Schizophreniform Disorder Related Hospitalizations: A Clinical and Demographic Analysis of a National Hospitalization Database

Hospitalizações por Perturbação Esquizofreniforme: Uma Análise Clínica e Demográfica de uma Base de Dados Nacional

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ABSTRACT

Introduction: Schizophreniform disorder manifests itself with similar symptoms to schizophrenia, but it is distinguished from the latter by its shorter duration, varying between at least one and six months. This study aimed to describe and analyze schizophreniform disorder related hospitalizations in a national hospitalization database.

Methods: We planned a descriptive retrospective study using a nationwide hospitalization database containing all hospitalizations registered in Portuguese mainland public hospitals from 2008 to 2015. Hospitalizations with a primary diagnosis of schizophreniform disorder were selected based on the International Classification of Diseases version 9, Clinical Modification (ICD-9-CM) code of diagnosis 295.4x. Data regarding birth date, sex, residence address, diagnoses, length of stay, discharge status, and hospital charges were obtained. Comorbidities were analyzed using the Charlson Index Score. Independent Sample *t* tests were performed to assess differences in continuous variables with a normal distribution and Mann-Whitney-U tests when no normal distribution was registered.

Results: In Portuguese mainland public hospitals, a total of 594 hospitalizations with a primary diagnosis of schizophreniform disorder occurred during the eight-year study period. Most, 72.1% (n = 428), were observed in male patients. The mean age at admission was 34.34 years in male patients and 40.19 years in female patients. The median length of stay was 17.00 days and in-hospital mortality was 0.5% (n = 3). Only 6.1% (n = 36) of the hospitalization episodes had one or more registered comorbidities. Forty-one readmissions were documented.

Conclusion: Hospitalizations with a primary diagnosis of schizophreniform disorder occur more frequently in young male patients. This is, to the best of our knowledge, the first nationwide study analyzing all hospitalizations due to this diagnosis in Portugal.

Keywords: Hospitalization; Psychotic Disorders

RESUMO

Introdução: A perturbação esquizofreniforme manifesta-se com sintomas semelhantes aos da esquizofrenia, mas distingue-se desta pela sua duração mais curta, que varia entre um e seis meses. O objetivo deste estudo foi descrever e analisar as hospitalizações por perturbação esquizofreniforme numa base de dados nacional de internamentos.

Métodos: Planeámos um estudo retrospetivo, utilizando uma base de dados de hospitalizações a nível nacional, contendo todos os internamentos registados em hospitais públicos de Portugal Continental entre 2008 e 2015. As hospitalizações com diagnóstico primário de perturbação esquizofreniforme foram selecionadas com base no código de diagnóstico 295.4x da Classificação Internacional de Doenças versão 9, Modificação Clínica (CID-9-CM). Foram obtidos dados relativos à data de nascimento, ao sexo, à zona de residência, aos diagnósticos, à duração do internamento (*length of stay*), ao estado de alta e às despesas hospitalares. As comorbilidades foram analisadas com recurso à pontuação do índice de Charlson. Foram efetuados testes *t* para amostras independentes para avaliar diferenças em variáveis contínuas com distribuição normal e testes Mann-Whitney-U quando esta distribuição não foi registada.

Resultados: Nos hospitais públicos de Portugal Continental, ocorreu um total de 594 internamentos com o diagnóstico primário de perturbação esquizofreniforme durante o período de oito anos selecionado. A maioria, 72,1% (n = 428), estava associada a doentes do sexo masculino. A idade média de admissão foi de 34,34 anos nos homens e de 40,19 anos nas mulheres. A mediana do *length of stay* foi de 17,00 dias e a mortalidade intra-hospitalar foi de 0,5% (n = 3). Apenas 6,1% (n = 36) dos episódios de internamento tinham uma ou mais comorbilidades registadas. Foram documentados 41 reinternamentos.

Conclusão: As hospitalizações com o diagnóstico principal de perturbação esquizofreniforme ocorrem mais frequentemente em doentes jovens do sexo masculino. Tanto quanto é do conhecimento dos autores, este é o primeiro estudo de âmbito nacional que analisa todos os internamentos por este diagnóstico em Portugal.

Palavras-chave: Hospitalização; Perturbações Psicóticas

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KEY MESSAGES

- Schizophreniform disorder manifests itself with similar symptoms to schizophrenia. These two entities are distinguished by temporal criteria, with schizophreniform disorder's duration from onset being between one and six months.
- We found that, in Portugal, between 2008 and 2015, hospitalizations with a primary diagnosis of schizophreniform disorder occurred mainly in young male patients.
- Despite the existence of various limitations, this paper managed to describe and detail the clinical and sociodemographic trends of these patients.

INTRODUCTION

Psychosis can be defined as a clinical syndrome, composed of symptoms related to a change in the perception of reality. It can occur in a wide range of conditions, and therefore, the differential diagnosis of the first episode of psychosis includes psychiatric disorders as well as nonpsychiatric medical conditions that cause secondary psychosis.¹⁻³

Initially proposed by Gabriel Langfeldt in 1939 in the book "The Schizophreniform States", the term 'schizophreniform psychosis' referred to a group of psychoses similar to schizophrenia, but with a better prognosis.⁴ Afterwards, in 1980, the term 'schizophreniform disorder' appeared for the first time in the American psychiatric nomenclature, in the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (DSM-3).⁶ This diagnostic category meant to include patients with good-prognosis, nonaffective psychosis who could not yet be diagnosed with schizophrenia, since the symptoms lasted less than six months.⁶

Since then, many studies have questioned the validity of schizophreniform disorder as a distinct diagnostic entity.^{6,7}

A review of the literature on schizophreniform disorder by Strakowski concluded that "the vast majority of patients diagnosed with schizophreniform disorder go on to develop other psychiatric syndromes", such as schizophrenia or schizoaffective disorder. Even though there were patients who exhibited recovery consistent with the original diagnosis, the author stated that this subgroup was composed of a very small percentage of people, since "the rate of schizophreniform disorder has been observed to be less than 5% of all patients with a first episode of psychosis".^{6,8,9}

The fact that this entity revealed itself to be so unstable led to it being considered as having no diagnostic value.⁷ Moreover, since the main concern was generally related to the alternative diagnosis that the patient would later acquire, the use of this term in clinical practice was considered to provide little prognostic information.⁶

Strakowski, who proposed replacing this diagnosis with "psychosis not otherwise specified", claimed the term 'schizophreniform' was suggestive of a possibly wrong association with schizophrenia, potentially leading to inappropriate treatment.⁶

At the moment, it is still possible to find this diagnosis in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, text revision (DSM-5-TR).¹⁰ However, it is not present in the current International Classification of Diseases, 11th edition (ICD-11),¹¹ or in the International Classification of Diseases, 10th edition (ICD-10),¹² despite having appeared in the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).¹³ In ICD-10, the diagnoses of schizophreniform disorder and brief psychotic disorder are replaced by acute and transient psychotic disorders.¹⁴

According to the DSM-5-TR, psychotic disorders such as schizophrenia and schizophreniform disorder "are defined by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia) and negative symptoms".¹⁰ These two entities are distinguished by temporal criteria, with schizophreniform disorder's duration from onset being between one and six months.³

In the literature, the difference between sexes in firstepisode psychosis is a controversial topic.¹⁵ While some authors claim that schizophreniform disorder affects mostly men, others argue that this entity affects both sexes equally.^{16,17} Its age of onset is between 18 and 24 years old for men and between 24 and 35 years old for women.¹⁸ The incidence rate is currently higher in developing countries.¹⁹

This disorder disturbs people's daily lives and has a huge impact on their performance at work or school, leading to a higher risk of depression and suicide.²⁰⁻²²

Furthermore, research also shows that "psychotic disorders are considered to be the most expensive mental illnesses in terms of costs of care per patient".²³

Even though many studies have been developed to describe psychotic disorders, their focus usually consists of schizophrenia, consequently, there is not enough evidence available about schizophreniform disorder trends.

In Portugal, to our knowledge, no study has yet been carried out on schizophreniform disorder hospitalizations at a national level. Therefore, the primary aim of this study Cosme Ferreira S, et al. Terapêutica substitutiva com imunoglobulina G polivalente: particularidades de um coorte Português, Acta Med Port 2024 Dec;37(12):823-830

was to analyze schizophreniform disorder hospitalizations in a nationwide administrative database. The secondary aims consisted of describing and detailing the clinical and

sociodemographic trends of these patients.

METHODS

Study design

A descriptive retrospective observational study was carried out using a database provided by Administração Central do Sistema de Saúde I.P. (ACSS).

Setting

The study included information from all schizophreniform disorder hospitalizations registered in Portuguese mainland public hospitals from 2008 to 2015.

Participants

In Portugal, most hospitalizations in all medical specialties take place in the public sector (approximately 70%).²⁴ Therefore, all patients admitted to public hospitals between 2008 and 2015 were included in this study. This was the selected time interval since, until 2008, some psychiatric hospitals were excluded from the database because they were not regarded as acute care level hospitals.

The identification of hospitalizations with a primary diagnosis of schizophreniform disorder was based on the International Classification of Diseases version 9, Clinical Modification (ICD-9-CM) code of diagnosis 295.4x.

The database does not have an identification variable for each patient. Therefore, we carried out an anonymous identification process through a sequential count of matching cases based on three variables: date of birth, residence address and sex.

Variables and statistical methods

For each patient hospitalized with a primary diagnosis of schizophreniform disorder, we gathered data about birth date, sex, residence address, diagnoses, lenght of stay (LoS), discharge status and hospital charges.

Categorical variables were described as absolute values and relative frequencies. The variable 'age' was presented as mean ± standard deviation (SD). Length of stay was described using median and interquartile range (IQR).

For the variables 'sex', 'age', 'LoS' and 'in-hospital mortality', we performed a subgroup analysis dividing the patients into two groups – the first group was aged 40 years or younger and the second group was aged older than 40 years old. This analysis was executed, taking into account that acute episodes of schizophrenia are more common up to the age of 40 and thinking of schizophreniform disorder as a potential diagnosis prior to a diagnosis of schizophrenia. Comorbidities were analyzed using the Charlson Index $\ensuremath{\mathsf{Score.}^{25}}$

Independent sample *t* tests were performed to assess differences in continuous variables with a normal distribution and Mann-Whitney-U tests when no normal distribution was registered. A significance level of 0.05 was considered.

To analyze the evolution of the number of hospitalizations over time, we performed a linear regression between the variables 'year' and 'number of hospitalizations per year'.

To obtain the mean direct estimated cost of each hospitalization, we calculated the mean of the variable 'hospital charges'.

All data was analyzed using IBM SPSS Statistics TM[®] v29 for MacOS[®].

Data sources

To calculate hospitalization charges, expenditure tables related to the Portuguese National Health Service hospital reimbursements, defined by a governmental decree in 2009 (in Diário da República),²⁶ were used. These costs were estimated by implementing a diagnosis-related groups (DRG)-based budget allocation model.

The number of Portuguese inhabitants was obtained in Instituto Nacional de Estatística (INE) reports, to determine hospitalization rates per 100 000 inhabitants.

Data access and cleaning methods

For this analysis, we used a database including anonymized data from all schizophreniform disorder's hospitalizations registered in Portuguese public hospitals from 2008 to 2015. There were no missing data concerning the analyzed variables.

Ethical considerations

The study design was approved by the Ethical Committee of the Faculty of Medicine, University of Porto (220/CE-FMUP/2023).

RESULTS

In Portuguese public hospitals, between 2008 and 2015, there was a total of 594 hospitalizations with a primary diagnosis of schizophreniform disorder, comprising a total of 553 patients.

The majority of these hospitalizations occurred in male patients (72.1%; n = 428), while, in terms of age at admission, female patients were older than male patients, with a mean age of 40.19 vs 34.34, respectively (p < 0.001). Individuals aged between 31 and 50 years old had the biggest percentage of hospitalizations (43.3%; n = 257), followed by those between 18 and 30 years old (35.0%; n = 208) and between 51 and 70 years old (13.5%; n = 80). Also, 6.7%

of the hospitalizations belonged to patients under 18 years old (n = 40) and the remaining 1.5% to those older than 70 years old (n = 9). Women had a median LoS of 20.00, while men had a median LoS of 16.50. The difference between the median LoS in the two sexes was not statistically significant (p = 0.050). In-hospital mortality was 0.5%, with the occurrence of three deaths. Patients with fatal outcomes were all aged over 45 and two of them had registered comorbidities (Table 1).

Another analysis dividing the patients into two groups first group aged 40 years or younger and the second group aged older than 40 - revealed that 65.3% (n = 388) of the hospitalizations occurred in the first group and 34.7% (n = 206) in the second. In the first group, most patients were male (78.6%; n = 305) and the mean age at admission was 27.71 for men and 27.53 for women. Additionally, the difference between the median LoS in both sexes (17.00 in male patients vs 20.00 in female patients) was not statistically significant (p = 0.068). Regarding the group of people aged over 40, 59.7% (n = 123) of the hospitalizations occurred in male patients and the remaining 40.3% (n = 83) in female patients. A mean age at admission of 50.78 for men and 52.86 for women was registered. Once again, there were no statistically significant differences (p = 0.280) between the median LoS in both sexes (16.00 in men vs 19.00 in women). It is also worth mentioning that, between the two groups, the difference between the median LoS was not statistically significant (p = 0.718) (Table 2).

Between 2008 and 2015, forty-one readmissions were registered. 92.7% (n = 38) of these belonged to male pa-

tients; 48.8% (n = 20) of the readmissions occurred in patients aged between 18 and 30 years old and 43.9% (n = 18) in patients aged between 31 and 50 years old. There was one patient included in the 51 - 70 age group and two individuals older than 70 years old. No underaged patients were readmitted. There were no statistically significant differences regarding the median LoS between men and women (p = 0.352). Furthermore, there were also no differences concerning the median LoS in primary hospitalizations *versus* readmissions (p = 0.416).

To analyze the evolution of the number of admissions over the entire study period, a linear regression between the variables year and number of hospitalizations per year was performed, which was not statistically significant (r = 0.322; p = 0.436). 2015 was the year with the most patients admitted to Portuguese public hospitals (17.3%; n = 103), which equals 1.04 hospitalizations per 100 000 inhabitants. This year was also the one in which the mean age of the hospitalized patients was higher (39.26) and with the shortest median LoS (12.00) (Table 3).

Only 6.1% (n = 36) of the hospitalization episodes had one or more registered comorbidities. The mean Charlson Comorbidity Index Score between all patients was 0.08. Most of the individuals (91.6%) were non-smokers.

The mean direct estimated cost of each hospitalization was €3598.48.

DISCUSSION

This study aimed to analyze schizophreniform disorder hospitalizations in a nationwide administrative database,

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				<i>p</i> -value
Hospitalizations (n)	594			
Patients (n)	553			
Sex (n; %)				
Male	428; 72.1%			
Female	166; 27.9%			
Age (years)	Male	Female	Total	
Mean (SD)	34.34 (12.898)	40.19 (15.353)	35.98 (13.867)	< 0.001
Age group (years)	Male (n; %)	Female (n; %)	Total (n; %)	
< 18	26; 6.1	14; 8.4	40; 6.7	
18 - 30	172; 40.2	36; 21.7	208; 35.0	
31 - 50	186; 43.5	71; 42.8	257; 43.3	
51 - 70	39; 9.1	41; 24.7	80; 13.5	
> 70	5; 1.2	4; 2.4	9; 1.5	
Lenght of stay (days)	Male	Female	Total	
Median ± IQR	16.50 (8.00; 27.00)	20.00 (10.00; 29.25)	17.00 (8.00; 28.00)	0.050
In-hospital mortality (n; %)	3; 0.5			

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	Α	ge ≤ 40 years o	ld	Age > 40 years old				
				<i>p</i> -value				<i>p</i> -value
Hospitalizations (n)	388				206			
Sex (n; %)								
Male		305; 78.6%				123; 59.7%		
Female		83; 21.4%				83; 40.3%		
Age (years)	Male	Female	Total		Male	Female	Total	
Mean (SD)	27.71 (6.745)	27.53 (7.503)	27.67 (6.905)		50.78 (9.305)	52.86 (9.665)	51.62 (9.483)	
Lenght of stay (days)	Male	Female	Total		Male	Female	Total	
Median ± IQR	17.00 (8.00; 28.00)	20.00 (13.00; 30.00)	17.00 (9.00; 28.00)	0.068	16.00 (7.00; 27.00)	19.00 (8.00; 29.00)	18.00 (7.00; 28.00)	0.280
p-value (comparison between both groups)				0.7	18			
In-hospital mortality (n; %)		0; 0				3; 1.5		

Table 2 – Data analysis dividing the patients into two groups: first group aged 40 years or younger and second group aged older than 40

describing and detailing the clinical and sociodemographic trends of these patients.

Schizophreniform disorder manifests itself similarly to schizophrenia but is distinguished from the latter by temporal criteria. It is an entity still not well conceptualized, suffering many changes throughout the various classification systems. Consequently, there is a scarcity of studies on this topic.

We gathered a total of 594 hospitalizations, corresponding to 553 patients, in Portuguese mainland public hospitals, between 2008 and 2015. Most of these (72.1%) belonged to male patients. The mean age at admission in men was 34.34 vs 40.19 in female patients. Individuals aged between 31 and 50 years old had the highest percentage of hospitalizations. The median LoS was 20.00 in women and 16.50 in men. In-hospital mortality was 0.5%. Forty-one readmissions were documented, 92.7% of these in males. Between 2008 and 2015, we observed an increase in the number of hospitalizations, much at the expense of the number of admissions in 2015. Only 6.1% of the hospitalization episodes had one or more registered comorbidities. The mean direct estimated cost of each hospitalization was €3598.48.

Our findings showed that, in Portugal, between 2008 and 2015, hospitalizations with a primary diagnosis of schizophreniform disorder occurred mainly in male patients, which supports the thesis that this entity affects mostly men and not both sexes equally.¹⁶

As for age at admission, schizophreniform disorder's age of onset is between 18 and 24 years old for men and 24 and 35 years old for women.¹⁸ This was not the case in our results, with individuals aged between 31 and 50 years old having the biggest percentage of hospitalizations. The mean age at admission in male patients was 34.34, while it was 40.19 in female patients. The large number of patients over the age of 40 (as shown in Table 2) could be explained by errors inherent to the database. Additionally, considering that two-thirds of patients with this diagnosis are eventually diagnosed with schizophrenia or schizoaffective disorder, and bearing in mind that, in schizophrenia, late-onset (after the age of 40) is common in women, this could be another reason for the high number of patients in this age group.¹⁰

Table 3 – Sociodemographic and clinica	characteristics of schizophreniform	disorder hospitalizations per vear

Year	Hospitalizations (n; %)	Hospitalizations per 100 000 inhabitants	Mean age (years)	Median LoS (days)								
2008	64 (10.8)	0.64	35.17	17.00								
2009	83 (14.0)	0.83	34.12	20.00								
2010	72 (12.1)	0.72	35.18	21.00								
2011	63 (10.6)	0.63	35.02	20.00								
2012	81 (13.6)	0.81	34.31	20.00								
2013	70 (11.8)	0.70	36.14	17.50								
2014	58 (9.8)	0.59	37.84	16.00								
2015	103 (17.3)	1.04	39.26	12.00								
Total	594	N.A.	35.98	17.00								
Total	594	N.A.	35.98	17.00								

Nevertheless, women were significantly older at admission, a fact that is in line with what is reported in other studies. To better illustrate this, a study found that, among patients with a first episode of schizophrenia/schizophreniform disorder, women had a later age of onset (approximately four years later than men).¹⁶

Given that acute episodes of schizophrenia are more common up to the age of 40 and thinking of schizophreniform disorder as a potential diagnosis prior to a diagnosis of schizophrenia, we performed a sub-analysis, dividing the patients into two age groups: under 40, and over 40 years old. In the first group, the mean age at admission was 27.71 for men and 27.53 for women. Therefore, analyzing only this subgroup, the mean age at admission is closer to what is expected in this diagnostic entity. Despite this, the difference between the mean age of female and male patients vanished when only patients aged 40 years or younger were taken into consideration (Table 2).

Since in the literature schizophreniform disorder is often grouped together with schizophrenia or other psychotic disorders, there is a scarcity of studies solely on this topic.¹⁴ This lack of knowledge makes it difficult to compare the data obtained here with information previously provided by other authors.

Still, a study on the prevalence of institutionalized and noninstitutionalized people with schizophrenia in Denmark showed that male sex was associated with higher relapse rates.²⁷ Also, another study found that women had shorter hospitalizations.²⁸ Our study demonstrated that most readmissions occurred in men. Nonetheless, we could not find any statistically significant differences between the median LoS in both sexes.

A total of 41 readmissions were documented, which corresponds to 6.9% of all hospitalizations. Since this is a diagnosis with a limited timeframe (between one and six months), this percentage of readmissions could be explained by the occurrence of misdiagnosis or coding errors at the time of readmission.

During the study period, in-hospital mortality was 0.5%. These three deaths occurred in patients older than 50 years old and two of them had other comorbidities. Consequently, it is not possible to conclude whether these fatal events were associated with the underlying psychiatric disease.

The mean direct estimated cost of each hospitalization was €3598.48, a value similar to the one that was found in a study that analyzed schizophrenia hospitalizations in Portugal.²⁹

The presented discrepancies can be explained by the existence of limitations in this study.

First of all, since this analysis was made using an administrative database, the quality of the data here presented is influenced by the reliability of the information registered by the clinician, as well as the accuracy of the diagnostic and coding processes. Hence, this could lead to the occurrence of an information bias.

In Portugal, during the period included in this study, even though ICD-10 was already in use in clinical practice, ICD-9-CM was still being used, so there may also have been errors in the transition between these classification systems.

Furthermore, as only hospitalized patients were selected, and these tend to be more severe cases than the ones who do not need hospitalization, a selection bias may have occurred.

The unit of analysis in this study was the hospitalization and not the patient. Therefore, the fact that readmitted patients are included in the calculations more than once may create some bias in the results, which is another limitation.

The database did not have a variable for substance abuse. Given that this is a frequent cause of secondary psychosis, it would be important to have this information to assess diagnostic accuracy.³⁰

Like previously mentioned, the fact that schizophreniform disorder is often grouped with other disorders in previous studies makes it difficult to understand whether our results are in line with the reality found in the bibliography.

By carrying out this study, we were able to analyze a nationwide administrative database of hospitalizations in patients with a primary diagnosis of schizophreniform disorder, describing and detailing their clinical and sociodemographic trends. Nevertheless, given the limitations of the study and the fact that it focuses on a limited period between 2008 and 2015, it is possible that the data does not represent the current Portuguese situation regarding schizophreniform disorder's hospitalizations.

Considering the limitations of the study, in order to better understand the characteristics of this disorder, it would be pertinent to carry out new studies including other variables in the analysis, such as secondary causes of psychosis and the treatment used in each patient.

Despite the limitations mentioned above, this study presents itself with several strengths.

First of all, to our knowledge, it is the first retrospective study on schizophreniform disorder hospitalizations at a national level in Portugal.

Furthermore, by using an administrative database, we were able to gather a large sample and to analyze a large set of variables, evaluating a series of outcomes.

This has helped to provide a comprehensive overview of the trends of this diagnosis in Portugal, which is a great advantage of using large databases.

Overall, schizophreniform disorder is an entity that is still not well conceptualized, and that has undergone changes throughout the various classification systems. For this

reason, the attempt to generalize these results must be made with caution. More epidemiologically based studies with more restrictive classification criteria are therefore needed.

CONCLUSION

We concluded that hospitalizations with this primary diagnosis occur mainly in young male patients. This disorder is accompanied by a major economic impact and a huge burden of illness, which highlights the need for early intervention in these cases.

Despite its limitations, the use of large administrative databases in healthcare provides a broad view of a particular diagnosis, proving to be advantageous in descriptive studies such as this one. Further studies are needed to better understand the characteristics of this disorder and its translation to a clinical setting.

AUTHOR CONTRIBUTIONS

ITC, AF, MGP: Study design, statistical analysis, writing and critical review of the manuscript.

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

All authors approved the final version to be published.

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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.

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