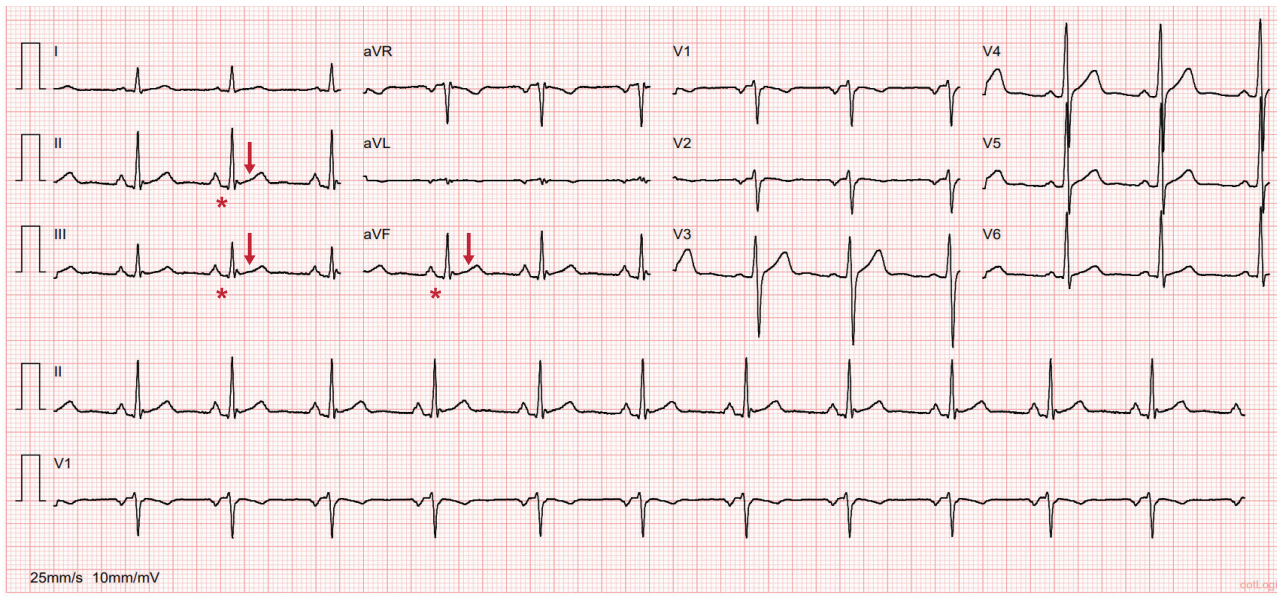


Figure 1 – Electrocardiogram showing slight inferior leads PR depression (*) and early repolarization pattern (arrow)

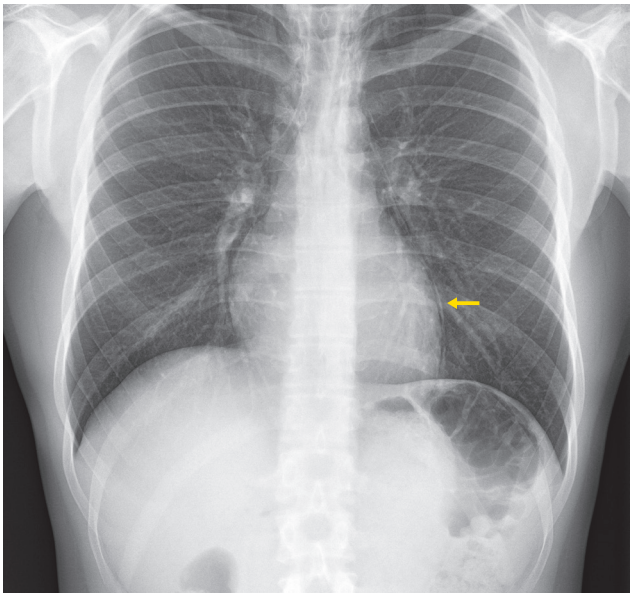


Figure 2 – Radiography of the chest showing pneumomediastinum (yellow arrow)

Hamman's sign. Also, it highlights the importance of anamnesis and auscultation in the differential diagnosis of chest pain.

AUTHOR CONTRIBUTIONS

MPS, AC, RC: Study design and writing of the manuscript.

MLC, ST: Critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Subki AH, Almani IM, Albeity A, Aljabri BK, Alsolaimani R, Halabi H. Spontaneous pneumomediastinum and subcutaneous emphysema in dermatomyositis: a case series and literature review. J Inflamm Res. 2023;16:1431-41.
2. Brugioni L, Niederhausern F, Gozzi C, Martella P, Romagnoli E, Aramini B, et al. Aurea diagnosis of pneumomediastinum. A case report. Ital J Med. 2020;14:179-83.
3. Chaudhary H, Yousaf Z, Nasir U, Waheed T, Syed K. Spontaneous pneumomediastinum mimicking acute pericarditis. Clin Case Rep. 2021;9:e05156.
4. Jimidar N, Lauwers P, Govaerts E, Claeys M. The clicking chest: what exactly did Hamman hear? A case report of a left-sided pneumothorax. Eur Heart J Case Rep. 2020;4:1-5.
5. Alexandre AR, Marto NF, Raimundo P. Hamman's crunch: a forgotten clue to the diagnosis of spontaneous pneumomediastinum. BMJ Case Reports. 2018;2018:bcr2018225099.

Mariana PEREIRA SANTOS✉[1,2], Andreia CAMPINAS[1,2], Rui COELHO[2,3], Maria Luísa CAIADO[1], Severo TORRES[1,2]

1. Cardiology Department. Centro Hospitalar Universitário de Santo António (CHUdSA). Porto. Portugal.
2. Instituto de Ciências Biomédicas Abel Salazar (ICBAS). School of Medicine and Biomedical Sciences. Universidade do Porto. Porto. Portugal.
3. Medicine Department. Centro Hospitalar Universitário de Santo António (CHUdSA). Porto. Portugal.

✉ **Autor correspondente:** Mariana Pereira Santos. marianapfdsantos@gmail.com

Recebido/*Received*: 18/12/2023 - **Aceite/*Accepted*:** 26/02/2024 - **Publicado *Online*/*Published Online*:** 08/04/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21115

O Respeito pela Capacidade de Decisão do Doente Tratado Involuntariamente ao Abrigo da Nova Lei de Saúde Mental

The Respect for the Decision-making Capacity of Patients Treated Involuntarily Under the New Mental Health Law

Palavras-chave: Portugal; Psiquiatria/legislação e jurisprudência; Psiquiatria/tendências; Saúde Mental/tendências
Keywords: Mental Health/trends; Portugal; Psychiatry/legislation & jurisprudence

Caro Editor,

Foi com interesse que lemos Fernando Vieira *et al*,[1] que bem sumariza os principais vetores de mudança na nova Lei de Saúde Mental (LSM).

Sem prejuízo da relevância dos demais, pretendemos densificar uma das principais concretizações da capacidade jurídica do doente em tratamento involuntário (TI), como preconizado pela Convenção dos Direitos das Pessoas com Deficiência (tratando-se aqui de "incapacidades duradouras físicas, mentais, intelectuais ou sensoriais, que em interação com várias barreiras podem impedir a sua plena e efetiva participação na sociedade em condições de igualdade com os outros").[2]

De acordo com a nova LSM, a pessoa em TI tem o especial dever de submissão ao tratamento, sem prejuízo de "participar, na medida da sua capacidade, na elaboração e execução do respetivo plano de cuidados e ser ativamente envolvida nas decisões (...) do processo terapêutico", tendo em atenção que "as restrições aos direitos, vontade e preferências (...) são as estritamente necessárias e adequadas à efetividade do tratamento, à segurança e à normalidade do funcionamento da unidade de internamento".[3]

Além da harmonização com o regime das Diretivas Antecipadas de Vontade, assinalamos aqui uma mudança de paradigma no tratamento coercivo da doença mental.

Segundo a anterior LSM, o tratamento era decidido de acordo com o melhor interesse médico, sinónimo do melhor tratamento disponível para o caso em particular (com a devida exceção da psicocirurgia), ao impor que "o internado tem o especial dever de se submeter aos tratamentos medicamente indicados", sem prever qualquer participação no seu plano de tratamento.[4]

Tal decorria não só de uma presunção de incapacidade para essa participação, como lhe era negada uma decisão de substituição (onde se incluem as Diretivas Antecipadas de Vontade, o Procurador de Cuidados de Saúde ou até o envolvimento de familiares), em contramão com o doente avaliado como incapaz para consentir um tratamento numa enfermaria médico-cirúrgica (internado por patologia não psiquiátrica),[5] caso em que se procede de acordo com o melhor interesse do doente, mesmo quando este não coincide com o melhor interesse médico, respeitando, assim, a Convenção de Oviedo.[6]

O novo regime não implica uma inversão completa, mas o melhor interesse médico tem agora de ser temperado com o interesse do doente, salvaguardada a "efetividade do tratamento" e "segurança (...) da unidade de internamento". Implica, também, a avaliação da capacidade de decisão do doente para participar no seu plano de tratamento, um desafio acrescido à equipa que o assiste.

Com estas alterações, calibrou-se a restrição do direito à liberdade subjacente ao TI em Portugal, corrigindo-se aquele que era o meio menos restritivo possível para o levar a cabo (princípio estruturante da LSM), que tem agora uma maior amplitude, com reconhecimento na lei de um espaço de reserva de capacidade de escolha (e, portanto, jurídica) do doente.

CONFLITOS DE INTERESSE

O autor declara não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Vieira F, Cabral A, Trancas B, Almeida F, Barreto H, Robalo I, et al. Novos tempos, novas realidades, novas leis: a continuidade, a mudança e os novos-velhos desafios em psiquiatria e saúde mental em Portugal. Acta Med Port. 2023;36:773-5.
2. Portugal. Resolução da Assembleia da República n.º 56/2009. Diário da República, I Série, n.º 146 (2009/07/30). p.4906-29.
3. Portugal. Lei n.º 35/2023. Diário da República, I Série, n.º 141 (2023/07/21). p.2-23.
4. Portugal. Lei n.º 36/1998. Diário da República, I Série A, n.º 169 (1998/07/24). p.3544-50.
5. Vicente F, Nascimento M, Oliveira C, Tomé C, Vieira C, Luís A. Avaliação da capacidade de decisão em Psiquiatria de Ligação. Psilogos. 2016;14:38-49.
6. Portugal. Resolução da Assembleia da República n.º 1/2001. Diário da República, I Série A, n.º 2 (2001/01/03). p.14-36.

Filipe VICENTE✉[1]
1. Serviço de Psiquiatria e Saúde Mental. Hospital Garcia de Orta. Unidade Local de Saúde de Almada-Seixal, EPE. Almada. Portugal.
✉ **Autor correspondente:** Filipe Vicente. filipe.l.vicente@gmail.com
Recebido/*Received*: 07/02/2024 - **Aceite/*Accepted*:** 04/03/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21352

Levodopa-Carbidopa: Um Caso Incomum de Intoxicação Medicamentosa Voluntária

Levodopa-Carbidopa: An Unusual Case of Voluntary Drug Intoxication

Palavras-chave: Antiparkinsonianos/intoxicação; Levodopa/intoxicação; Overdose de Medicamento/complicações
Keywords: Antiparkinson Agents/poisoning; Drug Overdose/complications; Levodopa/poisoning

Poucos são os casos conhecidos de intoxicação medicamentosa voluntária com levodopa-carbidopa de ação prolongada. Na quase inexistente literatura, apresenta-se com taquicardia, xerostomia, retenção urinária, alucinações, hipotensão transitória e, dada a ação prolongada, a sintomatologia poderá perdurar no tempo ou ocorrer em picos.[1]

Apresentamos o caso de uma mulher de 64 anos de idade, autónoma, com antecedentes conhecidos de perturbação depressiva (com internamento prévio na Psiquiatria), asma, hipertensão arterial, doença de Parkinson, portadora de derivação ventrículo-peritoneal por hidrocefalia, com seguimento médico irregular. Estava medicada habitualmente com levodopa-carbidopa-entacapona, ácido alendrónico, bisoprolol, venlafaxina, clobazam, esomeprazol, monteluscate, oxibutinina e pregabalina. Ingeriu 50 comprimidos de levodopa-carbidopa-entacapona (200 + 50 + 200 mg) duas horas antes da ativação de meios de emergência pré-hospitalar. Foi admitida na sala de reanimação, com alucinações visuais e agitação psico-motora, objetivando-se abertura ocular espontânea, pupilas midriáticas não reativas, discurso incoerente, pontuando 13 na escala de coma de Glasgow (O4, V4, M5), taquicardia e icterícia. Foi submetida a lavagem gástrica, com posterior administração de 50 g de carvão ativado. Após algaliação, por retenção urinária e para monitorização dos débitos urinários, observou-se saída de urina vermelho-fluorescente (Fig. 1). Dos exames complementares de diagnóstico realizados, destacava-se alcoolémia de 61 mg/d (acima do limite de 50 mg/dL), bilirrubina sérica e transaminases dentro dos valores de referência. Apresentava ainda benzodiazepinas na urina; o eletrocardiograma evidenciava ritmo sinusal sem alterações agudas.

Figura 1 – Saco coletor com urina vermelho-fluorescente imediatamente após algaliação na sala de reanimação

Foi transferida para a Unidade de Cuidados Intermédios, com os diagnósticos de intoxicação medicamentosa voluntária com parkinsonismo secundário e síndrome depressivo recorrente. Observaram-se dois episódios de hipotensão e seis de taquicardia autolimitados. Manteve-se tratamento de suporte com oxigenoterapia, fluidoterapia massiva e diuréticos. A melhoria do estado neurológico foi notória, tal como hemodinâmica e dos parâmetros analíticos.

Foi observada pela Psiquiatria ao quarto dia dada a sua perturbação depressiva recorrente, fortemente relacionada com a situação clínica subjacente, que a vinha a tornar cada vez mais dependente de terceiros nos meses anteriores. Por manter parkinsonismo assimétrico ligeiro de predomínio direito com algum grau de rigidez e sem tremor, reintroduziu-se, com apoio da Neurologia, levodopa, e iniciou-se o plano de reabilitação. À data da alta apresentava-se calma, com discurso coerente e organizado, manifestando arrependimento para o gesto autolítico, aceitando a proposta terapêutica.

Neste caso, as alterações do estado de consciência e hipotensão foram interpretadas no contexto de intoxicação por levodopa, enquanto a icterícia e coloração da urina se deveram à intoxicação por entacapona (a hipótese de insuficiência hepática como causa de icterícia foi excluída dado a doente não apresentar evidência laboratorial de lesão hepática e hiperbilirrubinémia), os mecanismos subjacentes aos quais se encontram descritos noutras fontes bibliográficas.[1,2]

CONTRIBUTO DOS AUTORES

SAC: Colheita e interpretação de dados, redação do artigo,
CJ, MV: Colheita de dados, revisão crítica do artigo.
RFA, TM: Revisão crítica do artigo.

PROTEÇÃO DE PESSOAS E ANIMAIS

Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial atualizada em 2013.

CONFIDENCIALIDADE DOS DADOS

Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação de dados.

CONSENTIMENTO DO DOENTE

Obtido.

CONFLITOS DE INTERESSE

Os autores declaram não ter conflitos de interesse relacionados com o presente trabalho.

FONTES DE FINANCIAMENTO

Este trabalho não recebeu qualquer tipo de suporte financeiro de nenhuma entidade no domínio público ou privado.

REFERÊNCIAS

1. Gael D, Christophe R, Françoise F. Acute overdose with controlled-release levodopa-carbidopa. Clin Toxicol. 2008;46:274-7.
2. Sun HL, Seong JY, Seokyong R, Seung WC, Hye JK, Tae KK, et al. Levodopa-carbidopa-entacapone overdose presenting as altered mental status, xanthoderma, and yellowish sclera. Signa Vitae. 2018;14:75-7.

Sara ALEIXO CABRITA✉[1], Catarina JORGE[1], Miguel VARELA[2], Rui FERREIRA ALMEIDA[2], Tatjiana MIHAILOVIC[1]
1. Serviço de Medicina Interna 2. Centro Hospitalar e Universitário do Algarve. Faro. Portugal.
2. Serviço de Medicina Intensiva 1. Centro Hospitalar e Universitário do Algarve. Faro. Portugal.
✉ **Autor correspondente:** Sara Aleixo Cabrita. sara.aleixo.d@gmail.com
Recebido/*Received*: 29/12/2023 - **Aceite/*Accepted*:** 08/03/2024 - **Publicado *Online*/*Published Online*:** 10/04/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21161

Improving the Care of Hip Fracture Patients Through Orthogeriatrics

Melhorando o Tratamento dos Doentes com Fratura da Extremidade Proximal do Fémur Através da Ortogeriatria

Keywords: Health Care Costs; Health Services for the Aged; Hip Fractures/therapy
Palavras-chave: Custos de Cuidados de Saúde; Fracturas do Colo do Fémur/tratamento; Serviços de Saúde para Idosos

Dear Editor,

We appreciated the recent letter to the editor by Barcelos *et al* addressing the costs of hip fractures (HF) in postmenopausal women in Portugal.[1] The authors rightly highlight HF as a public health concern due to their high incidence, costs, and morbimortality. We fully support their emphasis on prevention and the proposed indicators for primary care use.

While primary prevention is crucial, we believe it is essential to shed light on the current landscape of HF acute care. Most HF cases involve older patients, with over 95% attributed to falls. These fractures result from a combination of bone fragility and an increased fall risk.[2] The vulnerable clinical profile of older HF patients, including multimorbidity and geriatric syndromes, contributes to a higher risk of perioperative complications and poor surgical outcomes, mortality (approximately 20%), gait impairment and permanent disability (approximately 50%).[2]

To address this clinical complexity, prestigious scientific societies and healthcare systems advocate for the multidisciplinary co-management of acute fractures.[2] Orthogeriatric care models, involving collaboration between Traumatology and Geriatrics, have demonstrated improved clinical outcomes and cost-effectiveness.[2] However, in many Portuguese hospitals, older patients with HF are exclusively managed by orthopedic surgeons, and so the care regarding acute complications, chronic conditions, fall risk assessment, and osteoporosis treatment may be overlooked. Portugal's performance in HF surgery, according to the Organisation for Economic Co-operation and Development's (OECD) "Health at a Glance 2023" report, falls short, with only 46.5% undergoing surgery within 48 hours (*versus* the OECD average of 80.1%).[3] Delayed surgery beyond 48 hours increases one-month mortality by 41.5%.[4] Orthogeriatric input can reduce time-to-surgery.[2]

The conventional orthopedic care model, with no multidisciplinary approach, pose unnecessary risks and increase the risk of adverse events. Collaboration between internists trained in geriatrics and orthopedic surgeons is not just feasible but crucial. The implementation of Orthogeriatric care pathways aims to address fractures through a multidisciplinary approach, with the primary goal of reducing morbidity, mortality, and enhancing functionality.[2]

The relatively few existing orthogeriatrics units face challenges in gaining acceptance and recognition from peers and hospital managers.[5] Additionally, there is an urgent need for the widespread adoption of perioperative management for HF patients[6] supported by an anesthesiology team, and a Fracture Liaison service with support from a Rheumatology team.[7] However, the optimal multidisciplinary team for hip fracture management should ideally comprise a diverse array of professionals, such as geriatricians, orthopedic surgeons, anesthesiologists, rheumatologists, physiatrists, physiotherapists, occupational therapists, nutritionists, specialized nurses, social workers, psychologists, and clinical pharmacologists. The recently established Fragility Fracture Network - Portugal, supported by its international counterpart, will address all of these challenges.

The undeniable evidence supporting the cost-effectiveness and improved outcomes of orthogeriatrics units underscores the need to overcome ideological misconceptions. It is crucial to prioritize the maintenance of functionality and quality of life for older individuals while ensuring the sustainability of health services.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

MA has received support from Boehringer-Ingelheim, Bristol-Myers-Squibb, Merck Sharp & Dohme, AstraZeneca, Tecnimede, and Bayer for attending meetings and/or travel.

SD has received payment for expert testimony from Escola Nacional de Saúde Pública; is part of the executive board of the European Geriatric Medicine Society; is part of Núcleo de Geriatria da Sociedade Portuguesa da Medicina Interna, and Fragility Fracture NetworkFFN Portugal.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Barcelos A, Gonçalves J, Mateus C, Canhão H, Rodrigues AM. Costs of hip fractures in postmenopausal women in Portugal: a study from the payer's perspective. Acta Med Port. 2023;36:848-9.
2. Falaschi P, Marsh D, editors. Orthogeriatrics: the management of older patients with fragility fractures. 2nd ed. Cham: Springer; 2021.
3. Organisation for Economic Co-operation and Development. Health at a Glance 2023 Country Note - Portugal. [cited 2024 Mar 22]. Available from: https://www.oecd.org/portugal/health-at-a-glance-Portugal-EN.pdf
4. Shiga T, Wajima Z, Ohe Y. Is operative delay associated with increased mortality of hip fracture patients? Systematic review, meta-analysis, and meta-regression. Can J Anaesth. 2008;55:146-54.
5. Magalhães P, Gonçalves M, Silva F, Fernandes T, Oliveira A, Veríssimo R. Implementation of orthogeriatrics in Portugal. Cureus. 2023;15:e35361.
6. Carteiro J, Dinis M, Valente J, Resende A. #35900 POMAHR – perioperative management of patient with hip fracture in Centro Hospitalar Universitário Lisboa Norte (CHULN). Reg Anesth Pain Med. 2023;48:sA227.
7. Silva SP, Mazeda C, Vilas-Boas P, Portelada M do C, Eugénio G, Barcelos A. The impact of a Fracture Liaison service after 3 years on secondary fracture prevention and mortality in a Portuguese tertiary center. Arch Osteoporos. 2023;19:4.

Mariana ALVES[1,2], Sofia DUQUE[3,4,5]

1. Faculdade de Medicina. Universidade de Lisboa. Lisboa. Portugal.
2. Unidade de Ortogeriatria. Serviço Medicina. Centro Hospitalar Lisboa Norte. Lisboa. Portugal.
3. Instituto de Medicina Preventiva e Saúde Pública. Faculdade de Medicina. Universidade de Lisboa. Lisboa. Portugal.
4. Hospital Cuf Descobertas. Lisboa. Portugal.
5. Núcleo de Estudos de Geriatria. Sociedade Portuguesa de Medicina Interna. Lisboa. Portugal.

✉ **Autor correspondente:** Mariana Alves. marianaalves88@gmail.com

Recebido/*Received*: 31/12/2023 - **Aceite/*Accepted*:** 11/03/2024 - **Publicado *Online*/*Published Online*:** 24/04/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21169

An Algorithm for Waiting Times between Imaging Studies with Contrast Media and Prevention of Interference in Clinical Laboratory Tests

Algoritmo para Tempos de Espera entre Exames de Imagem com Meios de Contraste e Prevenção de Interferência em Testes Laboratoriais

Palavras-chave: Algoritmos; Guidelines de Prática Clínica; Meios de contraste/normas; Técnicas laboratoriais clínicas/métodos
Keywords: Algorithms; Clinical Laboratory Techniques/methods; Contrast Media/standards; Practice Guidelines

To the Editor,

Safety and appropriateness are at the core of diagnostic test prescribing, which contribute to a value-based approach and good use of healthcare resources. However, it is well established that clinicians are often unaware, unfamiliar, in disagreement, or fail to implement guidelines when making referrals, either to radiological imaging or clinical laboratory tests.[1,2]

Contrast-enhanced imaging studies like computed tomography (CT) and magnetic resonance (MR) are critical for the diagnosis and follow-up of a wide array of diseases and are usually of two types: iodine-based and gadolinium-based media, respectively.[3] Contrast media (CM) are mostly eliminated by glomerular filtration but also by hepatic excretion of up to 50% in the case of gadolinium-based media.[4,5] In patients with normal glomerular filtration rate (90 mL/min/1.73 m^2), the half-life of both contrast media in plasma is close to two hours, increasing progressively up to 30 hours in those with advanced kidney impairment (< 30 mL/min/1.73 m^2).[4] Therefore, kidney function should be determined beforehand by means of the estimated glomerular filtration rate (eGFR) for all patients undergoing contrast-enhanced imaging studies, within seven days for those with kidney impairment, and within three months for all other patients.[3]

Recently, the Contrast Media Safety Committee (CMSC) of the European Society of Urogenital Radiology (ESUR) issued guidelines on waiting times between imaging studies with intravascularly administered contrast media, namely, successive administration of iodine-based contrast in CT, gadolinium-based contrast in magnetic resonance (MR), or a combination of both.[5] These recommendations are meant to avoid the accumulation of CM with potential safety issues, namely nephrotoxicity, and to avoid interference between imaging studies, as iodine-based contrast influences MR signal intensity and gadolinium-based contrast influences CT attenuation. Interference of CM with clinical laboratory tests has also been addressed by the CMSC of ESUR along with the Preanalytical Working Group of the European Society of Laboratory Medicine (PWG-EFLM) Science Committee, through the development of recommendations to perform those prior to radiological imaging with CM or to delay blood or urine collection based on clearance kinetics and the patient's kidney function.[4]

Based on both guidelines, a single algorithm (Fig. 1) was developed that can be used by prescribing clinicians and by Radiology and Laboratory professionals to schedule

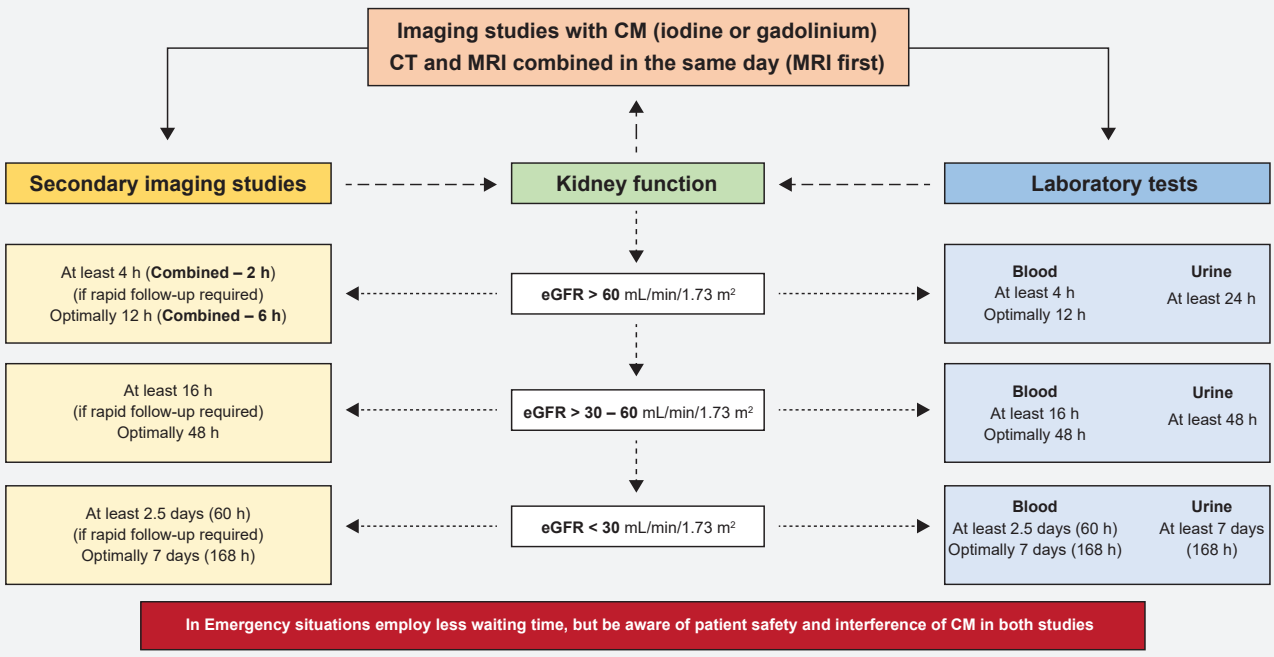


Figure 1 – Algorithm for waiting times between imaging studies with contrast media and prevention of interference in clinical laboratory tests
CM: contrast media; CT: computed tomography; MRI: magnetic resonance imaging; eGFR: estimated glomerular filtration rate

imaging studies with CM and clinical laboratory tests in a safe and timely manner. Adherence to this algorithm has the potential to ensure best practice and prevent patients from facing clinically important adverse events resulting from CM interference.

COMPETING INTERESTS

The author has declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Bouëtté A, Karoussou-Schreiner A, Ducou Le Pointe H, Grieten M, de Kerviler E, Rausin L, et al. National audit on the appropriateness of CT and MRI examinations in Luxembourg. Insights Imaging. 2019;10:54.
2. Devis L, Catry E, Honore PM, Mansour A, Lippi G, Mullier F, et al. Interventions to improve appropriateness of laboratory testing in the intensive care unit: a narrative review. Ann Intensive Care. 2024;14:9.
3. European Society of Urogenital Radiology Contrast Media Safety Committee. ESUR guidelines on Contrast Agents v10.0. Vienna: ESUR; 2018.
4. van der Molen AJ, Krabbe JG, Dekkers IA, Geenen RW, Bellin MF, Bertolotto M, et al. Analytical interference of intravascular contrast agents with clinical laboratory tests: a joint guideline by the ESUR Contrast Media Safety Committee and the Preanalytical Phase Working Group of the EFLM Science Committee. Clin Chem Lab Med. 2023;62:608-14.
5. van der Molen AJ, Dekkers IA, Geenen RW, Bellin MF, Bertolotto M, Brismar TB, et al. Waiting times between examinations with intravascularly administered contrast media: a review of contrast media pharmacokinetics and updated ESUR Contrast Media Safety Committee guidelines. Eur Radiol. 2024;34:2512-23.

Francisco FREITAS✉[1]
1. Microbiology Laboratory. Department Clinical Pathology. Viseu Dão-Lafões Local Health Unit. Viseu. Portugal.
✉ **Autor correspondente:** Francisco Freitas. francyske@gmail.com
Recebido/*Received*: 31/01/2024 - **Aceite/*Accepted*:** 18/03/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21296

Using Large Cohort Data to Strengthen Information-Based Public Health Policies: An Appeal to Portuguese Authorities

Utilização de Grandes Bases de Dados Longitudinais para Fortalecer as Políticas de Saúde Pública Baseadas em Informação: Um Apelo às Autoridades Portuguesas

Keywords: Biomedical Research; Health Information Management; Datasets; Portugal; Public Health; Registries; Research Design
Palavras-chave: Datasets; Desenho de Investigação; Gestão da Informação em Saúde; Investigação Biomédica; Portugal; Registos; Saúde Pública

Dear Editor,

Everyday millions of bytes of data are generated by routine activities of healthcare systems. Nevertheless, health researchers opt for primary data collection. This decision is often justified by the low quality of existing data, legal and bureaucratic processes impeding timely access, and/or important discrepancies between the needed data and the data that is available.

In Portugal, national data is siloed. Health data is collected in different datasets, is not interoperable or linked, with one identifier per dataset and several data 'owners'. Therefore, health data is not being used to anywhere near its full potential, leading to 'data wastage', hampered research and development (R&D) competitiveness, increased costs, and potentially slower responses to emerging health problems.

We argue that improved, ethical usage of national data registries to support public health decisions is paramount to Portuguese R&D strategy, competitiveness, and building an epidemiological milieu. Some of the research priorities funded through national and international research agencies can be addressed through the analysis of this data, allowing for more complex analyses, faster results, and a lower cost.

The existing unclear, unstructured processes for accessing data are a great disadvantage for Portuguese researchers. Even in cases where researchers are granted access, not all the necessary data to test the hypothesis are provided (e.g., date of birth, borough/parish, sex). Some can be denied due to concerns regarding confidentiality/anonymity of subjects in the datasets, making testing for potential confounders in the data *de facto* impossible)

Having clear paths to access big datasets would increase the relevance, efficiency and usefulness of the data collection, and its quality. Having several dataset users can help in identifying errors and pitfalls, bridging information needs and demand for data.

The Nordic countries are an example to follow, where national registries and the use of a single unique identifier enable the development of large cohort studies involving millions of participants,[1-3] with adequate censoring for death and migration, based on individual-level data collected for administrative purposes, either individually or per groups of countries.[4]

In Denmark, for instance, researchers can access anonymized raw data, use the Statistics Denmark's online research machine to analyze large datasets and transfer the results of the analysis afterwards.[5]

It is our hope that the Portuguese authorities, including the Ministries of Health, Education, Science and Technology will be inspired by these examples and derive a strategy to increase access and usefulness of the national registries, otherwise, Portuguese researchers and the country will lose its R&D competitiveness.

AUTHOR CONTRIBUTIONS

IF: Study design and writing of the manuscript.

FSB, CSB, PF, HB: Study design and critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

Fundação para a Ciência e Tecnologia ref. EXPL/SAU-EPI/0067/2021.

REFERENCES

1. Rod NH, Andersen TO, Severinsen ER, Sejling C, Dissing A, Pham VT, et al. Cohort profile: The SmartSleep Study, Denmark, combining evidence from survey, clinical and tracking data. BMJ Open. 2023;13:e063588.
2. Karlstad Ø, Hovi P, Husby A, Härkänen T, Selmer RM, Pihlström N, et al. SARS-CoV-2 vaccination and myocarditis in a Nordic cohort study of 23 million residents. JAMA Cardiol. 2022;7:600-12.
3. Maret-Ouda J, Tao W, Wahlin K, Lagergren J. Nordic registry-based cohort studies: possibilities and pitfalls when combining Nordic registry data. Scand J Public Health. 2017;45:s14-9.
4. Laugesen K, Ludvigsson JF, Schmidt M, Gissler M, Valdimarsdottir UA, Lunde A, et al. Nordic health registry-based research: a review of health care systems and key registries. Clin Epidemiol. 2021;13:533-54.
5. Statistics Denmark. Data for research. [cited 2024 Jan 23]. Available from: https://www.dst.dk/en/TilSalg/Forskningsservice.

Inês FRONTEIRA✉*[1,2], Frederik SCHALTZ-BUCHHOLZER[3], Christine STABELL BENN[3,4], Paulo FERRINHO*[2,5], Henrique BARROS*[6,7,8]

* Equally shared authorship position

1. Comprehensive Health Research Centre (CHRC). NOVA Medical School. Universidade NOVA de Lisboa. Lisbon. Portugal.
2. Associação Portuguesa de Epidemiologia. Porto. Portugal.
3. Odense Patient data Explorative Network (OPEN). Bandim Health Project. Institute of Clinical Research. Odense University Hospital/University of Southern Denmark. Odense. Denmark.
4. Danish Institute for Advanced Study. University of Southern Denmark. Odense. Denmark.
5. Global Health and Tropical Medicine. Instituto de Higiene e Medicina. Universidade NOVA de Lisboa. Lisbon. Portugal.
6. Epidemiology Research Unit (EPIUnit). Instituto de Saúde Pública. Universidade do Porto. Porto. Portugal.
7. Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional (ITR). Porto. Portugal.
8. Departamento de Ciências da Saúde Pública e Forenses e Educação Médica. Faculdade de Medicina. Universidade do Porto. Porto. Portugal.

✉ **Autor correspondente:** Inês Fronteira. ines.fronteira@ensp.unl.pt

Recebido/*Received*: 05/02/2024 - **Aceite/*Accepted*:** 21/03/2024 - **Publicado/*Published*:** 02/05/2024

https://doi.org/10.20344/amp.21329

www.actamedicaportuguesa.com