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ORIGINAL ARTICLE

Long-term survival in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: Insights from a referral center in Portugal

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KEYWORDS
Pulmonary hypertension;
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Abstract
Objectives: This study aims to assess the long-term survival of pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) patients followed in a Portuguese pulmonary hypertension (PH) referral center.
Methods: We studied PAH and CTEPH patients diagnosed between January 2005 and December 2016. Cumulative survival was estimated using the Kaplan-Meier method. Survival trends were compared over two periods (2005-2010 vs. 2011-2016).
Results: Of the 142 studied PH patients (age 54±18 years; 31% male), 47 had CTEPH and 95 had group 1 PH. Most patients with CTEPH and idiopathic/heritable PAH (I/HPAH) were in NYHA III-IV at diagnosis (64% and 57%, respectively). At the time of death, 31% of patients with connective tissue disease (CTD)-associated PAH (CTD-PAH) and all I/HPAH patients were on double or triple combination therapy. No patient underwent lung transplantation. Pulmonary endarterectomy or angioplasty were performed in 36% of CTEPH patients. Age at diagnosis tended to increase over time in CTD-PAH (53±15 vs. 63±15 years; p=0.13) and I/HPAH (39±15 vs. 51±19 years; p=0.10). The five-year survival estimates for I/HPAH, CTD-PAH and CTEPH patients were 80%, 52%, and 81%, respectively. Over time, CTD-PAH and CTEPH showed better five-year survival (33 vs. 67% and 77 vs. 84%), but I/HPAH did not (84 vs. 75%).

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Conclusions: Our data indicate a trend toward improved survival over time of CTD-PAH and CTEPH patients treated at a Portuguese referral PH center. Earlier diagnosis, increasing use of parenteral prostanoids, and surgical treatment may further improve PH prognosis.

PALAVRAS-CHAVE
Hipertensão pulmonar;
Hipertensão arterial pulmonar;
Sobrevivência;
Hipertensão pulmonar tromboembólica crónica

Sobrevivência a longo prazo na hipertensão arterial pulmonar e na hipertensão pulmonar tromboembólica crónica: dados de um centro de tratamento em Portugal

Resumo
Introdução: Este estudo tem como objetivo avaliar a sobrevivência a longo prazo em doentes com hipertensão arterial pulmonar (PAH) e hipertensão pulmonar tromboembólica crónica (CTEPH) seguidos num centro de tratamento.
Métodos: Doentes diagnosticados com PAH ou CTEPH entre janeiro 2005 e dezembro 2016 foram incluídos. A sobrevivência cumulativa foi estimada utilizando o método Kaplan-Meier. Compararam-se os padrões de sobrevivência de dois períodos (2005-2010 *versus* 2011-2016).
Resultados: Foram estudados 142 doentes (54 ± 18 anos; 31% homens), 47 diagnosticados com CTEPH e 95 com PAH. A maioria dos doentes com CTEPH e etiologia idiopática/hereditária (I/HPAH) apresentava classe funcional NYHA III-IV ao diagnóstico (64% e 57%, respetivamente). Aquando da morte, 31% dos doentes com doença do tecido conjuntivo (CTD) e todos os doentes com H/IPAH recebiam terapia dupla ou tripla. Nenhum doente realizou transplante pulmonar. Endarterectomia pulmonar (PEA) ou angioplastia foram realizadas em 36% dos doentes com CTEPH. A idade de diagnóstico de H/IPAH (39 ± 15 *versus* 51 ± 19 anos; p = 0,10) e CTD (53 ± 15 *versus* 63 ± 15 anos; p = 0.13) tendeu a aumentar. A sobrevivência a cinco anos foi estimada em 80%, 52% e 81% para H/IPAH, CTD e CTEPH, respetivamente. No 2.º período, a sobrevivência a cinco anos melhorou nos doentes com CTD e CTEPH (33% *versus* 67% e 77% *versus* 84%), mas não nos I/HPAH (84% *versus* 75%).
Conclusões: Existe uma tendência de melhoria na sobrevivência de doentes com CTD-PAH e CTEPH tratados num centro de referência português. O diagnóstico precoce, o uso de prostanoides parenterais e a disponibilização de tratamentos cirúrgicos poderão traduzir-se em ganhos adicionais de sobrevida.

Introduction

Pulmonary hypertension (PH) is characterized by an increase in pulmonary artery pressure. It can be associated with a wide range of conditions,[1] the most common of which are left heart disease and lung disease, in which PH has considerable prognostic significance but no indication for specific therapy.[2] The distinction between these causes and less frequent causes of PH such as pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) is often challenging and always critical, since the latter have an ominous prognosis without specific treatment.[3,4] Ten specific pulmonary vasodilators are currently available for PAH and there is robust evidence on the clinical benefits of pulmonary endarterectomy (PEA) for CTEPH patients.[2]

Despite notable advances in recent decades, rare diseases such as PAH and CTEPH still present numerous challenges. Early diagnosis is fundamental but still an unmet need. The more advanced the functional class at diagnosis, the worse the prognosis.[5,6] Regarding treatment, generalization of data from clinical trials is not straightforward, as these trials' study populations often differ from real-world patients.[7] Observational data from registries and cohort studies are accordingly crucial to provide insights on epidemiology, adherence to guidelines, effectiveness of treatments, and outcomes in clinical practice. Several international registries and PH referral center cohort studies have been published.[8] However, available data on PAH and CTEPH patients followed in Portugal are limited, especially in terms of long-term mortality.[9–11]

We studied PAH and CTEPH patients followed in a Portuguese PH referral center with the following aims: (1) to describe patients' clinical, functional and hemodynamic profile at diagnosis; (2) to characterize the use of specific pulmonary vasodilator treatments; and (3) to examine long-term mortality and survival trends between different time periods.