

Pulmonary Arteriopathy in Patients with Mild Pulmonary Valve Abnormality without Pulmonary Hypertension or Intracardiac Shunt

Karam Obeid^{1*}, Subeer K. Wadia, MD², Gentian Lluri, MD, PhD², Cherise Meyerson, MD³, Gregory A. Fishbein, MD³, Leigh C. Reardon, MD², Jamil Aboulhosn, MD²

¹ Department of Biological Sciences, Old Dominion University, Norfolk, Virginia, USA

² Department of Internal Medicine, Ahmanson/UCLA Adult Congenital Heart Disease Center, Los Angeles, California, USA

³ Department of Pathology, Ronald Reagan/UCLA Medical Center, Los Angeles, California, USA

Abstract

Background: The natural history of pulmonary artery aneurysms (PAA) without pulmonary hypertension, intracardiac shunt or significant pulmonary valvular disease has not been well studied. This study looks to describe the outcome of a cohort of adults with PAA without significant pulmonic regurgitation and stenosis. Imaging modalities utilized to evaluate pulmonary artery (PA) size and valvular pathology are reviewed.

Methods: Patients with PAA followed at the Ahmanson/UCLA Adult Congenital Heart Disease Center were included in this retrospective analysis. The criteria for patient inclusion were PAA size ≥ 2.5 cm without intracardiac shunting, more than mild pulmonary valve stenosis and regurgitation, or pulmonary hypertension. PAA size gathered from initial imaging was compared to the most recent to quantify PAA growth over time. CT, MRI and echocardiography results were compared.

Result: Eleven patients were included; Eight females and mean age of 57 (range 25-80). Eight patients were > 50 years of age. Five patients had PAA > 4 cm and were ≥ 50 years old. PAA size increased at a mean rate of 0.5 cm over a mean follow-up of 10 years. Echocardiography demonstrated significant correlation to CT/MRI ($r=0.93$, $p<0.001$).

Conclusion: Most PAA cases are present in patients older than 50 years. Long-term follow-up suggests a

benign course without episodes of dissection or rupture despite 6/11 patients with PAA ≥ 5 cm. PA dilation progresses slowly over time and does not appear to cause secondary events. Echocardiography correlates well with magnetic resonance imaging and computed tomography and is useful in measuring PAA over time.

Copyright © 2018 Science International Corp.

Key Words

Pulmonary artery aneurysm • Pulmonary stenosis • Pulmonary hypertension • Aortic aneurysm

Introduction

Pulmonary artery aneurysm (PAA), as an isolated finding, is a rare condition of unclear clinical significance that is not well described in the literature. Deterling and Clagett [1] reported an occurrence of eight PAA in 109,571 post-mortem examinations, corresponding to an estimated prevalence of one PAA per 13,696 necropsies. Greene and Baldwin [3] described four criteria for defining PAA: 1) Dilation of the pulmonary artery (PA) (including or excluding the branches), 2) lack of intracardiac shunt, 3) lack of chronic cardiac conditions and 4) lack of systemic arterial disease.



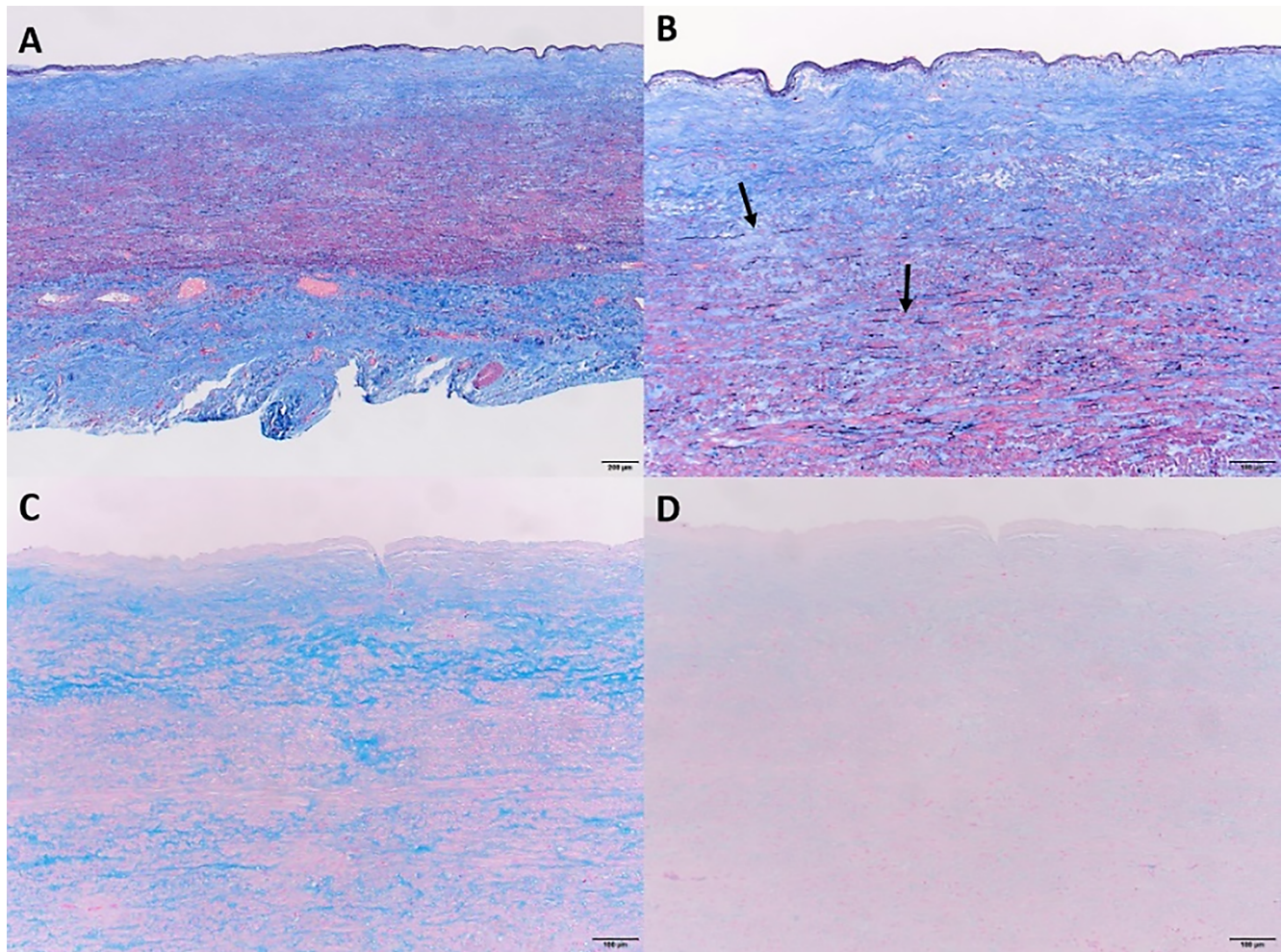


Figure 1. Pulmonary artery histology from a patient with Pulmonary artery aneurysm. *Panel A.* Trichrome/elastin stain demonstrating severe elastic fiber loss (40x) consistent with grade 3 arteriopathy (Niwa et al, *Circulation* 2001). *Panel B.* At high power, there is disruption (arrow) and fragmentation of the remaining elastic fibers (trichrome/elastin, 100x). *Panel C.* The alcian blue stain highlights transmucoid extracellular matrix accumulation (100x). *Panel D.* The extracellular mucoid matrix materials (glycosaminoglycans) are digested following treatment with hyaluronidase (100x).

When pulmonary aneurysms do occur, they are usually secondary to a variety of factors, most commonly pulmonary arterial hypertension and/or congenital cardiac shunts. Less commonly pulmonary artery aneurysms may be secondary to infection (syphilis and tuberculosis), congenital arteriopathy (e.g. Marfan and Turner syndrome), auto-immune conditions (Behcet's) or congenital pulmonary valve abnormalities (Tetralogy of Fallot with absent pulmonary valve, pulmonary stenosis and/or regurgitation) [2]. Pulmonary artery dilation may be present in patients with pulmonary valve stenosis, however, catastrophic complications such as dissection or rupture

are rare (Roberts WC et al. *AJC* 2017, Adodo et al. *Ann Thorac Surg* 2017, Koretzky *Circulation* 1969). The histopathologic characteristics are similar to those seen in the aortas of those with congenital aortic valve disease [9]. The association between aortic dilation and congenital aortic stenosis is well known, however, the degree of aortic dilation is not directly related to the degree of valvular stenosis. This suggests a congenital etiology to the aortopathy in bicuspid aortic valve patients that may be independent of valvular hemodynamics. Could a similar logic exist for congenital pulmonary valve stenosis? The definition of an aneurysm is "focal dilation of a blood vessel involving all

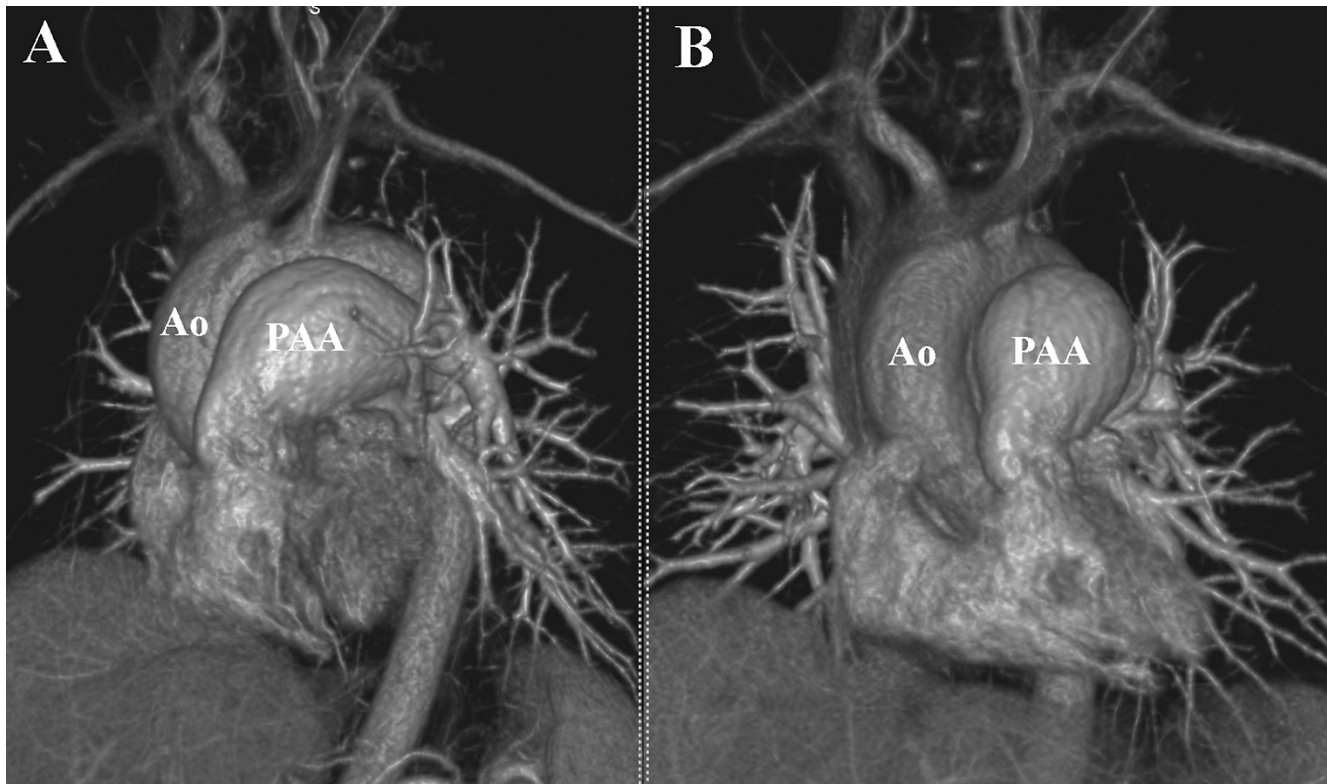


Figure 2. Cardiac MRI with feraheme contrast of a patient with Pulmonary Artery Aneurysm demonstrating severe dilation of the main pulmonary artery. *Panel A.* Left anterior oblique view. *Panel B.* Frontal view.

three layers of the vessel wall” [4]. There have been several suggested definitions for pulmonary artery aneurysm. Nguyen et al [5] defined a PAA as the “focal dilation of the artery beyond its maximal normal caliber”. There is no clear consensus on the upper limit of normal size for the main pulmonary artery in adult patients. In this study, we considered PAA to be a dilation of the main and/or proximal branch pulmonary artery of ≥ 2.5 cm. The histopathologic characteristics of PAA include fragmentation and loss of elastin fibers (Figure 1). Patients with PAA are generally asymptomatic and the diagnosis is often made incidentally on chest or cardiac imaging. This study seeks to describe the imaging modalities utilized to make the diagnosis of PAA and monitor for growth or complications, the natural history of this condition and review the existing literature. Moreover, commonly utilized imaging modalities for the diagnosis and follow-up of PAA, such as echocardiography and cross-sectional imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI), are compared (Figure 2).

Methods

A retrospective review of the Ahmanson/UCLA Adult Congenital Heart Disease Center database was performed to identify a cohort of patients with PAA. The criteria for patient inclusion were dilated main and/or branch pulmonary artery ≥ 2.5 cm, lack of significant pulmonary valvular disease, absence of congenital cardiac shunt and/or pulmonary hypertension, and absence of a clear secondary etiology. Transthoracic echocardiographic and cross-sectional imaging (CT and/or MRI) imaging data were gathered and compared. The first recorded PAA size from each imaging modality was compared to the most recent PAA size allowing estimation of rate of growth over time.

Results

Eleven patients with PAA were identified from a total of 4,857 patients in the Ahmanson/UCLA Adult Congenital Heart Disease database. Patients with

Table 1. Baseline and follow-up imaging characteristics of 11 pulmonary artery aneurysms (PAA) patients. Mean follow-up duration is 10 years.

Patient	Gender	Age (years)	Initial PAA size (cm)	PAA size at latest follow-up (cm)	Follow-up duration (years)	Rate of PAA growth (cm/year)
1	M	65	3.7	3.8	12	.01 cm/year
2	M	30	5	5	5	0 cm/year
3	M	77	4.5	5	15	.03 cm/year
4	F	53	3.8	3.8	1	0 cm/year
5	F	52	4.8	5.3	18	.03 cm/year
6	F	80	7.3	7.5	2	0.1 cm/year
7	F	71	3.1	4.3	11	0.1 cm/year
8	F	25	2.8	3.9	14	0.08 cm/year
9	F	69	5.9	6.5	13	0.05 cm/year
10	F	70	4	5.4	16	0.09 cm/year
11	F	43	4.6	4.7	5	0.02 cm/year

greater than mild pulmonary valve stenosis or regurgitation and any of the secondary causes of pulmonary artery aneurysm were excluded. All patients had mild pulmonary valve stenosis and 9/11 had mild pulmonary regurgitation. Eight of the eleven patients were female, mean age 57 (range 25-80) (Table 1). Eight of the eleven (73%) were above 50 years of age. Five patients (46 %) had PAA > 4 cm and all were \geq 50 years old. PAA size increased at a mean rate of 0.5 cm over a mean follow-up of 10 years, and an increase in PAA size was noted in nine patients. PAA size increased at <0.1 cm/year in all patients (Figure 3). For the assessment of PAA size, echocardiography demonstrated a significant correlation to CT/cMRI ($r=0.93$, $p<0.001$). There were no instances of pulmonary artery dissection or rupture despite 6/11 patients with PAA > 5 cm. Additionally, there were no instances of coronary artery compression and no evidence of progressive pulmonary valvular abnormalities over 10 years.

The mean systolic gradient across the pulmonic valve measured by Doppler was 7.3 (+/- 3 mmHg) and 7/11 patients had evidence of pulmonary valve systolic doming by echocardiography. Ten patients underwent cardiac MRI imaging at some point in their care, of these eight had evidence of pulmonary valve doming, and one patient had a bicuspid pulmonic valve. A bicuspid aortic valve was present in one patient who also had dilation of the ascending aorta

and whereas another patient had pectus excavatum and mitral valve prolapse without dilation of the aorta. Pulmonary ejection sounds were auscultated in eight patients and pulmonary ejection murmurs were heard in all eleven patients. Pulmonic valve clicks or murmurs led to further investigation and discovery of PAA by echocardiography in nine patients. Incidental discovery occurred by chest CT in one patient with frequent pulmonary infections and another patient with a thyroid cyst.

Discussion

Pulmonary arterial aneurysm (PAA) may occur in a variety of settings and is often associated with pulmonary arterial hypertension or congenital cardiac shunts. The condition has been described in patients with pulmonary valve pathology, but long-term data on clinical significance and progression is lacking. This study sought to delineate the long-term outcomes in a cohort of adults with no more than mild pulmonary valve dysfunction and PAA. Long-term follow-up suggests a benign course without catastrophic complications of rupture or dissection despite 6/11 patients having a PAA \geq 5 cm. The dilation of the pulmonary artery occurred slowly over time and did not seem to cause any secondary clinical complications such as

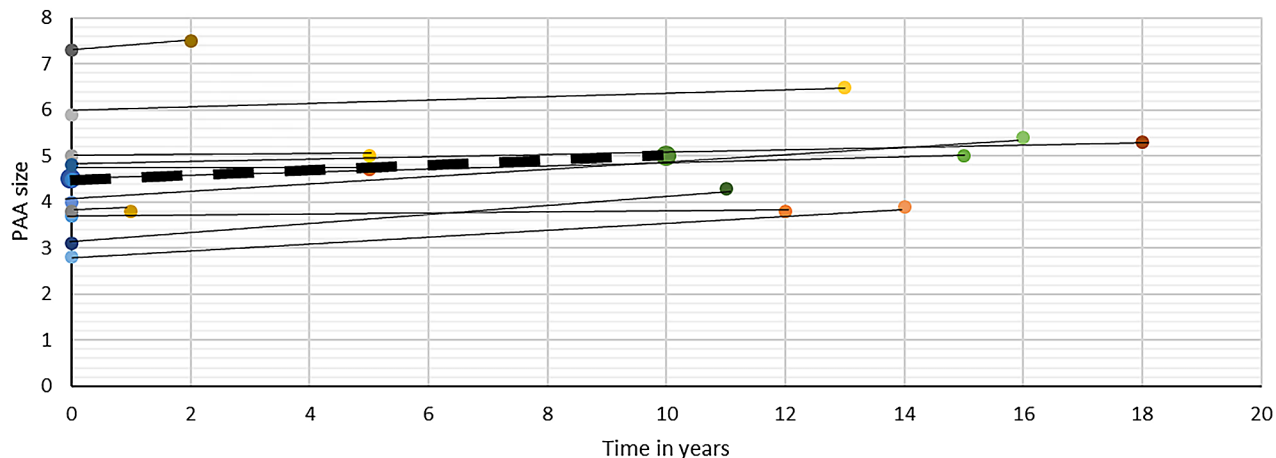


Figure 3. Rate of change in Pulmonary Artery Aneurysm size in 11 patients over time. The bold and dashed line is the mean rate of growth in the entire cohort over 10 years.

progressive pulmonary valve regurgitation or coronary artery compression.

Niwa et al. [9] described the histopathologic characteristics of thirteen patients with PAA and compared the findings to seventy-three patients with aortic aneurysms due to a variety of causes. One patient with PAA and pulmonary valve stenosis was included and had evidence of advanced (grade 3) medial wall abnormalities of collagen deposition, ground substance and loss of elastin fibers (Figure 1). There are rare reports of aortopathy in patients with pulmonary valve stenosis and PAA. In 1959, Evans and Dauncey [7] described a case of aortic dissection in a patient with moderate pulmonary valve stenosis with “post-stenotic” pulmonary artery dilation. However, the occurrence of congenital pulmonic and aortic valve disease is unusual. In congenital aortic or pulmonic valve stenosis, the relationship of severity of stenosis to the degree of arterial dilation and histopathologic abnormalities has been questioned. Niwa et al. [9] suggest that aortic and pulmonic arterial dilation are independent of the degree of valvular stenosis or regurgitation and more likely due to an inherent congenital arteriopathy. This assertion is supported by the eleven patients described in this cohort, all of whom had pulmonary artery dilation in the absence of significant pulmonic valve stenosis. Therefore, “post-stenotic” pulmonary arterial dilation

is not included in this cohort given the absence of significant pulmonary valve stenosis.

Patients were generally diagnosed because echocardiographic imaging was performed to evaluate for pulmonic valve ejection sound and/or systolic flow murmurs in the pulmonic position. There were two incidental diagnoses made on chest imaging to evaluate other conditions.

In regard to imaging modalities, it was encouraging to note that echocardiography correlated well with cross-sectional imaging by MRI or CT. Echocardiography is widely available, cost-effective and does not involve radiation. Given the slow rate of PAA growth (~ 5 mm over 10 years), yearly imaging is unnecessary.

The following limitations are present in our study. The sample size for this study is eleven patients. No definitive claims can be made with a small sample size. This study is also retrospective. Even though the current progression of the patients in our study is good, we can't be sure that they will continue on the same trajectory.

Conclusions

Pulmonary artery aneurysms are described in patients with congenital pulmonary valve pathology of mild functional significance. Most cases were present in patients older than 50 years. Long-term follow-up

suggests a benign course without dissection or rupture despite the majority of patients with PAA > 5 cm. Pulmonary arterial dilation progresses slowly over time and does not appear to cause any secondary clinical events. Echocardiography correlates well with MRI or CT and is useful in measuring PAA over time. Yearly imaging is unnecessary given the slow rate of progression.

References

1. Deterling RA, Clagett OT. Aneurysm of the Pulmonary Artery: Review of the Literature and Report of a Case. *Am heart j.* 1947;34:471-499. DOI: [10.1016/0002-8703\(47\)90527-9](https://doi.org/10.1016/0002-8703(47)90527-9)
2. Theodoropoulos P, Ziganshin BA, Tranquilli M, Eleftheriades JA. Pulmonary Artery Aneurysms: Four Case Reports and Literature Review. *Int J Angiol.* 2013; 22:143–148. DOI: [10.1055/s-0033-1347907](https://doi.org/10.1055/s-0033-1347907)
3. Greene DG, Baldwin ED, Baldwin JS, Himmelstein A, Roh CE, Cournand A. Pure Congenital Pulmonary Stenosis and Idiopathic Congenital Dilatation of the Pulmonary Artery. *Am j medicine.* 1949;6:24-40. DOI: [10.1016/0002-9343\(49\)90004-2](https://doi.org/10.1016/0002-9343(49)90004-2)
4. Kreibich M, Siepe M, Kroll J, Höhn R, Grohmann J, Beyersdorf F. Aneurysms of the Pulmonary Artery. *Circulation.* 2015;131:310-316. DOI: [10.1161/CIRCULATIONAHA.114.012907](https://doi.org/10.1161/CIRCULATIONAHA.114.012907)
5. Nguyen ET, Silva CI, Seely JM, Chong S, Lee KS, Müller NL. Pulmonary Artery Aneurysms and Pseudoaneurysms in Adults: Findings at CT and Radiography. *Am J Roentgenol.* 2007;188:W126-W134. DOI: [10.2214/AJR.05.1652](https://doi.org/10.2214/AJR.05.1652)
6. Adodo DK, Kloeckner M, Bergoend E, Couetil JP. Pulmonary Artery Dissection: A Case Treated by Homograft Replacement. *Ann thorac Surg.* 2017;103: e47-e49. DOI: [10.1016/j.athoracsur.2016.06.052](https://doi.org/10.1016/j.athoracsur.2016.06.052)
7. Evans B, Dauncey TM. Dissecting Aneurysm of the Aorta Associated with Congenital Pulmonary Valvular Stenosis. *Br Heart J.* 1959;21:139-41. DOI: [10.1136/hrt.21.1.139](https://doi.org/10.1136/hrt.21.1.139)
8. Roberts WC, Grayburn PA, Guileyardo JM, Stoler RC. Full Development of Consequences of Congenital Pulmonic Stenosis in Eighty-Four Years. *Am J Cardiol.* 2017;119:1284-1287. DOI: [10.1016/j.amjcard.2016.11.069](https://doi.org/10.1016/j.amjcard.2016.11.069)
9. Niwa, K, Perloff JK, Bhuta SM, Laks H, Drinkwater DC, Child JS, et al. Structural Abnormalities of Great Arterial Walls in Congenital Heart Disease. *Circulation.* 2001;103:393-400. DOI: [10.1161/01.CIR.103.3.393](https://doi.org/10.1161/01.CIR.103.3.393)
10. Koretzky ED, Moller JH, Korn ME, Schwartz CJ, Edwards JE. Congenital Pulmonary Stenosis Resulting from Dysplasia of Valve. *Circulation.* 1969;40:43-53. DOI: [10.1161/01.CIR.40.1.43](https://doi.org/10.1161/01.CIR.40.1.43)

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

[Comment on this Article or Ask a Question](#)

Cite this article as: Obeid K, Wadia SK, Lluri G, Meyerson C, Fishbein GA, Rear-don LC, Aboulhosn J. Pulmonary Arteriopathy in Patients with Mild Pulmonary Valve Abnormality without Pulmonary Hypertension or Intracardiac Shunt. *Structural Heart Disease.* 2017;4(3):79-84. DOI: <https://doi.org/10.12945/j.jshd.2018.040.18>