Complex Congenital Heart Disease: The Influence of Prenatal Diagnosis

Cardiopatias Congénitas Complexas: Influência do Diagnóstico Pré-Natal

Marta CORREIA[1], Fabiana FORTUNATO[2], Duarte MARTINS[3], Ana TEIXEIRA[3], Graça NOGUEIRA[3], Isabel MENEZES[3], Rui ANJOS[3]

Acta Med Port 2015 Mar-Apr;28(2):158-163

ABSTRACT

Introduction: Complex congenital heart disease is a group of severe conditions. Prenatal diagnosis has implications on morbidity and mortality for most severe conditions. The purpose of this work was to evaluate the influence of prenatal diagnosis and distance of residence and birth place to a reference center, on immediate morbidity and early mortality of complex congenital heart disease.

Material and Methods: Retrospective study of complex congenital heart disease patients of our Hospital, born between 2007 and 2012.

Results: There were 126 patients born with complex congenital heart disease. In 95%, pregnancy was followed since the first trimester, with prenatal diagnosis in 42%. There was a statistically significant relation between birth place and prenatal diagnosis. Transposition of great arteries was the most frequent complex congenital heart disease (45.2%), followed by pulmonary atresia with ventricular septal defect (17.5%) and hypoplastic left ventricle (9.5%). Eighty-two patients (65.1%) had prostaglandin infusion and 38 (30.2%) were ventilated before an intervention. Surgery took place in the neonatal period in 73%. Actuarial survival rate at 30 days, 12 and 24 months was 85%, 80% and 75%, respectively. There was no statistically significant relation between prenatal diagnosis and mortality.

Discussion: Most patients with complex congenital heart disease did not have prenatal diagnosis. All cases with prenatal diagnosis were born in a tertiary center. Prenatal diagnosis did not influence significantly neonatal mortality, as already described in other studies with heterogeneous complex heart disease.

Conclusion: prenatal diagnosis of complex congenital heart disease allowed an adequate referral. Most patients with complex congenital heart disease weren't diagnosed prenatally. This data should be considered when planning prenatal diagnosis of congenital heart disease.

Keywords: Heart Defects, Congenital; Prenatal Diagnosis.

RESUMO

Introdução: As cardiopatias congénitas complexas são patologias graves, e o diagnóstico pré-natal poderá ter implicações sobre a morbilidade e a mortalidade. O objetivo deste trabalho foi estudar a influência do diagnóstico pré-natal e da distância do local de parto a um centro de referência, na morbilidade imediata e mortalidade precoce de um grupo de doentes com cardiopatias congénitas complexas.

Material e Métodos: Análise retrospetiva dos doentes com cardiopatias congénitas complexas, seguidos no nosso hospital, nascidos entre 2007 e 2012.

Resultados: Identificaram-se 126 doentes com cardiopatias congénitas complexas. Em 95% a gravidez foi vigiada desde o primeiro trimestre existindo diagnóstico pré-natal em 42%. Houve relação estatisticamente significativa entre o local do parto e a existência de diagnóstico pré-natal. A cardiopatia congénita complexa mais frequente foi a transposição das grandes artérias (45,2%), seguida da atresia da pulmonar com comunicação interventricular (17,5%) e ventrículo esquerdo hipoplásico (9,5%). Oitenta e dois doentes (65,1%) foram medicados com prostaglandinas e 38 (30,2%) foram ventilados antes de uma intervenção. A cirurgia ocorreu no período neonatal em 73%. A sobrevida atuarial aos 30 dias, 12 e 24 meses foi 85%, 80% e 75%, respetivamente. Não houve relação estatisticamente significativa entre diagnóstico pré-natal e mortalidade.

Discussão: A maioria dos doentes com cardiopatias congénitas complexas não teve diagnóstico pré-natal. Nos casos com diagnóstico pré-natal houve referenciação e parto num centro terciário. Não houve associação estatisticamente significativa entre diagnóstico pré-natal e mortalidade neonatal, como já descrito em séries heterogéneas de cardiopatia congénita complexa.

Conclusão: A maioria dos doentes com cardiopatias congénitas complexas não teve diagnóstico pré-natal. Estes dados devem ser tomados em conta no planeamento do diagnóstico pré-natal das cardiopatias congénitas.

Palavras-chave: Cardiopatias Congénitas; Diagnóstico Pré-natal.

INTRODUCTION

Congenital heart diseases are the most frequent major birth defects and those with higher clinical relevance, with 0.5 to 1% prevalence in the neonatal period.[1-3] About half of the cases are clinically severe requiring surgical correction in neonatal period or during the first years of life.[2]

Complex congenital heart diseases (CCHD) are included in a group of serious disorders mostly presenting with abnormal segmental arrangement such as for instance hypoplastic left heart syndrome (HLHS), great arteries transposition (GAT) and univentricular heart. These are the most serious among congenital heart diseases, more complicated and therefore represent a greater therapeutic

1. Serviço de Pediatria. Hospital Vila Franca de Xira. Vila Franca de Xira. Portugal.
2. Serviço de Pediatria. Hospital de Caldas da Rainha. Centro Hospitalar Oeste. Caldas da Rainha. Portugal.
3. Serviço de Cardiologia Pediátrica. Hospital de Santa Cruz. Centro Hospitalar de Lisboa Ocidental. Lisboa. Portugal

Recebido: 21 de Agosto de 2014 - Aceite: 20 de Janeiro de 2015

challenge. Some studies have shown that in some of these heart defects (such as in GAT), prenatal diagnosis (PND) allows for an adequate timing and for childbirth to be planned to occur in a maternity hospital with close links to reference centres in Cardiology and Paediatric Heart Surgery, with a resulting positive impact on morbidity and mortality.[4-7]

There are no studies published up to date in Portugal regarding the benefits of PND in this group of disorders. National coverage with foetal echocardiography is apparently asymmetric and therefore PND in congenital heart diseases is mainly available in major urban centres.

OBJECTIVES

Our study aimed to determine the influence of (i) PND and (ii) the distance from the place of childbirth to a reference centre with foetal echocardiography facility, on immediate morbidity and mortality rate. The group of patients with CCHD was defined by the presence of abnormal segmental arrangement, including hypoplastic left heart syndrome, great arteries transposition, univentricular heart and valvular atresia.

MATERIAL AND METHODS

This was a case study in children with CCHD (defined as any abnormal heart segmental arrangement) attending the Paediatric Cardiology Department at our hospital. It included children born between January 2007 and December 2012. The patients with a CCHD prenatal diagnosis and intrauterine foetal death or whenever a termination of pregnancy had occurred were excluded from the study. Clinical records were analysed in order to assess the following parameters: date of birth, gender, place of residence, pregnancy follow-up, prenatal diagnosis (PND) testing, gestational age at which time CCHD was diagnosed, childbirth location, prostaglandin therapy, need for ventilation, severe acidosis (pH < 7.2) prior to the first therapeutic procedure, type and date of the first therapeutic procedure (catheter therapy or surgery) and mortality. As regards the patient's place of residence and childbirth location, the distance to a tertiary referral hospital with Paediatric Cardiology facility was analysed and patients were classified as: group 0 (when the place of residence was the same as where the tertiary referral hospital was located; group < 100 km; group 101-200 km; group 201-300 km; > 300 km; Madeira & Azores islands and abroad, in countries with no PND availability. Comparisons between groups were established according to PND availability and proximity to a tertiary referral hospital. Statistical analysis used the PASW Statistics 18® software ($p < 0.05$).

RESULTS

Over the 6-year timeframe of our study, 126 new-born babies with CCHD were diagnosed, according to the described definition. Childbirth annual distribution is shown in Fig. 1. The distance from patient's place of residence to a tertiary Paediatric Cardiology referral hospital is shown in Table 1 and no statistically significant difference was found between groups of patients who underwent PND *vs.* no PND. A 1.8:1 male/female ratio was found.

Pregnancy was medically followed up in 124 patients (98.4%) and in 120 from the first trimester onwards. The age at the time when CCHD was diagnosed is shown in Table 1. In total, 42 patients with CCHD underwent PND. Childbirth location was in the same municipality as the closest tertiary Paediatric Cardiology referral hospital in 64 patients (Table 1), with a statistically significant difference between childbirth location and the presence of PND ($p < 0.001$). All PND-screened patients living further than 100 km away from a tertiary referral hospital had childbirth programmed for that hospital and not in their area of residence.

Great arteries transposition (45.2%), followed by pulmonary valve atresia with interventricular communication (17.5%) were the most frequent CCHD found (Fig. 2), with a higher number of PND-screened patients with more severe CCHD such as hypoplastic left heart syndrome (HLHS).

In total, 82 patients (65.1%) were treated with prostaglandins, from which 31 had undergone PND testing. Of note, ventilation before surgery was required in 38 patients (30.2%) and included 17 clinical situations where ventilation is usually not indicated and which may even be considered deleterious or inappropriate. Nine patients presented with severe pre-procedure acidosis, with a statistically non-significant relationship ($p = 0.06$) between the absence of PND testing and the need for ventilation or the presence of severe acidosis. When we analysed both the presence of acidosis and the need for ventilation, we did not find any statistically significant difference regarding the outcome between the groups with *vs.* without PND

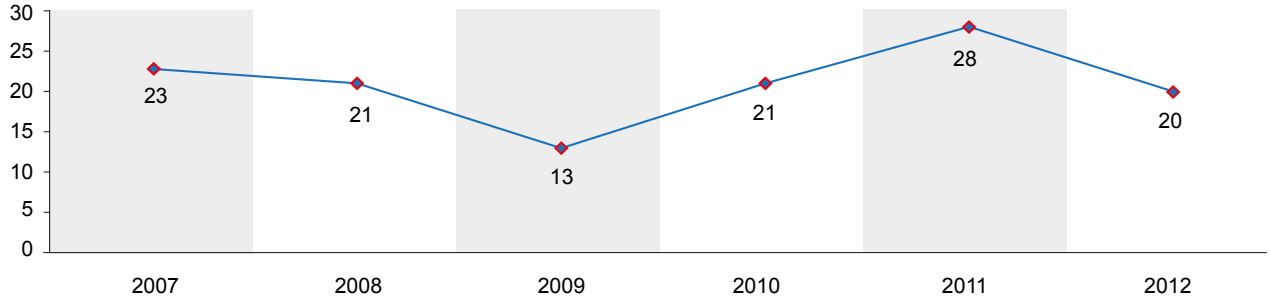

Figure 1 – Annual distribution of new-borns with CCHD

Table 1 - Characteristics of CCHD patients PND-screened *vs.* non-PND-screened, referred to our Hospital from2007 to 2012

Variable	PND testing (%)	No PND testing (%)	*p*-value
CCHD	42 (33)	84 (67)	
Distance from place of residence to a tertiary referral hospital			0.09
0 km	10	8	
≤ 100 km	12	44	
101-200 km	3	2	
201-300 km	10	14	
> 300 km	2	3	
Madeira and Azores islands	5	12	
Undetermined	0	1	
Age at time of diagnosis			
< 24 WG	20 (16)	NA	
≥ 24 WG	22 (17)	NA	
1st week of life	NA	70 (56)	
2nd week of life	NA	5 (4)	
> 2nd week of life	NA	9 (7)	
Distance from childbirth location to a tertiary referral hospital			0.001
0 km	42	23	
≤ 100 km	0	27	
101-200 km	0	0	
201-300 km	0	15	
> 300 km	0	1	
Madeira and Azores islands	0	14	
Undetermined	0	4	

WG – weeks of gestation; NA – not applicable

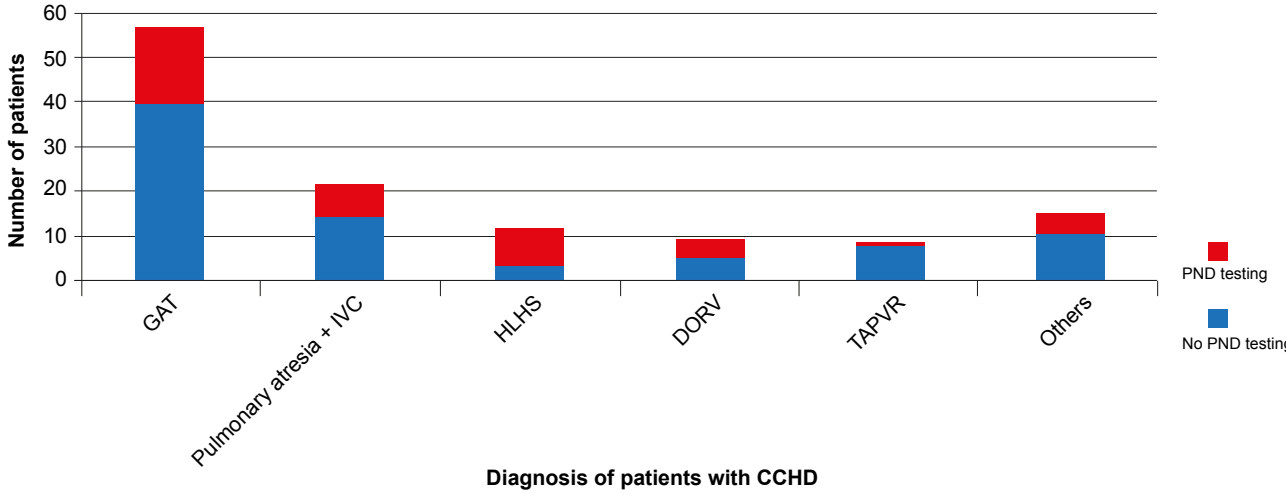

Figure 2 – Patients with CCHD referred to our Hospital in neonatal period from 2007 to 2012

GAT = Great Arteries Transposition; IVC = Interventricular communication; HLHS = Hypoplastic Left Heart Syndrome; DORV = Double Outlet Right Ventricle; TAPVR = Total Anomalous Pulmonary Venous Return

testing (p = 0.892). Likewise, the logistic regression for the composite outcome regarding PND testing and childbirth location did not show any differences.

In total, 73% of the patients underwent surgery in the neonatal period (and this was the first therapeutic procedure in 60% of the patients). A seven-day median age of children was found at the time of the first therapy procedure; 76 patients underwent surgery whilst 46 underwent catheter therapy (Table 2). The Rashkind atrial septostomy was mostly used for the

Table 2 - Therapy procedures performed in patients with CCHD referred to our Hospital, 2007 to 2012

Variable	n	%
First approach		
Catheter therapy	46	36.5
Surgery	76	60.3
Catheter therapy + Surgery	2	1.6
Not performed	2	1.6
Catheter therapy		
Rashkind septostomy	41	32.5
Neonatal hybrid approach	4	3.2
Percutaneous valvuloplasty	1	0.8
Not performed	80	63.5
Surgery		
Arterial switch	61	48.4
Blalock-Taussig shunt	28	22.2
Pulmonary Artery Banding	11	8.7
TAPVR correction	6	4.8
Others	18	14.0

TAPVR = Total Anomalous Pulmonary Venous Return

latter (41). In patients with GAT, septostomy was performed on average, on the second day of life. Surgery was successful in 70 patients (55.6%). The arterial switch was the most common type of surgery used (61), followed by the Blalock-Taussig shunt (28) and pulmonary artery banding (11).

In total, 12 deaths occurred in the post-surgical period, with statistically non-significant relationship between mortality in the neonatal period and PND testing or distance from childbirth location to a reference referral hospital.

In our group of patients, 85% 30-day actuarial survival was found, 80% at 12 months and 75% at 24 months (Fig. 3). There was non-statistically significant difference in survival curves from the patients with *vs.* without PND testing (Fig. 4).

DISCUSSION

We should mention that most patients in our study did not undergo PND testing, even though CCHD included the most severe heart defects. Congenital heart disease PND screening rates of 47.3% have been described in France, 49% in the USA and 52.8% in Australia.[7,8,13] Guidelines regarding the indication for foetal echocardiography were published in Portugal by the *Direção Geral da Saúde* in 2006, establishing that, in most pregnancies, a reliable second-trimester ultrasound screening allows for the identification of most of the foetuses with an indication for ecocardiography.[14] PND testing is technically not difficult

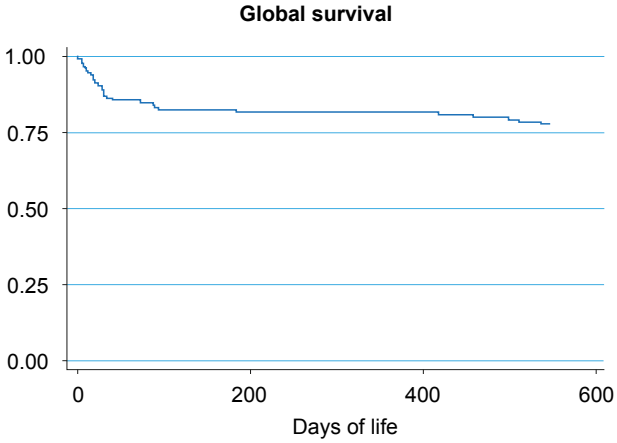

Figure 3 – Actuarial survival curve for all CCHD

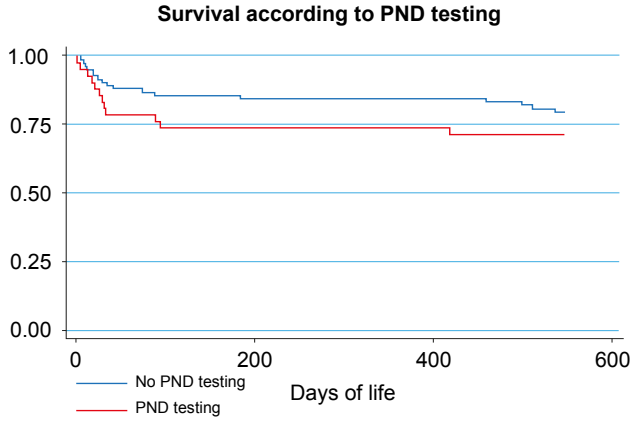

Figure 4 – Actuarial survival curve for CCHD in PND-screened *vs.* non-PND-screened patients. There is statistically no significant difference between both curves - $p = 0.167$

to perform although it requires adequate training of health professionals involved, mainly including obstetricians and paediatric cardiologists.

Contrary to our expectations, our study did not find that PND-screened patients had lower mortality and morbidity. The advantage of PND testing of severe heart defects was demonstrated for the first time in 1999, in a French study with a very homogeneous group of patients, with simple GAT.[7] In other studies, this benefit has been difficult to prove,[10,11] the latter probably explained by the heterogeneity of CCHD and different survival rates for each pathology. When the group of patients is restricted to specific congenital heart disorders, an improvement in short-term and long-term outcome in PND-screened patients is found.[12] In our group of patients and when analysing only patients with GAT, we found that in the PND-screened patient group there was no severe acidosis, unlike the non-PND-screened patient group, where this occurred in 13% of the patients. The same was found regarding ventilation, with differences of 24 to 43%, respectively, when comparing the PND and no PND groups. However, this correlation was not statistically significant. The severity of pathologies may be another explanation for the absence of any benefit regarding PND testing in our study, as patients with more severe pathologies will most probably be diagnosed in the prenatal period and will probably also have a worse outcome.

Even though our study did not show a higher survival related to PND testing, there are certainly several other major benefits. It has been shown that PND testing of complex heart disorders is associated to a better outcome in different specific pathologies, namely in GAT (as in about 12% of the patients a Rashkind septostomy is needed on the first hour of life,[7] which would only be possible when delivery occurs in a tertiary referral hospital) and a correct prediction of surgical approach in the case of complex GAT.[4,9] PND testing allows for better counselling and also for adequate perinatal planning, namely regarding childbirth location. Therefore, PND testing leads to lower rates of postnatal transportation and, when this is necessary, to shorter and safer transportation of new-born babies, mainly with less use of invasive ventilation or inotropic medication.[15] We should also mention the fact that all PND-screened new-born babies referred to our centre were born in a tertiary referral hospital, showing that the referral network is efficient when PND testing is performed.

The small number of patients referred to only one centre is a limitation to our study, as well as the fact that some immediate post-delivery data regarding clinical severity were not available, as many deliveries occurred in other hospitals.

CONCLUSIONS

Our study involving patients born between 2007 and 2012 demonstrates that most patients with CCHD did not undergo any PND testing. This finding supports the need to re-structure the entire circuit of diagnosis of patients with CCHD, including professional training in obstetric ultrasound, as well as referral guidelines when the presence of foetal pathology is suspected. It is interesting to find that, in this group of patients with CCHD, those living away from major urban centres do not show any lower rate of PND testing when compared to those living closer to tertiary referral hospitals. It should be mentioned that referral network involving our hospital was efficient in all patients PND-screened and born in tertiary referral hospitals, allowing for lower early neonatal morbidity.

Our study is a contribution for a wider reflection on how to more efficiently implement PND testing for congenital heart diseases in Portugal.

OBSERVATIONS

This study was in part presented as oral communication named *"Cardiopatias congénitas complexas e diagnóstico pré-natal: casuística de um centro de referência"*, at the *XLII Jornadas Nacionais de Neonatologia/V Jornadas Internacionais de Neonatologia*; Lisbon, 14-15th November 2013.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

FINANCIAL SUPPORT

The authors declare there was no financial support in writing this manuscript.

REFERENCES

1. Berkley E, Goens M, Karr S, Rappaport V. Utility of fetal echocardiography in postnatal management of infants with prenatally diagnosed congenital heart disease. Prenat Diagn. 2009;29:654–8.
2. Nelle M, Raio L, Pavlovic M, Carrel T, Surbek D, Meyer-Wittkopf M. Prenatal diagnosis and treatment planning of congenital heart defects - possibilities and limits. World J Pediatr. 2009;5:18-22.
3. Wald N, Morris J, Walker K, Simpson J. Prenatal screening for serious congenital heart defects using nuchal translucency: a meta-analysis. Prenat Diagn. 2008;28:1094–104.
4. Lhomme D, Khoshnood F, De Vigan C, Vodovar V, Goujard J. Population-based evaluation of newborns with congenital heart disease in France, 1983–2000: a trends in prenatal diagnosis, pregnancy termination, and perinatal mortality. Pediatrics. 2005;115:95-101.
5. Germanakis I, Sifakis S. The impact of fetal echocardiography on the prevalence of liveborn congenital heart disease. Pediatr Cardiol. 2006;27:465–72.
6. McBrien A, Andrew S, Craig B, Dornan J, Casey F. Major congenital heart disease: antenatal detection, patient characteristics and outcomes. J Matern Fetal Neonatal Med. 2009;22:101-5.
7. Bonnet D, Coltri A, Butera G, Fermont L, Bidois J, Kachaner J, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation. 1999;99:916-8.
8. Chew C, Halliday JL, Riley MM, Penny DJ. Population-based study of antenatal detection of congenital heart disease by ultrasound examination. Ultrasound Obstet Gynecol. 2007; 29:619–24.
9. Pascal CJ, Huggon I, Sharland GK, Simpson JM. An echocardiographic study of diagnostic accuracy, prediction of surgical approach, and outcome for fetuses diagnosed with discordant ventriculo-arterial connections. Cardiol Young. 2007;17:528-34.
10. Mahle WT, Clancy RR, McGaurn SP, Goin JE, Clark BJ. Impact of

prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. Pediatrics. 2001;107:1277-82.
11. Raboisson MJ, Samson C, Ducreux C, Rudigoz RC, Gaucherand P, Bouvagnet P, et al. Impact of prenatal diagnosis of transposition of the great arteries on obstetric and early post natal management. Eur J Obstet Gynecol Reprod Biol. 2009;142:18-22.
12. Fuchs IB, Muller H, Abdul-Khaliq H, Harder T, Dudenhausen JW, Henrich W. Immediate and long-term outcomes in children with prenatal diagnosis of selected isolated congenital heart defects. Ultrasound Obst Gynecol. 2007;29:38-43.
13. Israel SW, Roofe LR, Saville BR, Walsh WF. Improvement in antenatal diagnosis of critical congenital heart disease - implications for postnatal care and screening. Fetal Diagn Ther. 2011;30:180-3.
14. Diagnóstico Prenatal de Cardiopatias Congénitas. Circular Normativa nº 11/DSMIA da Direcção Geral da Saúde. Lisboa: DGS; 2006.
15. Gupta N, Leven L, Stewart M, Cheung M, Patel N. Transport of infants with congenital heart disease: benefits of antenatal diagnosis. Eur J Pediatr. 2014;173:655-60.

Marta CORREIA, Fabiana FORTUNATO, Duarte MARTINS, Ana TEIXEIRA, Graça NOGUEIRA, Isabel MENEZES, Rui ANJOS

Complex Congenital Heart Disease: The Influence of Prenatal Diagnosis

Acta Med Port 2015:28:158-163

Publicado pela **Acta Médica Portuguesa**, a Revista Científica da Ordem dos Médicos

Av. Almirante Gago Coutinho, 151
1749-084 Lisboa, Portugal.
Tel: +351 218 428 215
E-mail: submissao@actamedicaportuguesa.com
www.actamedicaportuguesa.com
ISSN:0870-399X | e-ISSN: 1646-0758