Aneurysms of the Pulmonary Artery

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Pulmonary artery (PA) aneurysms (PAAs) are rare and infrequently diagnosed. Deterling and Clagett1 discovered 8 cases of PAAs in 109,571 consecutive postmortem examinations. PAAs generally occurred in a younger age group than aortic aneurysms with an equal sex incidence.2 Eighty-nine percent of all PAAs were located in the main PA, whereas only 11% were located in the pulmonary branches.3 When affecting the PA branches, PAAs in the left PA were more common than in the right PA.1

Definition
An aneurysm is defined as a focal dilatation of a blood vessel involving all 3 layers of the vessel wall. Pseudoaneurysms, on the other hand, do not involve all layers of the arterial wall but possess a higher risk of rupture. In computed tomography, the upper limit for adults of the main PA diameter is 29 mm, and the upper limit of the interlobar PA is 17 mm.4 Therefore, Nguyen et al5 describe a PAA as a focal dilatation of the PA beyond its maximal normal caliber. In contrast, Brown and Plotnick6 define a PAA as a PA with a diameter exceeding 40 mm, distinguishing between an ectasia of the PA and a true PAA. However, both definitions do not relate the PAA threshold to body dimensions or to the diameters of other vessels.

In our center, the upper limit of the main PA diameter (29 mm) was defined as a PAA. In case of a PAA in children, the PAA size was compared with the normal values according to the method of Kampmann et al.7 In high-risk patients, the size of the PAA was indexed to the body weight according to patients presenting with an aneurysm of the aorta.

Origin
Various origins of PAA have been described, allowing us to differentiate among congenital causes, acquired causes, and idiopathic PAA (Table 1).

Congenital Causes
Congenital causes have been recognized as the major reason for PAA formation. More than 50% of all cases were associated with congenital heart disease.1,2

In general, it is presumed that increased flow caused by left-to-right shunt results in increased hemodynamic shear stress on the vessel walls and therefore promotes aneurysm formation in the PAs.3 The 3 most frequent congenital heart defects associated with a PAA are, in decreasing order, persistent ductus arteriosus, ventricular septal defects, and atrial septal defects.1,2,8

The aortic valve has also been identified as a major congenital cause of PAA formation. In fact, the fourth and fifth most frequent causes of PAA formation are a hypoplastic aortic valve and a bicuspid aortic valve, respectively.1,2,8

Pulmonary valve stenosis, including postvalvular stenosis, has frequently been described as an isolated cause of PAA formation.5,9 In fact, early pulmonary valve commissurotomy in the patient’s history may precipitate aneurysm formation because of an eccentric right ventricular outflow jet, which may lead to weakening of the vascular wall.5 Furthermore, 1 case report described PAA formation in a patient presenting with the Noonan syndrome, a relatively common autosomal-dominant congenital disorder that is also associated with pulmonary stenosis.6

Many patients with PAA also present with pulmonary valve regurgitation, and even though it is more plausible that it is a consequence of annulus dilatation by the PAA, it may also be an independent etiologic factor in the formation of a PAA.1,10

Patients with the congenital malformation of an absent pulmonary valve syndrome represent a PAA subset that might link pulmonary valve regurgitation to PAA formation (Figure 1). Absent pulmonary valve syndrome has been described as a rare variant of tetralogy of Fallot but has also been associated with ventricular septal defects and Uhl anomaly and very seldom occurs as an isolated congenital heart defect.11,12 In fact, early mortality in patients with absent pulmonary valve syndrome is high as a result of significant PAA formation and bronchi compression.12

Other congenital causes associated with the formation of aneurysms resulting from deficiencies of the vessel walls and vascular wall abnormalities have been connected to PAA formation. Those include the Ehlers-Danlos syndrome, the Marfan syndrome, and cystic medial necrosis.13,14

Acquired Causes
There are various reports of infectious causes for PAA formation. In the past, untreated syphilis and tuberculosis have frequently been associated with PAA formation. In patients with advanced syphilis, PAA formation almost always occurs in the large PAs, whereas patients with advanced tuberculosis...
are at high risk of intraparenchymal PAA formation.15,16 Pseudoaneurysms secondary to pulmonary tuberculosis, also known as Rasmussen aneurysms, usually involve the upper lobes in the setting of reactivation tuberculosis.16 Today, pyogenic bacteria are an increasingly common cause of PA pseudoaneurysm formation.17 In addition, septic embolisms caused by bacterial endocarditis, seen mainly in intravenous drug users, have been recognized as a cause of PAA formation.4,8 Moreover, there are reports linking fungal pneumonia to PAA formation.17

Vasculitis of the PAs has been identified as an acquired cause of PAA formation. The Behçet syndrome is a chronic multisystem form of vasculitis characterized by recurrent oral and genital ulcers in combination with uveitis. It is most commonly seen in Southeast Asia and may result in PAA formation.18

PA hypertension (PAH) is an important cause of PAA formation10,14,20 and has been suggested to be a clinical symptom of an existing PAA.21 PAH is a clinical syndrome characterized by an increase in pulmonary vascular resistance leading to failure of the right side of the heart and ultimately to death.22 In fact, PAA formation has been classified according to the updated National Institute for Health and Clinical Excellence classification of pulmonary hypertension into 5 groups: group 1, PAH (idiopathic, heritable, drug-/toxin-induced, and associated with connective tissue disease, portal hypertension, congenital heart diseases, schistosomiasis, HIV infections, pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis, and persistent pulmonary hypertension of the newborn); group 2, PAH resulting from disease of the left side of the heart; group 3, PAH caused by lung diseases or hypoxia; group 4, chronic thromboembolic pulmonary hypertension; and group 5, pulmonary hypertension with unclear multifactorial mechanisms.25

Chronic pulmonary embolism is also a relatively common cause of PAA, and such aneurysms tend to be associated with mural thickening, webs, or intramural thrombi that can calcify.5 Primary lung cancer and pulmonary metastasis can cause erosion into the PAs, resulting in pseudoaneurysm formation. Moreover, primary tumors arising from the PAs such as leiomyosarcoma or angiosarcoma may lead to focal expansion and aneurysmal dilatation of the PA wall.26

Over the last years, an increasing number of iatrogenic causes of PAA formation have been reported. PAH formation has been described as a rare complication after several cardiac surgeries, including surgical palliation of tricuspid atresia, Fenning technique treatment for D-transposition of the great vessels, the Blalock-Taussig shunt procedure, and PA banding.27–30 Wrongly positioned Swan-Ganz catheters were described as an increasingly frequent cause of iatrogenic PA pseudoaneurysms, with a 0.2% incidence of rupture and hemorrhage after catheter insertion. When the catheter is inserted too far into the PAs, the tip of the catheter may erode the arterial wall, causing weakening and dilatation of the vessel. Hence, the artery ruptures or a pseudoaneurysm forms.31 Other rare iatrogenic causes of PAA formation include chest tube insertion, conventional angiography, and surgical resection or

Table 1. Causes of PAA

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Heart defects</th>
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<tr>
<td>Persistent ductus arteriosus</td>
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<td>Ventricular septal defects</td>
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<tr>
<td>Atrial septal defects</td>
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<td>Hypoplastic aortic valve</td>
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<td>Bicuspid aortic valve</td>
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<td>Pulmonary valve stenosis</td>
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<td>Pulmonary regurgitation</td>
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<tr>
<td>Absent pulmonary valve</td>
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<tr>
<td>Connective tissue abnormalities</td>
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<tr>
<td>Ehlers-Danlos syndrome</td>
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<td>Marfan syndrome</td>
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<tr>
<td>Cystic medial necrosis</td>
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<tr>
<td>Acquired</td>
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<tr>
<td>Infectious</td>
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<td>Syphilis</td>
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<td>Tuberculosis</td>
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<td>Pyogenic bacteria</td>
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<td>Septic embolisms</td>
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<tr>
<td>Bacterial and fungal pneumonia</td>
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<tr>
<td>Vasculitis</td>
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<tr>
<td>Behçet syndrome</td>
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<tr>
<td>Hughes-Stovin syndrome</td>
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<tr>
<td>Pulmonary arterial hypertension</td>
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<tr>
<td>Chronic pulmonary embolism</td>
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<tr>
<td>Neoplasm</td>
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<td>Primary lung cancer</td>
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<tr>
<td>Pulmonary metastasis</td>
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<tr>
<td>Iatrogenic</td>
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<td>Cardiac surgery</td>
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<td>Catheters</td>
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<td>Chest tubes</td>
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<td>Angiography</td>
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<td>Surgical resection</td>
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<td>Biopsy</td>
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PAA indicates pulmonary artery aneurysm.
biopsy. Moreover, PA pseudoaneurysm formation after penetrating trauma such as stab and gunshot wounds has been reported.

**Idiopathic**

Idiopathic PAA formation is rare, but an increasing number of cases are being reported in the literature. Greene and Baldwin have defined 4 pathological criteria for an idiopathic PAA: simple dilatation of the pulmonary trunk with or without involvement of the rest of the arterial tree, the absence of intracardiac or extracardiac shunts, the absence of chronic cardiac or pulmonary disease, and the absence of arterial disease such as syphilis or more than minimal atheromatosis or arteriosclerosis of the pulmonary vascular tree.

**Pathophysiological Considerations**

There are very limited data on the pathophysiological processes that are relevant or evident in PAA formation. Cystic medial necrosis was observed in many perioperative samples of the vascular wall, but there are also reports of normal histological architecture. It has been proposed that structural changes in elastin and collagen under the influence of an increased PA pressure may lead to PA dilatation. From a hemodynamic perspective, perturbation from an abnormally opening pulmonary valve or shear stress resulting from shunt flow may induce apoptosis, remodeling, and aneurysmal transformation of the vessel wall. In the presence of regurgitation, the hemodynamic stress may be exacerbated as stroke volume is increased, resulting in larger root aneurysm.

**Clinical Manifestation**

In general, clinical manifestations of PAA remain nonspecific, whereas most patients with a PAA, even those with large PAA diameters up to 70 mm, have no complaints. Clinical symptoms include dyspnea, chest pain, hoarseness, palpitation, and syncopal episodes. Bronchus compression by a large PAA may be responsible for cyanosis, cough, and increasing dyspnea, pneumonia, fever, and bronchiectasis. Among all reported cases, one third of the patients died as a result of rupture, which underlines the fact that not all PAAs progress to the rupture state.

Depending on the underlying condition responsible for PAA formation, patients frequently present with right atrial and ventricular hypertrophy, right heart failure, tricuspid regurgitation caused by annulus dilatation, and mild pericardial and pleural effusion. Dissection of a PAA is a rare but life-threatening complication that occurs in up to 19% of all PAA patients without PAH. PA dissection occurs almost exclusively in an artery dilated by an aneurysm rather than in a normal-sized PA. The most common site of dissection is the main PA trunk (in 80%), and only 15% of all PAA dissections are diagnosed in alive patients. Clinical symptoms include severe dyspnea, retrosternal chest pain, central cyanosis, cardiogenic shock, and sudden death.
death. Cardiac tamponade resulting from dissection of a PAA has been identified as the major cause of death.39,40,42

Diagnosis
During auscultation, a systolic heart sound is generally present and might be combined with a diastolic murmur.3,34–36 The ECG shows signs of right ventricular or right atrial hypertrophy.41 In a standard x-ray (Figure 2), a PAA may appear as a hilar enlargement, a lung nodule, or a pulmonary mass.3,35 Some x-rays illustrate an aneurysmal main PA segment or dilatation of the PA.3,36 Transthoracic or transesophageal echocardiography is an important tool to evaluate heart function and valvular function to reveal shunts and may show the presence of a PAA.9,20,34,36,40,41 A bronchoscopy may show compression of the bronchus.35 Angiography allows delineation of the PAA within the pulmonary vasculature, involvement of the vascular structure, and assessment of the right-side hemodynamic pressure. However, an angiography can visualize only the patent lumen of the PAA, and it is invasive.9,35 In general, contrast-enhanced computed tomography (Figure 3) confirms the diagnosis and provides useful information on size, number, location, and extent of the PAA.20,34–36,40,41 Furthermore, magnetic resonance imaging (Figure 4) or 4-dimensional magnetic resonance imaging may show arterial wall thickening, provide information on blood flow, and characterize aortic and pulmonary hemodynamics without any radiation exposure.43

Treatment
Overall, the optimal treatment of PAA remains uncertain. There is no clear guideline for the best therapeutic approach, and there is limited experience because of the infrequency of the disease.

Conservative and Interventional Treatment
The law of Laplace dictates that wall stress, the most important determinant of progression to rupture, is directly proportional to the pressure and radius of the vessel wall and is inversely proportional to the wall thickness. Therefore, conservative treatment seems reasonable for asymptomatic patients with PAA with no significant PAH and apparent stability in PAA diameter.9,14,40 Shunt flow or valvular pathologies cause persistent hemodynamic stress, which may be responsible for PAA formation and dilatation and should therefore be a contraindication for conservative treatment.14 Overall, idiopathic PAA seem to be a relatively benign condition, and conservative observation may be reasonable when there is normal PA pressure, in contrast to patients with aneurysms of the aorta.44

In case of PAH, treatment should include calcium channel blockers, diuretics, and anticoagulants, and patients may benefit from the use of vasoactive substances such as endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, and prostacyclin derivatives.45 Nevertheless, the majority of patients with normalized pressure still show an increase in PAA diameter. A phenomenon well known from aneurysms of the aorta: Hypertension is an important underlying cause of aneurysm formation of the aorta, but further dilatation of the aneurysm is independent of systemic blood pressure.46 In general, patients with PAH should be seriously considered for surgical treatment, and an aggressive surgical approach has
been advocated for patients with PAH owing to the risk of impending dissection and rupture. However, patients with PAH may have a high surgical risk and may need a heart-lung transplantation. Even though there are reports of relatively long survival without surgery, surgical therapy seems to be the only treatment with the possibility of effective long-term survival.3

In case of vasculitis, immunosuppressive medication seems to be the logical therapy. However, the effect has to be monitored carefully because some drugs might be ineffective in vascular Behçet syndrome, and there currently is no satisfactory medical treatment for the Hughes-Stovin syndrome.18,19

Interventional treatment is a relatively new treatment option for PAAs, and coil embolization seems to be a good treatment option for iatrogenic causes and small branches.47 In addition, there was a report of complete occlusion of a dissected PAA by a covered stent.38

### Indication for Surgical Treatment

Overall, surgery remains the cornerstone of therapy for lesions involving the main pulmonary trunk, and evidence suggesting an absolute diameter threshold for surgery of the main PA is lacking. However, from our clinical experience and scientific knowledge of all the available data about aortic aneurysms, we suggest operating on adults with pulmonary trunk aneurysms ≥5.5 cm according to the guidelines for aortic disease.3

In case of conservative treatment, it is our opinion that patients should be re-evaluated regularly, and a change in treatment should strongly be considered in case of compression of adjacent structures, thrombus formation in the aneurysm sack, ≥5-mm increase in the diameter of the aneurysm in 6 months, the appearance of clinical symptoms, evidence of valvular pathologies or shunt flow, and verification of PAH.10,34,35,44

In case of symptomatic pulmonary valve regurgitation and right ventricular dilatation, the timing of surgical intervention should be determined by changes in right ventricular size and function rather than the size of the PAA itself.10,34 Moreover, in cases of PAH or an underlying tissue disease, surgery seems to be the treatment of choice.20 However, for this patient group with an aggressive underlying cause of the PAA such as patients presenting with idiopathic PAH who already have a very limited life span despite the introduction of new pharmaceutical therapy options, a more careful therapeutic approach seems reasonable. In general, it is our opinion that PAH is an indication for a surgical therapy with the size limit of 5.5 cm according to Table 2. This relates more in these patients than in other groups to the natural progression of the disease resulting from the instability of the aneurysm. However, if there is clear evidence that the natural course of the underlying disease will severely limit the mid- and long-term postoperative survival, we are very reluctant to and cautious about operating on this patient group.

Other authors proclaimed that once a PAA has been diagnosed it should be operated on because of the possible fatal outcome, including failure and rupture of the right side of the heart,3 whereas Seguchi et al36 recommend surgery for all PAAs with a diameter ≥60 mm. Unfortunately, because of the infrequency of the diagnosis and because of the different causes of the formation of a PAA, it is, for now, not possible to define a single scientifically proven threshold. However, we suggest that a recommendation according to the vast data on the progression of aortic aneurysms is the most appropriate. In addition, from our own clinical experience, a greater PAA diameter is associated with a higher postoperative morbidity.

Early surgery should be considered in patients with a reasonable surgical risk. Progression of diameter increases surgical risk as a result of impaired cardiac function and difficult ventilation owing to chronic bronchus obstruction and atelectasis. Surgery in a younger patient reduces postoperative morbidity and mortality.28

In case of rupture, surgery is the only possible life-saving treatment option.34 In addition, dissection is an indication for surgery in case of reasonable preoperative morbidity.10,20

### Surgical Treatment

Aneurysmorrhaphy is a simple, non–time-consuming possibility for surgical repair of a PAA.3 However, it only decreases the diameter of the vessel; it does not treat the abnormal vessel wall. In addition, it might increase overall wall stress according to the law of Laplace. Today, aneurectomy and repair or replacement of the right ventricular outflow tract seem to be the methods of choice.10,34 Moreover, aneurectomy is the only feasible treatment for patients with connective tissue disorders.34 With respect to extension of the PAA, different replacement strategies are possible. The most common procedure is the replacement of the PA and the pulmonary trunk with a conduit starting in the right ventricular outflow tract. This can be performed with Gore-Tex or Dacron tubes, homografts, or xenografts (porcine aortic grafts or bovine jugular conduits).10,34 Another possible option may be a valve-sparing surgical approach comparable to the David procedure. However, in case of involvement of the pulmonary valve, repair or replacement should seriously be considered for relief of right ventricular volume overload and hemodynamic burden on the vessel wall. In fact, sole aneurysmorrhaphy without pulmonary valve replacement was associated with late recurrence of PA dilatation, possibly because of persistent hemodynamic stress.14

Treatment of distal PAA may be more difficult and may require lung resection, and it is more often considered fatal.40 Lung or combined heart-lung transplantation is the ultimate treatment, especially in patients with PAH.20,39

### Table 2. Recommended Indications for Surgery*

| Absolute PAA diameter ≥5.5 cm | Increase in the diameter of the aneurysm of ≥0.5 cm in 6 mo | Compression of adjacent structures | Thrombus formation in the aneurysm sack | Appearance of clinical symptoms | Evidence of valvular pathologies or shunt flow | Verification of PAH | Signs of rupture or dissection |

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PAA indicates pulmonary artery aneurysm; and PAH, pulmonary artery hypertension.

*Our conclusion from a review of the literature and from our own clinical experience.
In terms of surgical outcome, because no large series of PAA patients have been published, mortality and morbidity data cannot be provided. From our own clinical experience, perioperative morbidity is comparable to that of the repair of aneurysms of the ascending aorta. Significant postoperative problems include ventilation difficulties resulting from a tendency of the bronchi to collapse, atelectasis of the lung, and postoperative effusion in the former cavity of the aneurysm, which together may extend mechanical ventilation time and increase the risk for lung injury.

Still, it has to be considered that the indications for surgery listed in Table 2 may result in an earlier surgical intervention, which may create the need for reinterventions. Overall, the situation of those patients may be compared with that of patients after the Ross procedure, and this patient group shows low rates of degeneration, endocarditis, and thromboembolism for a period lasting >20 years after pulmonary valve replacement. In addition, a complete right ventricular outflow tract reconstruction by a valved bovine conduit (Contegra), an approach favored in our center, showed good long-term results. Therefore, we believe that the risk of reintervention after PAA surgery is outweighed by the risk reduction (dissection, rupture) resulting from an earlier surgery.

Conclusions

PAAs seldom occur, are rarely diagnosed, and do not present with distinct symptoms. To date, there are no clear guidelines or rules on the optimal treatment for patients with PAAs because of the small number of cases. On the basis of our clinical and scientific knowledge, we suggest operating on adults with pulmonary trunk aneurysms >5.5 cm according to the guidelines for aortic disease. In case of conservative treatment, it is our opinion that patients should be re-evaluated regularly, and a change in treatment should strongly be considered in case of compression of adjacent structures, thrombus formation in the aneurysm sac, ≥25-mm increase in the diameter of the aneurysm at 6 months, the appearance of clinical symptoms, evidence of valvular pathologies or shunt flow, or verification of PAH. In general, the PA and the pulmonary trunk can be replaced with a conduit starting in the right ventricular outflow tract. In case of no involvement of the pulmonary valve, a valve-sparing surgical approach comparable to the David procedure may be feasible.

Disclosures

None.

References


Key Words: aneurysm • arteries • blood vessels • surgery
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