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Review article

Interventional Therapies in Pulmonary Hypertension

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ABSTRACT

Despite advances in drug therapy, pulmonary hypertension—particularly arterial hypertension (PAH)—remains a fatal disease. Untreatable right heart failure (RHF) from PAH eventually ensues and remains a significant cause of death in these patients. Lowering pulmonary input impedance with different PAH-specific drugs is the obvious therapeutic target in RHF due to chronically increased afterload. However, potential clinical gain can also be expected from attempts to unload the right heart and increase systemic output. Atrial septostomy, Potts anastomosis, and pulmonary artery denervation are interventional procedures serving this purpose. Percutaneous balloon pulmonary angioplasty, another interventional therapy, has re-emerged in the last few years as a clear alternative for the management of patients with distal, inoperable, chronic thromboembolic pulmonary hypertension. The current review discusses the physiological background, experimental evidence, and potential clinical and hemodynamic benefits of all these interventional therapies regarding their use in the setting of RHF due to severe pulmonary hypertension.

Terapias intervencionistas en hipertensión pulmonar

Palabras clave:
Hipertensión pulmonar
Insuficiencia ventricular derecha
Terapias intervencionistas

RESUMEN

A pesar de los avances en el tratamiento farmacológico de la hipertensión pulmonar, en particular de la hipertensión arterial pulmonar (HAP), sigue siendo una enfermedad mortal. La insuficiencia ventricular derecha (IVD) debida a HAP refractaria a tratamiento finalmente se produce y permanece como una causa importante de muerte en estos pacientes. Disminuir la impedancia pulmonar con diferentes fármacos específicos para HAP es el objetivo terapéutico obvio en la IVD secundaria a una poscarga crónicamente aumentada. Sin embargo, se puede esperar una ganancia clínica potencial a partir de los intentos para descargar el corazón derecho y aumentar el gasto cardiaco. La septostomía auricular, la anastomosis de Potts y la denervación de la arteria pulmonar son procedimientos intervencionistas que sirven para este propósito. La angioplastia pulmonar percutánea con balón, otra terapia intervencionista, ha resurgido en los últimos años como una alternativa clara para el tratamiento de pacientes con hipertensión pulmonar tromboembólica crónica distal no operable. En esta revisión se presentarán los antecedentes fisiológicos, la evidencia experimental y los posibles beneficios clínicos y hemodinámicos de todas estas terapias de intervención con respecto a su uso en el contexto de la IVD secundaria a hipertensión pulmonar grave.

INTRODUCTION

Pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure (PAP) > 25 mmHg at rest, measured during right heart catheterization.[1] The term pulmonary arterial hypertension (PAH) describes a subpopulation of patients with PH (group 1 of the current clinical classification), characterized by the presence of precapillary PH including a pulmonary artery wedge pressure < 15 mmHg and a pulmonary vascular resistance > 3 Wood units.[1,2] PAH is a progressive and fatal disorder that affects the pulmonary vasculature and the heart and has no cure. Progressive right heart failure (RHF) remains the main cause of death in this population.

In the last 2 decades, there has been an extraordinary advance in the treatment of PAH. The use of PAH-specific drugs targeting dysfunctional pathways that lead to the characteristic vascular remodeling in this condition have improved both quality of life and survival.[1–3] However, PAH-specific drugs are not always available and, most importantly, not all patients respond.[1,4,5] Furthermore, many patients still deteriorate over time despite treatment and therefore other therapeutic alternatives should be considered. In this regard, dedicated interventions have been applied to selected patients with PAH.[1,3,6–15] These include established and more widespread procedures such as atrial septostomy (AS) and attractive emerging strategies, including a Potts shunt (anastomosis),[1,3,8–11]

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Abbreviations

AS: atrial septostomy
BDAS: balloon dilation atrial septostomy
BPA: balloon pulmonary angioplasty
CTEPH: chronic thromboembolic pulmonary hypertension
PADN: pulmonary artery denervation
PAH: pulmonary arterial hypertension
RHF: right heart failure
TPS: transcatheter Potts shunt

pulmonary artery denervation (PADN),[12–14] and balloon pulmonary angioplasty (BPA) in patients with inoperable chronic thromboembolic PH (CTEPH).[1,6,7,15] This review highlights current understanding and the potential role of all these interventions in the management of RHF in PH.

BALLOON ATRIAL SEPTOSTOMY

There is clinical and experimental evidence suggesting that an interatrial shunt may be of benefit in the setting of PAH. From a clinical standpoint, we know that primary PH patients with a patent foramen ovale live longer than those without a shunt.[16] In addition, we have recognized that patients with Eisenmenger's syndrome with a comparable degree of PH live longer and have less RHF than patients with primary PH.[17] Several experimental studies have shown the potential benefit of a right-to-left shunt in the setting of PH.[18,19] Years ago, several techniques to perform AS without thoracotomy were developed[20,21] and in 1983 Rich and Lam[22] performed the first AS in a patient with PAH. However, the precise role of AS in the management of PAH remains uncertain because most of our knowledge comes from small, noncontrolled series or case reports, and a somewhat generalized perception that the procedure carries an unacceptably high risk. Interestingly, experience with AS has increased considerably in the last few years (Figure 1).

Worldwide Experience With AS for PAH

Since the last review,[23] 5 more series[10,24–27] and case reports have been added.[28–31] To date, 461 procedures have been performed in 364 patients, as reported in 28 series (Table 1 of the supplementary material) and 26 case reports. Atrial septostomy has been performed both in child and adult populations (mostly women [68%]) with idiopathic PAH (76%) in advanced stages of the disease (functional classes III and IV) and failed medical treatment.

Persistent RHF alone (53.4%) or in combination with syncope (21.4%) remains the most common indication for the procedure (Table 2 of the supplementary material). Balloon dilatation AS (BDAS) accounts for by far the most widely used technique (83%). Reported series have shown beneficial hemodynamic effects, including a decrease of ~20% in right atrial pressure (RAP), an increase of about 30% in cardiac index and, as expected, a decrease of ~10% in arterial oxygen saturation (SaO_2%). Furthermore, mortality associated with the procedure has decreased significantly over the last few years (Figure 1).

Procedural Details of Technical Aspects

Balloon dilation AS involves a standard right-left heart catheterization. Septal puncture is performed in most instances using a standard Brockenbrough needle and a long sheath and dilator (ie, Mullins-type sheath) to cross the atrial septum. Sequential static atrial septoplasty is gradually performed using different sized noncompliant peripheral balloons in a careful and controlled (step-by-step) approach[32,33] (Figure 2). A decision on the final diameter of the septostomy is reached when the following hemodynamic changes are met: a drop in baseline SaO_2% of no more than 10%, and/or an increase in left ventricular end-diastolic pressure. We advocate maintaining the latter below 18 mmHg. Altogether, these recommendations are important to avoid refractory hypoxemia and/or pulmonary edema, 2 life-threatening complications of the procedure. In the worldwide experience, the mean size of the atrial shunt is 11 mm (range, 8-18). Reintervention has been repeated on 71 occasions due to spontaneous closure of the defect during follow-up.

Hemodynamic Consequences of AS

Hemodynamic changes after septostomy depend on baseline RAP[23] (Table); at higher baseline RAP, the more pronounced hemodynamic effect, especially in patients with RAP > 20 mmHg. However, it is this subset of patients who are deemed at high risk for complications including death during the procedure as a result of refractory hypoxemia. RAP > 20 mmHg has been associated with more than 10 times the risk of death in these patients.[23] We do not perform AS in this population. It may be considered that the best risk-benefit ratio is therefore for patients with an RAP between 10 and 20 mmHg. Finally, most published data concerning hemodynamic impact following BDAS has been in the resting condition; however, it is during exercise when septostomy could prove to be even more useful, as a pop-off safety valve.[18] This is highlighted by data showing improvement in exercise tolerance after creation of the atrial shunt.[33–35]

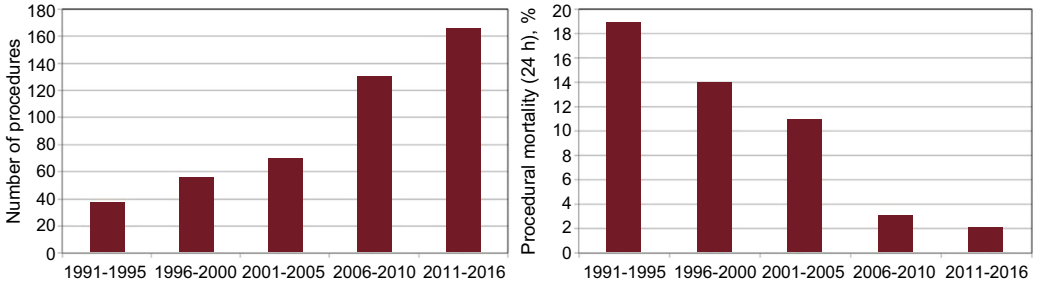

Figure 1. Worldwide experience with atrial septostomy in the treatment of pulmonary arterial hypertension. The left panel shows the number of procedures over the years. The right panel shows that the immediate procedure-related mortality has decreased as a result of experience and modifications to the technique.

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