Differences in Survival in Idiopathic Pulmonary Arterial Hypertension

Hiosam Bayoumi Hamuda

University of Debrecen Hungary

Abstract

Pulmonary hypertension is a prevalent complication of chronic obstructive pulmonary disease (COPD) that is associated with poor prognosis. Although pulmonary hypertension is usually diagnosed in patients with advanced disease, changes in pulmonary vessels are already apparent at early disease stages, and in smokers without airflow obstruction. Changes in pulmonary vessels include intimal hyperplasia, resulting from proliferating mesenchymal cells, and elastic and collagen deposition as well as endothelial dysfunction. Dysregulation of endothelium-derived mediators and growth factors and inflammatory mechanisms underlie the endothelial dysfunction and vessel remodeling. Circumstantial and experimental evidence suggests that cigarette smoke products can initiate pulmonary vascular changes in COPD and that, at advanced disease stages, hypoxia may amplify the effects of cigarette smoke on pulmonary arteries. Bone marrow-derived progenitor cells may contribute to vessel repair and to vessel remodeling, a process that appears to be facilitated by transforming growth factor-β. Pulmonary arterial hypertension (PAH) is a rare disease characterized by obstructive lesions of the small pulmonary vessels, leading to increased pulmonary artery pressure (PAP), right-sided heart failure, and death within several years. Despite the advent of improved therapies, outcome remains poor. Prognosis correlates with severity of right ventricular (RV) structure and function. More recently, male sex was identified as an independent predictor of mortality. Men treated with endothelin receptor antagonists had less 6-min walk distance (6MWD) improvement. The cause of these sex differences is unknown; however, a distinct vascular and/or RV response to medical therapies is one possibility. Considering the need for improved treatments and "personalized therapy," a better understanding of these sex differences would be important. The aim of our study was to investigate the role of the pulmonary vasculature and the right ventricle in explaining sex differences in the survival of treated idiopathic pulmonary arterial hypertension (IPAH). All patients with IPAH, anorexigen-associated PAH, and heritable PAH treated at the VU University Medical Centre (VUMC) between February 1999 and January 2011 were eligible. Diagnosis was according to the guidelines and included right-sided heart catheterization (RHC). Medical treatment comprised prostacyclin analogs, endothelin receptor antagonists, and phosphodiesterase type-5 inhibitors either alone or in various combinations. Patients with a positive vasodilator challenge were treated with calcium antagonists.1 This was a retrospective cohort study of patients enrolled in an ongoing prospective study to assess the clinical value of cardiac MRI (CMR) in PAH. All patients who had RHC and CMR performed prior to initiation of medical therapy. One hundred eighty-six patients (155 IPAH, 25 heritable PAH, and six anorexigen-associated PAH) were treated at the VUMC between February 1999 and January 2011. Eight-five patients were excluded. Reasons for exclusion were no MRI because of logistical reasons (n = 44), first-line treatment elsewhere (n = 25), contraindications for MRI (n = 11), and no PAH medication initiated (n = 5). Apart from age, indicates similar characteristics compared with those included for further analysis (n = 101).