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ORIGINAL ARTICLE

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Angiographically detectable Thebesian veins are a dynamic and reversible finding in the setting of congenital heart disease

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Abstract

Objective: Angiographically detectable Thebesian veins (ThVs) are a rare finding sometimes associated with coronary steal and myocardial ischemia in adults, but there are limited data regarding prominent ThVs in the setting of complex congenital heart disease (CHD). This study represents the largest series to date describing the presence and temporal changes of angiographically detectable ThVs in children with CHD.

Methods: This is a single center case series describing the clinical characteristics and coronary anatomy in children with CHD and angiographicall detectable ThVs. After identification of the index case, additional patients were identified in a prospective manner during the course of routine clinical care. We developed a qualitative scale to grade ThV burden, with changes tracked over time in the subset of patients who underwent serial cardiac catheterizations.

Results: A total of 10 patients are included in this report. There was a predominance of female gender (8 of 10 patients), right-dominant single ventricle physiology (7 of 10 patients), and heterotaxy syndrome (6 of 10 patients). The degree and location of epicardial coronary artery tortuosity was qualitatively related to ThV burden. The subset of patients who underwent serial cardiac catheterizations demonstrate that ThV dilation can progress or regress over time.

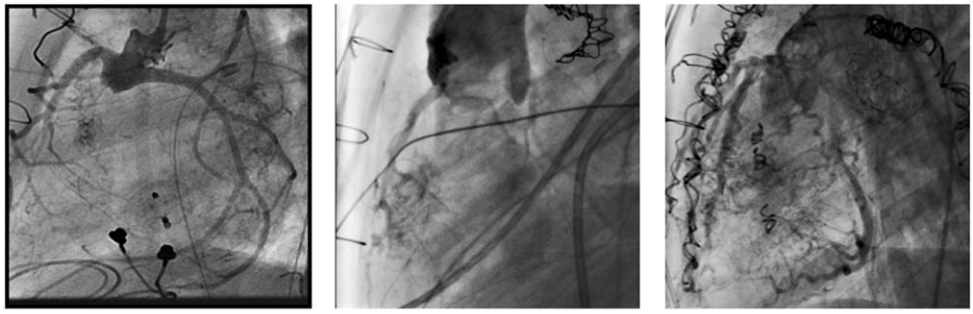
Conclusions: Angiographically detectable Thebesian veins are a rare finding in patients with congenital heart disease and may represent global changes in the coronary circulation. This is the first report, adult or pediatric, to demonstrate that ThV dilation is a dynamic process capable of both progression and regression. The physiologic impact of these findings remains to be elucidated.

KEYWORDS
congenital heart disease, coronary artery tortuosity, heterotaxy, Thebesian veins

1 | INTRODUCTION

Initially described by Vieussens in 1706 and further delineated by Thebesius in 1708, *venae cordis minimae*, commonly referred to as Thebesian veins (ThVs), are small, valveless venous channels running perpendicular to the endocardial surface. ThVs are present in all chambers of the heart, with greater density in the right versus the left ventricle. Three anatomic subtypes have been identified[1–3]; the first drain blood from the capillary bed directly into the cardiac chambers. The second are arterioluminal vessels, draining blood from the coronary arteries into the ventricles without traversing a capillary bed, thus behaving like a coronary cameral fistula and potentially compromising downstream myocardial perfusion. The third are venoluminal vessels that connect the coronary veins directly into the atrial or ventricular chamber.

While ThVs are a normal anatomic finding in all individuals, in adults, systems prominent enough to be seen by coronary angiography have a prevalence of only 0.08%-0.3%, and there are no data regarding the prevalence in children and/or the setting of congenital heart disease.[4] Though the exact physiologic role of ThVs is uncertain, they are estimated to carry 5%-10% of the total coronary venous return under baseline conditions, and the clinical significance, if any, of angiographically detectable ThVs remains unknown.[3,4]



Grade 0	No angiographically detectable ThVs.
Grade I	Angiographically detectable ThVs with partial opacification of the ventricular chamber (left).
Grade II	Angiographically detectable ThVs with opacification of the ventricular cavity and clearance of contrast in < 3 cardiac cycles (center).
Grade III	Angiographically detectable ThVs with opacification of the entire ventricular cavity or clearance of contrast in > 3 cardiac cycles (right)

FIGURE 1 Qualitative grading of Thebesian vein burden

There are a number of hypotheses regarding the implication of angiographically detectable ThVs in the setting of heart disease. Prominent ThVs could allow for an alternative route of myocardial venous drainage, and it has been established that ThVs are capable of carrying the bulk of venous return in situations where the epicardial coronary veins are compromised, or in the setting of coronary sinus ostial atresia.[5–7] Some investigators hypothesize that ThVs provide an alternative channel of nutrition to the myocytes in the setting of proximal coronary artery obstruction (via retrograde flow from the ventricles to the capillary network). Alternatively, high ThV burden (particularly the arterioluminal variety) can potentially be detrimental, hypothesized to cause coronary steal and myocardial ischemia in patients without coronary lesions or obstructions.[8–10]

In this report we present a series of patients with congenital heart disease and angiographically detectable ThVs as seen by aortic root or selective coronary angiography. In patients who underwent serial catheterizations we were able to demonstrate *de novo* and/or progressive development of angiographically evident ThVs, as well as regression over time, demonstrating that this is a dynamic process capable of responding to hemodynamic changes. Furthermore, in this series there is a qualitative association between tortuosity of the epicardial coronary arteries and the presence of angiographically detectable ThVs, suggesting global remodeling of the coronary circulation.

2 | METHODS

This study was conducted in accordance with guidelines as established by the Boston Children's Hospital Institutional Review Board. Given the descriptive nature of this work, the need for informed consent was waived. We initiated this study with no *a prior* data regarding which patients are most likely to manifest angiographically evident ThVs. After identification of the index case, a list of patients with similar angiographic findings was prospectively complied. Once we characterized the clinical traits and had collected a number of demonstrative angiograms, these data were then disseminated within our program, leading to the identification of additional patients. Furthermore, we searched our catheterization database and reviewed the angiograms for historical patients with clinical properties similar to those found in our initial cohort. All available angiographic data for each case were reviewed by the authors PT and DP, computed tomography and magnetic resonance imaging data were reviewed by author SG.

As this is an entirely descriptive study, all coronary angiography was done per operator discretion and as deemed clinically appropriate at the time of cardiac catheterization. The coronary circulation was evaluated via aortic root angiograms (contrast given at 0.8-1 mL/kg/s) or selective coronary angiography. We developed a qualitative grading scale to characterize the clinical diagnosis and extent of ThV burden, similar in concept to that described by Hunt et al for aortic regurgitation[11] (Figure 1). Grade 0 represents no detectable ThVs. In patients with Grade I ThVs there was faint and incomplete opacification of the ventricular chamber, with rapid clearance of contrast within 1–2 cardiac cycles. Grade II ThVs resulted in opacification of the entire ventricular chamber, with clearance of contrast within 3 cardiac cycles. With grade III ThVs there was opacification of the ventricular chamber with clearance of contrast requiring >3 cardiac cycles.

3 | RESULTS

Native anatomy and surgical history of the 10 patients in this cohort are summarized in Table 1. All patients had single ventricle physiology at the time ThVs were identified, and of these, 8 had a right-dominant ventricle. Six were established patients at our center and this subset had a median age at time of diagnosis of 4.0 years (range 0.5–21.6 years). The remaining four patients presented to our program after

TABLE 1 Demographic data

Case #	Gender	Native anatomy	Surgical history (age)	Age ThV first noted (years)	Grade and change over time (if any)	Genetic diagnosis
1	F	DORV superior inferior Vs, criss–cross AVV, VSD, AS,	1. Norwood + RmBTS (3 days) 2. Glenn + central shunt (4 months) 3. Takedown shunt + Fontan (2 years 8 months)	1.3	0 → III	None identified
2	F	DILV, PA	1. RmBTS (4 days) 2. Fontan (2 years) 3. Takedown Fontan + BDG, pulmonary vein sutureless repair (3 years 9 months)	3.8	I → III	HTX
3	M	DORV/PS	1. Kawashima (5 months) 2. Fontan (23 months)	5.3	0 → II	HTX
4	F	RdAVC	1. CoA repair, PAB (2 weeks) 2. BiV training with ASD repair, PAB revision. (6 months) 3. BiV repair with mitral valve repair (1 year 1 month) 4. Mitral valve revision (1 year 2 months) 5. Mitral valve replacement with Melody (1 year 3 months)	0.5	II → 0	T21
5	F	DORV, PA	1. BDG, RmBTS, fenestrated membrane in MPA (8 years) 2. Lateral tunnel Fontan (9 years)	9.0	III	HTX
6	F	DORV, balanced CAVC, sub/valvar PS.	1. RmBTS (5 years) 2. BiV repair (17 years)	17.2	II	HTX
7	F	Tricuspid atresia with TGA and unobstructed pulmonary outflow	1. PAB (1 month) 2. Takedown PAB + BDG. 3. VSD closure (11 months) 4. Fontan (2 years)	21.6	II	None identified
8	F	L-TGA, VSD, PA	1. BDG (2 years) 2. Takedown BDG, BiV repair with atrial switch/Rastelli (6 years)	6.3	II	None identified
9	F	RdAVC, TAPVR	1. Stage 1 Sano (6 days) 2. Glenn (4 months) 3. Fontan (2 years)	4.1	II	HTX
10	M	DIRV, TGA	1. LmBTS, APC ligation (6 years) 2. BDG (7 years)	7.8	I	HTX

Abbreviations used: APC, aortopulmonary collateral; ASD, atrial septal defect; AS, aortic stenosis; AVV, atrioventricular valve; BDG, bidirectional Glenn; BiV, biventricular; CAVC, complete atrioventricular canal; DILV, double inlet left ventricle; DIRV, double inlet right ventricle; DORV, double outlet right ventricle; HTX, heterotaxy syndrome; LmBTS, left modified Blalock-Taussig shunt; MPA, main pulmonary artery; PAB, pulmonary artery banding; PA, pulmonary atresia; PS, pulmonary stenosis; RdAVC, right dominant atrioventricular canal; RmBTS, right modified Blalock-Taussig shunt; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great arteries; T21, trisomy 21; VSD, ventricular septal defect.

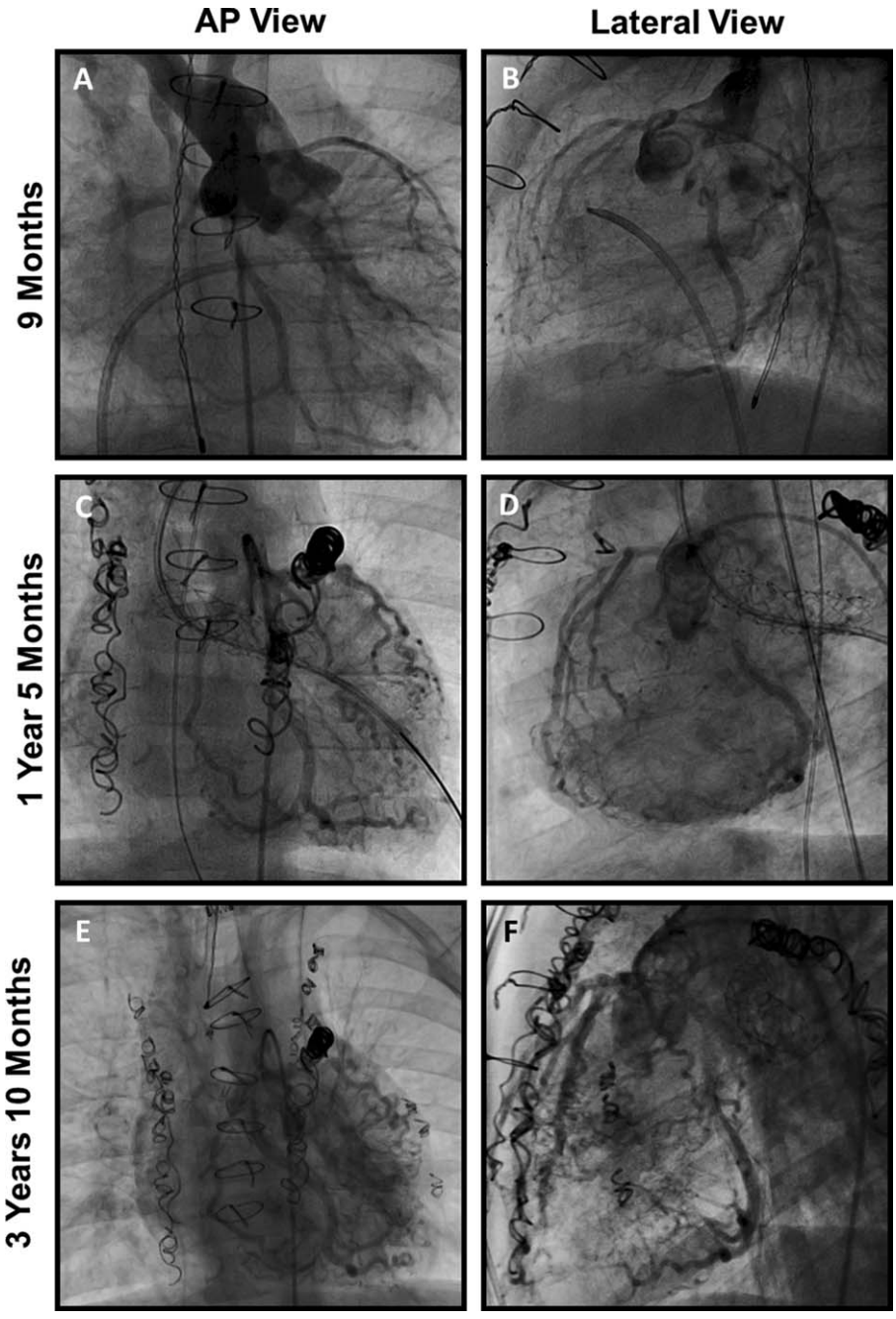


FIGURE 2 Development of angiographically detectable Thebesian veins. Serial AP and lateral views of root aortograms demonstrating progressive development of Thebesian veins. There are Grade 0 ThVs at 9 months of age (A, B), Grade II ThVs at 1 year 5 months of age (C, D), and Grade III ThVs at 3 years 10 months of age (E, F). In tandem with Thebeisan vein changes, there are progressive increases in the degree of epicardial coronary artery tortuosity

undergoing initial care at outside facilities, with ages ranging from 7 to 17 years, and diagnosis made on the initial preoperative catheterization. 8 patients were female and 6 patients had a diagnosis of heterotaxy syndrome. All had undergone at least two prior surgical palliations at the time of diagnosis.

Four patients in this report underwent serial cardiac catheterizations, demonstrating the dynamic nature of ThV findings. The most dramatic example is case #1 involving a young girl with double outlet right ventricle, superior/inferior ventricles, criss–cross atrioventricular valves, and a ventricular septal defect, who had been ultimately palliated to a lateral tunnel Fontan. Review of sequential aortic root angiograms demonstrates Grade I ThVs at 9 months of age, Grade II at 17 months of age, and then Grade III at 3 years 10 months of age (Figure 2). This final angiogram demonstrates no aortic insufficiency and significant angiographic ThVs with greater burden involving the right versus left ventricle, despite equal pressures in the setting of an unrestricted VSD. Also of note, there was a progressive increase in the degree of coronary artery tortuosity occurring in tandem with the increased ThV burden.

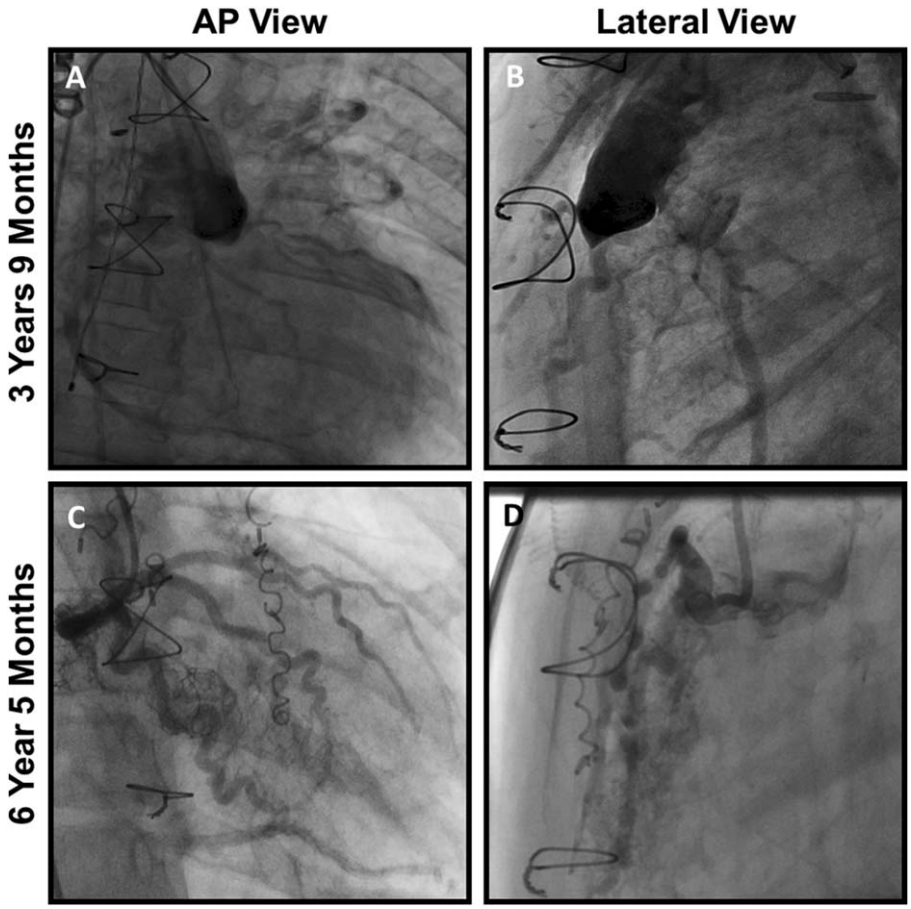


FIGURE 3 Development of angiographically detectable Thebesian veins. Serial AP and lateral views of root aortograms demonstrating progressive development of Thebesian veins. There is Grade I ThVs at 3 years 9 months age (A, B), and Grade III ThVs at 6 years 5 months of age (C, D). In tandem with Thebeisan vein changes, there are progressive increases in the degree of epicardial coronary artery tortuosity

Case #2 involves a young girl with double inlet left ventricle with pulmonary atresia and shows similarly progressive changes with Grade I ThVs noted at 3.75 years of age. Over the next 2.5 years there was marked progression with repeat catheterization showing Grade III ThVs (Figure 3) and a progressive increase in epicardial coronary artery tortuosity, similar to findings reported in case #1. Case #3 demonstrates less dramatic development of ThVs in a boy with double outlet right ventricle and pulmonary stenosis. He had Grade 0 ThVs noted at 4 months of age, progressing to Grade II on repeat study performed at 5 years of age (data not shown).

Case #4 demonstrates the reverse paradigm; ThV regression following normalization of hemodynamics. This patient is a young girl with trisomy 21 and a right-dominant atrioventricular canal. She underwent cardiac catheterization one month after surgery which involved ASD closure and revision of a previously placed pulmonary artery band as part of preparation for biventricular repair. During this initial study grade II ThVs were evident from both the RCA and LCA, though the total burden was qualitatively greater over the right ventricle, and there was qualitatively mild epicardial contrary artery tortuosity (Figure 4). Approximately 3 years after biventricular repair with normalization of right ventricular pressures and systemic saturations, repeat angiography demonstrated complete resolution of her angiographically detectable ThVs (Grade 0) and regression of coronary artery tortuosity.

The remaining 6 patients in this series each had only one documented coronary angiogram, thus changes over time could not be evaluated. Native anatomy, surgical history, and grade of ThV burden is reported in Table 1. In 5 of these 6 patients significant epicardial coronary artery tortuosity was again noted. In Patient #8 we note that within the same right coronary artery system there two marginal branches with tortuosity and ThVs involving the downstream myocardium, whereas the distal RCA demonstrates normal anatomy and minimal associated ThVs (Figure 5A, B). Likewise, in Patient #9 there is only Grade I ThV burden exclusively localized to the region of distal LAD tortuosity (Figure 5C, D).

Each of the 10 patients in this series subsequently underwent cardiopulmonary bypass for cardiac surgery and there were no documented instances of significant postoperative ventricular dysfunction, arrhythmia, or any findings to suggest myocardial ischemic changes due to poor myocardial protection during bypass. Patient #5 (Grade II ThVs) demonstrated mild RV dysfunction on the immediate postoperative transesophageal echocardiogram, but on subsequent imaging there was full recovery of function within 48 hours.

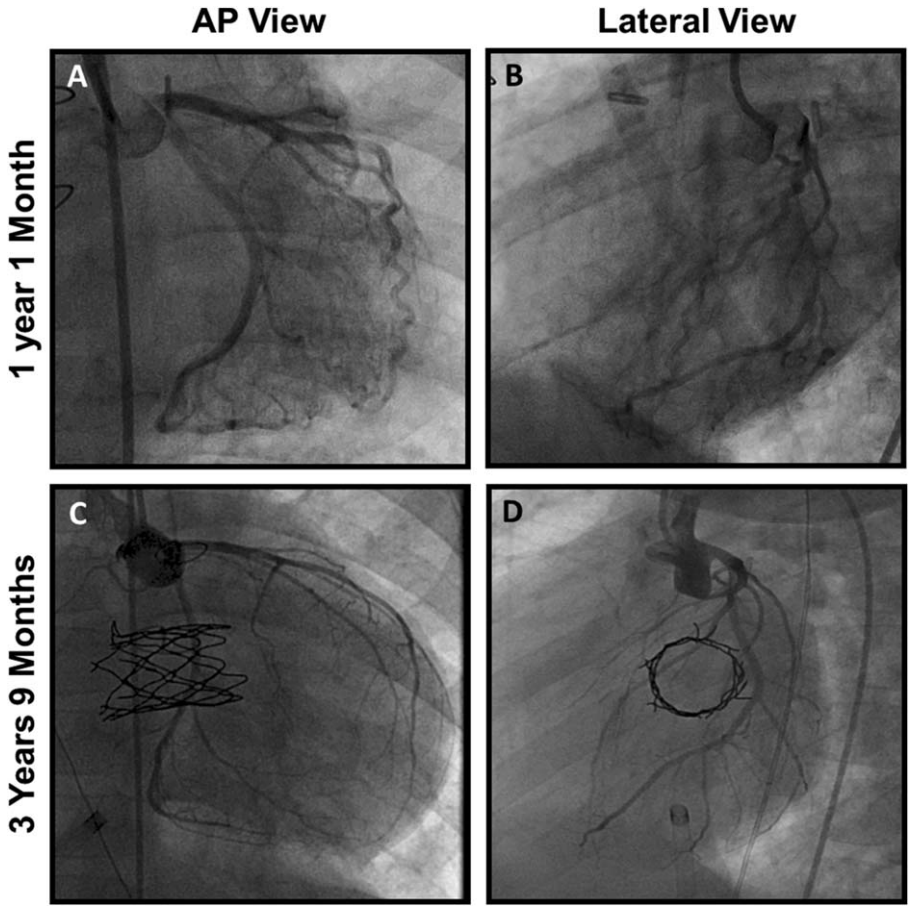


FIGURE 4 Regression of angiographically detectable Thebesian veins following biventricular repair. Serial AP and lateral views of selective left coronary artery angiograms demonstrating Grade II ThVs at 6 months of age (A, B). Approximately three years after successful biventricular repair there is complete resolution, with Grade 0 ThVs (C, D). There is qualitatively moderate epicardial tortuosity present in the original angiogram, with complete resolution seen in the latter study

All patients in this series underwent either cardiac computed tomography or cardiac magnetic resonance imaging during their course of care. In addition to the angiograms, these studies were reviewed for evidence of coronary sinus ostial atresia, but given the retrospective nature of this work, the data were not of sufficient quality to definitively assess patency of the coronary sinus.

4 | DISCUSSION

This is the largest report to date describing ThVs in children with congenital heart disease, and these data provide novel insight into the dynamic nature of this process. We demonstrate that ThV dilation can be acquired as evidenced by three patients with absent or trace angiographically detectable ThVs early in life, who then developed Grade II or III vessels over the course of years. Conversely, the process is reversible as seen by one patient who showed complete resolution after successful biventricular conversion. Interestingly, the degree and location of epicardial coronary artery tortuosity was qualitatively proportional to ThV burden, suggesting that the underlying process is one of global coronary vascular remodeling.

Although it is impossible to prove a causal relationship based on these data, it is interesting to note that at the time of diagnosis all patients in this study had single ventricle physiology with systemic cyanosis. Similar to pathologic series which demonstrate greater ThV density in the right versus left ventricle at baseline, angiographically detectable ThV burden in our cohort was qualitatively greatest in the right ventricle, and the only case showing resolution did so after conversion to a biventricular circulation with normalization of right-sided pressure and systemic oxygen saturation. Furthermore, we note the marked predominance of female gender (8 of 10 patients), right-dominant single ventricle physiology (7 of 10 patients), and heterotaxy syndrome (6 of 10 patients). These data then support a mechanism whereby systemic right ventricle pressures and/or chronic cyanosis might contribute to ThV enlargement, but further work is necessary to investigate this hypothesis.

While these data are the first to demonstrate the dynamic nature of ThV remodeling in the setting of congenital heart disease, we cannot determine if this process is an anatomic curiosity versus a significant effector of cardiac physiology? Not knowing what kind of ThVs are present (arterioluminal vs. venoluminal), we can only speculate about the theoretical physiologic impact. With predominantly venoluminal

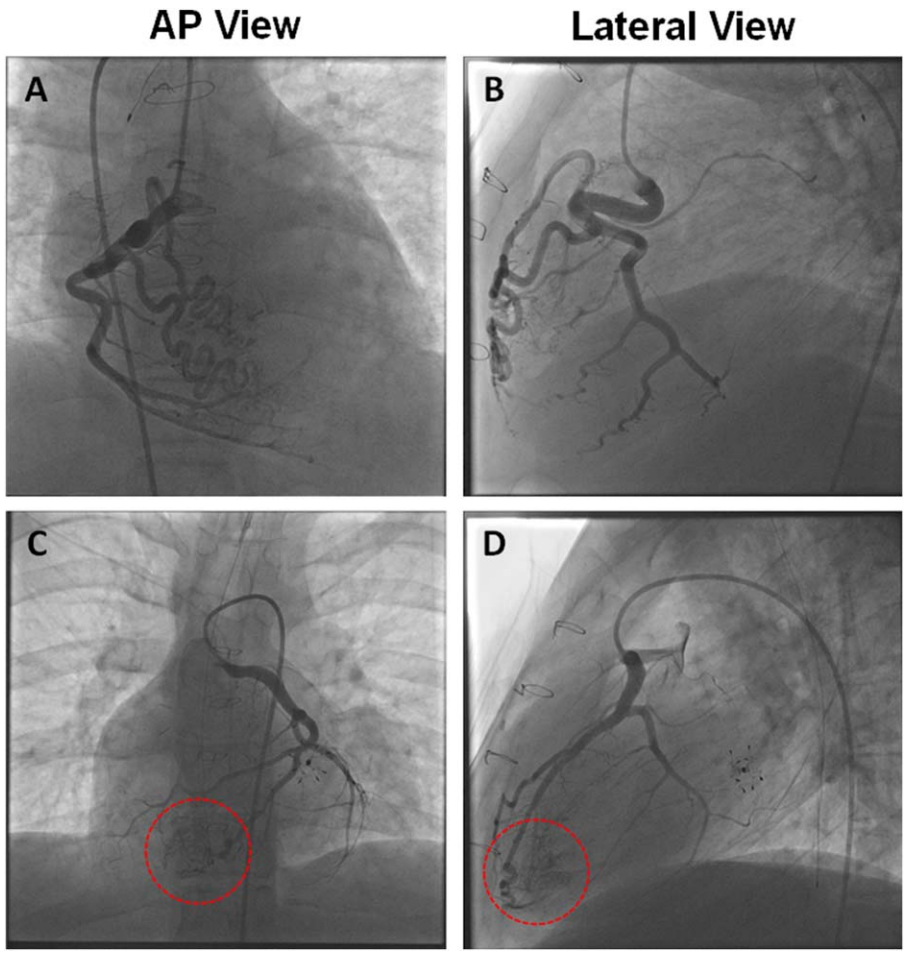


FIGURE 5 Angiographically detectable Thebesian Veins are associated with increased epicardial coronary artery tortuosity. Angiograms from Patient #8 (A, B) show marked coronary artery tortuosity involving two branches off the RCA, with associated ThVs. Conversely, the distal artery, with normal angiographic appearance, had no significant ThV burden. Angiograms from Patient #9 (C, D) show grossly normal coronary arteries with only distal tortuosity. ThV burden localizes to the region of arterial tortuosity

ThVs one would expect them to behave as coronary-cameral fistulae, resulting in a volume load to the ventricle secondary to of high flow through a low-resistance pathway. However, the epicardial coronary arteries upstream to the ThVs, while prominent and tortuous, were not markedly dilated, arguing against a significant volume load. Additionally, with venoluminal ThVs one potential consequence would be systemic hypoxemia. However, coronary artery flow at rest represents approximately 5%–10% of systemic venous return, and because dilated ThVs only drain part of the myocardium, this is unlikely to become clinically significant. Lastly, most patients with Fontan palliation have all coronary drainage exclusively to the pulmonary venous atrium, and this does not typically cause significant cyanosis. Areterioluminal (pre-capillary) ThVs, theoretically, may be associated with compromised oxygenation of the downstream myocardium supplied by these coronaries. To this end, we found no evidence of myocardial ischemia in these patients, either at baseline or after open-heart surgery, and no evidence of regional dyskinesis in regions of the myocardium with high ThV burden.

This study is limited by its descriptive nature and by the fact that ThVs have previously not been coded for in our database, making it almost certain that we are under-reporting this finding and that we are likely to have included only the most severe cases. There was no standardized protocol for imaging coronary arteries when ThVs were noted, thus our ability to judge total ThV burden may be limited. Because only 4 of our 10 patients had serial angiograms, our observations about the natural history of this finding remains largely anecdotal, but still demonstrate proof of principle. Also, despite having axial imaging on all patients, we were unable to accurately assess the status of the coronary sinus. This may be important information, especially in a population of patients with heterotaxy syndrome and a high prevalence of coronary sinus abnormalities.

5 | CONCLUSIONS

Angiographically detectable Thebesian veins are a rare finding in patients with congenital heart disease and can be a dynamic process with both progression and regression as demonstrated in this small series. The physiologic impact of these findings remains to be elucidated.

CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Paul Tannous: Lead author with substantial contribution to all elements of this project including design, interpretation of data, drafting and revision of this manuscript. Dr. Tannous has read and approves this submitted version.

Sunil J Ghelani: Contributing author with substation contribution including interpretation of all CT and MRI data, drafting and critical revision of the submitted version. Dr. Ghelani has read and approves this submitted version.

Audrey C. Marshall: Contributing author with substantial contribution to project design, interpretation of data, as well as drafting and revision of this manuscript. Dr. Marshall has read and approves this submitted version.

Diego Porras: Senior author with substantial contribution to project design, interpretation of data, as well as drafting and revision of this manuscript. Dr. Porras has read and approves this submitted version.

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