Shunts: When to Close Them and When to Create Them for Palliation

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Pulmonary hypertension, despite specific therapies, remains an incurable disease with a dreadful prognosis. A systemic-to-pulmonary shunt, if left unrepaired, can cause pulmonary arterial hypertension. With time, pulmonary vascular disease develops, and closure of the shunt becomes contraindicated. Operability criteria are not well defined and rely mainly on hemodynamic values that fail to predict long-term survival. Shunts can also be created in selected cases of advanced pulmonary hypertension, in view of off-loading the right ventricle and improving cardiac output at the cost of cyanosis. Shunt creation is not without risks and remains indicated only in selected severe cases.

INTRODUCTION

A shunt is an abnormal communication between the systemic and the pulmonary circulation, which are normally in series. Discussing shunts in pulmonary hypertension (PH) is both interesting and complicated, as the presence of a shunt can be a cause of PH, but the creation of a shunt represents a palliative procedure performed in a subset of idiopathic PH patients with severe disease. This antagonism makes more sense, however, when you consider timing.

Patients with a systemic-to-pulmonary shunt have increased pulmonary blood flow (PBF) and can develop pulmonary arterial hypertension (PAH) and increased pulmonary vascular resistance (PVR) over time. The definition of PH was updated in 2018 at the 6th World Symposium on Pulmonary Hypertension in Nice, and is a mean pulmonary artery pressure > 20 mm Hg assessed by a right heart catheterization.[1] PH secondary to systemic-to-pulmonary shunt is classified as PAH, Group 1 of the PH classification. In PAH, pulmonary wedge pressure is lower than 15 mm Hg and indexed pulmonary vascular resistance (PVRi) is elevated (> 3 Wood Units [WU] · m^2).[1]

Remembering the equation pulmonary pressure = PBF × PVR is very helpful to understand PAH. In patients with systemic-to-pulmonary shunts, the shear stress provoked by increased PBF damages the pulmonary vascular bed, resulting in endothelial dysfunction and remodeling of the pulmonary arteries. At the early stage of the disease, the increased pulmonary pressure usually reflects the increase in PBF previously described as "hyperkinetic PH." But progressively, pulmonary vascular disease also develops, and PVR increases. In Eisenmenger syndrome (ES), the most advanced form of PAH secondary to congenital heart disease, PVR exceeds systemic vascular resistance, leading to shunt reversal and cyanosis.[2]

Targeted therapies (phosphodiesterase-5 inhibitors, endothelin-receptor antagonists, and prostacyclin analogues) have improved the dreadful prognosis of most forms of PAH, including ES, but curative therapy remains elusive.

The guidelines are well established for the treatment of both ends of the spectrum of PAH secondary to a systemic-to-pulmonary shunt. When the PVR is low and increased pulmonary pressure is mainly due to increase in flow, there is no PAH by definition, and the shunt can safely be closed. When ES has developed, surgery is contraindicated and the patient should benefit from specific medical PAH therapies. The challenge remains in selecting candidates for shunt closure from among the patients with mild or moderate PVR elevation. Persisting PAH after shunt closure has a very poor prognosis, hence the importance of selecting candidates for surgery very carefully.[3,4] We will discuss management strategies for PAH secondary to systemic-to-pulmonary shunt, espe-

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cially operability criteria, in the section "When to Close a Shunt."

Observing that patients with ES have reported better survival than patients with idiopathic PAH, physicians have started to create shunts in severe idiopathic PAH to allow for right-to-left shunting.[5,6] The aim is to prolong survival, postpone lung transplant, or improve quality of life at the expense of systemic arterial desaturation. It is, however, important to note that most of the studies evaluating survival in ES do not take into account immortal time bias. Indeed, only patients surviving long enough to enter clinical follow-up at research institutions have been enrolled into these studies. Diller et al[7] nicely demonstrated that not dealing with this effect overestimates the survival prospects of ES patients. We will address the different types of palliative shunts, and the literature reporting outcomes of this strategy, in the section "When to Create a Shunt."

WHEN TO CLOSE A SHUNT

As overviewed in the introduction, outcomes of patients with congenital heart diseases and a systemic-to-pulmonary shunt, also called a left-to-right shunt, are of special interest in PH. The consequence of the shunt is increased PBF, creating shear stress in the endothelium of the pulmonary vascular bed, leading to thickened and stiff pulmonary arterioles through a cascade of events involving inflammation and remodeling. The PVR progressively increases and leads to PAH.

The velocity of those changes depends on many variables, most of which are not well understood. There is an interindividual variation, implying a role of genetics in the propensity to develop PAH. The location of the shunt also seems to be of importance. Posttricuspid shunts tend to develop PAH much faster than pretricuspid shunts, mainly because the pulmonary vascular bed faces an overload in pressure and increase in pulsatility on top of the volume overload.[8]

The consensus is to close a left-to-right shunt early in life, before the consequences to the pulmonary vascular bed become too severe or irreversible (generally less than 6 months for truncus arteriosus, atrioventricular septal defect, and transposition of the great arteries; less than 12 months for ventricular septal defect and patent ductus arteriosus; and less than 30-40 years for atrial septal defect). However, in some cases, a left-to-right shunt diagnosis is made once some degree of PAH already exists. So, when is it too late to close the shunt? This is a subject of great controversy. The Pediatric Task Force of the 6th World Symposium on Pulmonary Hypertension issued a table with very conservative hemodynamic criteria to be used as a "guidance for assessing operability in PAH associated with congenital heart disease."[1] As the authors outline, these recommendations are based on expert opinion rather than on robust data. The shunt is deemed operable when PVRi is < 4 WU $\cdot$ m^2, with favorable long-term outcome. It is also admitted that a shunt is inoperable when PVRi is > 8 WU $\cdot$ m^2. In between, there is a gray zone with suggested case-by-case decision making in tertiary centers, taking into account many variables such as the age of the patient, the type of shunt, the comorbidities, the resting and exercise saturation, and the clinical history.[1]

The American Heart Association and the European Pediatric Pulmonary Vascular Disease Network issued some slightly different guidelines, with shunt repair to be considered if PVRi is < 6 WU $\cdot$ m^2, or if the ratio of PVR:systemic vascular resistance is < 0.3 at baseline.[9,10] For patients with elevated PVRi, acute vasoreactivity testing can be used to help determine operability. Again, this approach is not based on any study, but rather reflects expert opinion. One of the main limitations is that a universal definition of a positive response to acute vasoreactivity testing in pediatrics and its ability to predict long-term outcome after surgery is still lacking.[11,12]

The Pediatric Task Force of the 6th World Symposium on Pulmonary Hypertension also emphasizes that the long-term outcome of shunt closure in patients with PAH and increased PVR is unknown.[1] Indeed, surviving shunt closure (operability) and normalizing hemodynamics with regression of the lesions in the pulmonary vascular bed (reversibility) are two different concepts.[13] As discussed previously, hemodynamics, although used widely, are not a good predictor of reversibility, and hence not a surrogate for long-term prognosis. Identifying criteria able to better discriminate patients who will benefit from shunt closure with reversal of PAH is needed.[13]

The importance of identifying patients who will normalize their hemodynamics after shunt closure is reinforced by the poor prognosis of persisting PAH after shunt closure. In the categories of PAH associated with congenital heart disease, persisting PAH after shunt closure carries the worst prognosis of PAH secondary to congenital heart diseases.[3,4,14] The strategy to repair the shunt and treat with targeted therapies can therefore not be recommended based upon the currently available data.

Another approach is the "treat with intent to repair," when patients are treated with pulmonary vasodilators in an effort to improve their hemodynamic parameters and then shunt closure is performed. This strategy aroused some interest when first reported; however, the literature on the subject is still very sparse. A few case reports and more recently a multicenter retrospective study of 69 patients have been published, but they mainly concern atrial septal defect, a pretricuspid shunt that seldom causes severe PAH and irreversible lesions.[15,16] No larger-scale studies are published or underway to the best of our knowledge. Moreover, the plausibility of this approach is questionable. We know that idiopathic PAH is not a disease that can regress and be cured with targeted therapies; why should PAH secondary to systemic-to-pulmonary shunt behave any differently? This strategy is hence not proven, and is not supported in the treatment algorithm of the international guidelines.

Other strategies worth mentioning in selected cases where the hemodynamics are not favorable are partial closure of the shunt (patch fenestration)[17] or pulmonary artery banding.[18] These approaches warrant further studies, and are beyond the scope of this article.

WHEN TO CREATE A SHUNT

Shunt creation has been performed in congenital heart surgery for more than

half a century, most often as a palliative procedure to provide pulmonary blood flow (ie, Potts shunt for cyanotic congenital heart diseases), or to create mixing between oxygenated and deoxygenated blood (ie, atrial septostomy in transposition of the great arteries[19]). As PH is a disease with a dreadful prognosis that no specific therapy can cure, physicians have been looking at other treatment strategies.

Based on the observation that patients with ES have a better survival than patients with idiopathic PAH, mainly because of decreased right ventricle (RV) afterload from right-to-left shunting,[5] the idea to perform a surgical or percutaneous shunt to create an "Eisenmenger physiology" arose.

Atrial septostomy has been performed as a palliative procedure for patients with refractory PAH since 1983.[20] In patients with a failing RV and elevated right atrial pressure (RAp), pretricuspid right-to-left shunting unloads the RV and improves left ventricular preload and systemic cardiac output. It is worth mentioning that unlike adults, children with PAH seldom have elevated RAp. Atrial septostomy has the advantage of being a percutaneous procedure, either via blade septostomy or balloon dilation of the atrial septum. It has been reported that atrial septostomy improves symptoms (most notably syncope) and quality of life in adults and children with PAH.[21] A meta-analysis has recently been published demonstrating benefits with this intervention.[22] It may also serve as a bridge to lung transplantation.[23] The procedural morbidity of atrial septostomy is mainly related to uncontrolled right-to-left shunting, resulting in insufficient PBF and profound hypoxemia in patients with elevated RAp and large defects. The relative contraindications for atrial septostomy are a mean RAp > 20 mm Hg, a resting oxygen saturation < 90%, and severe RV failure. Another longer-term disadvantage is the risk of paradoxical cerebral thromboembolism. The international guidelines suggest considering atrial septostomy in patients in World Health Organization (WHO) functional Group III and Group IV with recurrent syncope on combined medical therapy.[1]

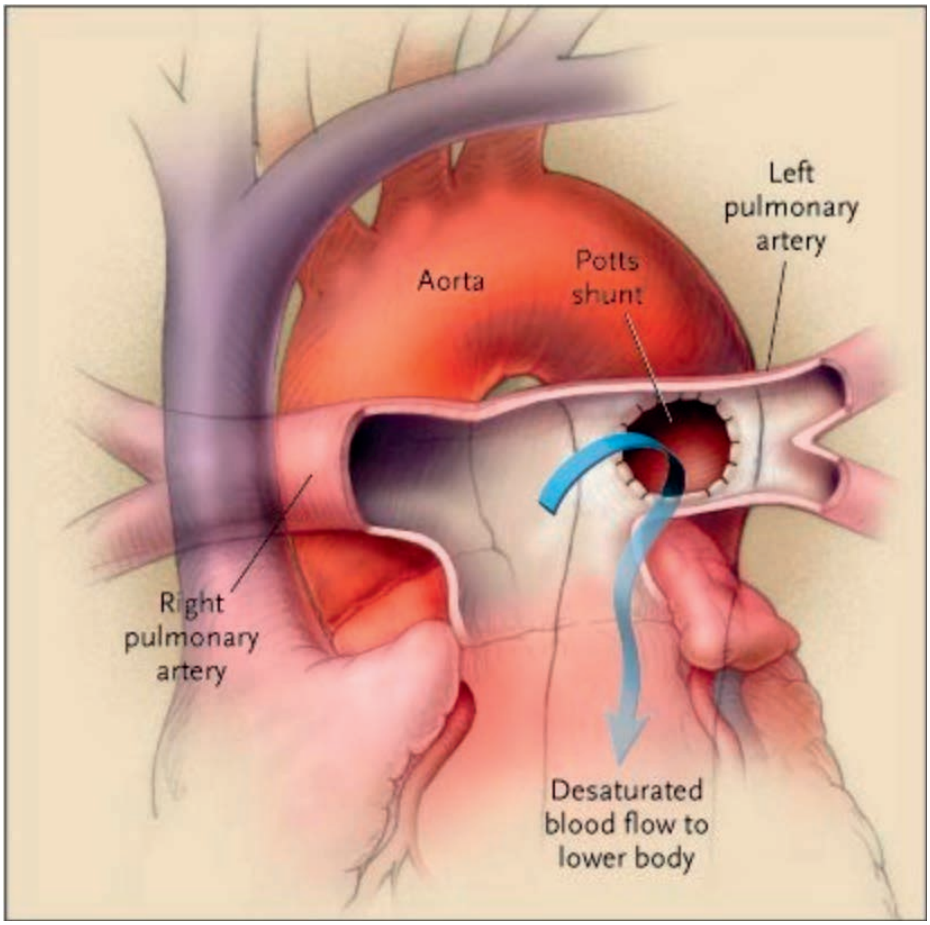

Figure 1: Reversed Potts shunt. The left pulmonary artery is anastomosed to the descending aorta, allowing the desaturated blood to go from the left pulmonary artery to the lower part of the body (arrow). Of note, the right pulmonary artery passes in front of the ascending aorta in the illustrated case, because a Lecompte maneuver has been performed. Reproduced with permission from Blanc et al.[24]

A reversed Potts shunt is the creation of a connection between the left pulmonary artery and the descending aorta, which allows right-to-left shunting (hence the term "reversed"; Figure 1).[24] It has the advantage over atrial septostomy of providing oxygenated blood to the brain and the coronary arteries and only causes desaturation of the lower body. The reversed Potts shunt relieves RV pressure overload in systole and in diastole, improves RV–pulmonary artery coupling, and improves left ventricular performance by reducing the interventricular septum left shift.[25] It has the potential to be effective before RV failure develops. The chief concern remains the risk of operating in PAH patients who have a nonnegligible anesthetic and surgical mortality. Transcatheter procedures have been performed in some highly experienced centers,[26,27] either by stenting an existing small patent ductus arteriosus, or by creating a transcatheter de novo stent–secured aortopulmonary connection, though this approach also appears to carry a high risk of severe complications. Regardless of the technique, reversed Potts shunt creation remains a high-risk procedure with a reported mortality of 12% to 30%.[26,28] One of the main complications is an early acute low-output state secondary to sudden reduction in the left ventricular preload. Despite the high periprocedural mortality, long-term results are very encouraging, with prolonged survival and improvement in functional status, allowing progressive weaning from prostanoids in children.[28] Further studies should help to understand if these favorable effects are long-lasting and further define the indications and contraindications of the procedure.

Table 1. Comparison of Atrial Septostomy and Reversed Potts Shunt[a]

	Advantages	Drawbacks
Atrial septostomy	Percutaneous procedure RV diastolic decompression Increases LV preload	May require repeated procedures (for spontaneous closure) Whole body desaturated Requires elevated RAp Risk of cerebrovascular events
Reversed Potts shunt	Preserved saturation to brain and coronaries Independent of RAp Reduces RV afterload RV systolic decompression, leading to better RV to pulmonary artery coupling Some RV diastolic decompression Improves septal geometry Improves LV performance	Surgical or high-risk percutaneous procedure Requires supra-systemic PAH Risk of decreasing LV preload

[a] RV indicates right ventricle; LV, left ventricle; RAp, right atrial pressure; PAH, pulmonary arterial hypertension.

As per the international guidelines, reversed Potts shunt "may be considered in patients with suprasystemic PH refractory to any medical treatment, including combined therapy presenting with WHO FC IV symptoms."[1] The recent implant of unidirectional valved anastomosis in PAH patients with infrasystemic pulmonary pressures offers new potential to use this approach at earlier stages of disease.[27,28]

Table 1 summarizes the main features of atrial septostomy and the reversed Potts shunt. Shunt creation remains a therapy used only in severe PAH cases, mainly because of the significant periprocedural mortality. With the improvement of procedural techniques and better patient selection, and after collecting longer-term follow-up data, we may well be tempted to offer shunt creation earlier in the course of PH. The creation of a shunt does not seem to contraindicate a future lung transplant, but might rather represent a valuable bridge to transplantation.

Apart from the question of the timing of the shunt, the application of the technique to other groups of PAH (eg, heritable PAH, PAH secondary to connective tissue disease) and to adult populations warrants further studies.

Finally, before reproducing ES physiology by means of shunt creation, it should be kept in mind that patients with ES do not have such a benign prognosis.[7]

CONCLUSION

Shunts and PAH have a complex relationship that evolves with time. In the early stages of PH secondary to left-to-right shunt, the best therapeutic option remains closing the shunt. When PH has developed with concomitant significant pulmonary vascular disease, the shunt should not be closed and patients should be treated with specific therapies. In severe cases of idiopathic PH, shunt creation (atrial septostomy or reversed Potts shunt) may represent a therapeutic option that improves functional status and may delay the need for lung transplantation in those who survive the high-risk procedure. Further studies are needed to assess the indications for shunt creation, as well as the long-term effects of this approach.

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