

# Pulmonary Vein Stenosis as a Cause of Pulmonary Hypertension in Trisomy 21

Adam Lobbestael, PhD<sup>1</sup>, Sana Khan<sup>2</sup>, Ahmed Deniwar, MD<sup>2</sup>, and Joseph Vettukattil, MBBS, MD<sup>2,1</sup>

<sup>1</sup>Michigan State University College of Human Medicine, Grand Rapids, Michigan  
<sup>2</sup>Betz Congenital Heart Center, Helen DeVos Children’s Hospital, Spectrum Health, Grand Rapids, Michigan

## Introduction

Congenital heart disease is observed in approximately 40% of patients with trisomy 21<sup>1</sup>. Within this subset of patients, pulmonary hypertension (PH) is a common manifestation<sup>2</sup>. Etiologies of PH in this setting are varied and often multifactorial. However, a definite cause is often not identified, and the PH is labeled as idiopathic<sup>3</sup>. One potential cause of PH is pulmonary vein (PV) stenosis. However, as illustrated by the following studies, this has previously been thought to be very rare.<sup>4</sup>

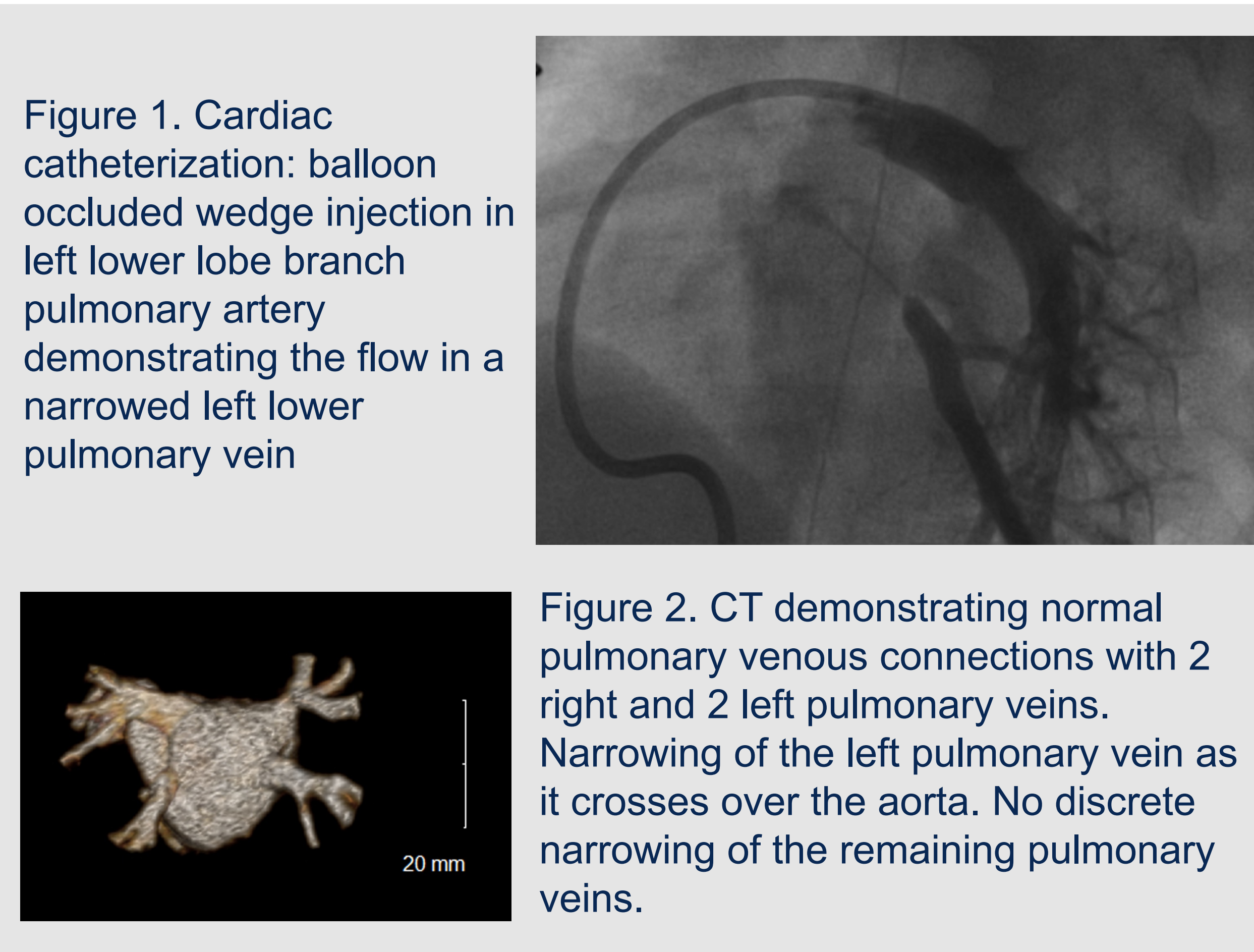
- Chi and Krovetz (1975): 69 children with Down syndrome, 90% with PH, none with PV stenosis<sup>5</sup>
- Wilson et al (1979): 82 patients with Down syndrome and PH, none with PV stenosis<sup>6</sup>
- Holt et al (2007): 98,126 patients with PH, 3 with PV stenosis and PH<sup>7</sup>

Nearly all patients with congenital heart disease undergo echocardiography, which can identify PV stenosis. However, echocardiography cannot be used to definitively rule out PV stenosis and cardiac catheterization or CT angiography must be performed to do so. Examples of catheter and CT findings of PV stenosis are shown in Figures 1 and 2, respectively. These diagnostic tests are performed in far fewer patients than echocardiography, which may allow PV stenosis to go undetected. Accordingly, the incidence of PV stenosis as a cause of PH in trisomy 21 patients may currently be underreported.

## Methods

A retrospective chart review was conducted on all trisomy 21 patients who presented to the Betz Congenital Heart Center between 2012 and 2022. For patients identified as having persistent PH, charts were reviewed to ascertain if PV stenosis had been diagnosed. Additionally, an independent review of diagnostic imaging in these patients was conducted

to further search for PV stenosis in patients without such diagnosis. Demographic information and data on diagnostic testing (echocardiography, cardiac catheterization, and CT angiography) was also collected. Using available data, the incidence of PV stenosis in trisomy 21 patients with PH presenting to our program was calculated.



## Results

81 patients were identified with trisomy 21 and PH. Among them, 8 (9.9%) were confirmed to have PV stenosis. Table 1 presents demographics of the patients with and without confirmed PV stenosis. Table 2 presents a summary of the diagnostic testing conducted for these patients. Of the 73 without confirmed PV stenosis, only 32 (43.8%) had diagnostic testing sufficient to rule out PV stenosis. Additionally, CT scans in this group of patients, whether designated as cardiac or otherwise, were obtained for a variety of indications and not necessarily to check pulmonary veins.

Table 1. Demographics and presence of pulmonary vein stenosis in patients with trisomy 21 and PH

	Patients with trisomy 21 and PH	Patients with trisomy 21, PH, and PV stenosis
Number of Patients	81	8
Sex		
Female	40 (49.4%)	4 (50%)
Male	41 (50.6%)	4 (50%)
Race		
African American	4 (4.9%)	0
Asian/Pacific Islander	3 (3.7%)	0
Hispanic or Latino	8 (9.9%)	0
Native American	0	0
White	63 (77.8%)	7 (87.5%)
Unknown	1 (1.2%)	0
Other	2 (2.5%)	1 (12.5%)
Current Age (years)		
Average	14.4	6.1
Median	7.3	5.2
Standard Deviation	17.6	4.4
Range	0.7 – 69	2.9 – 16.6
Confirmed PV Stenosis	8 (9.9%)	8 (100%)

Table 2. Summary of diagnostic testing in patients with trisomy 21 and PH

Diagnostic Testing	Pulmonary Vein Stenosis Confirmed (n = 8)	Pulmonary Vein Stenosis Not Confirmed (n = 73)
Cardiac Catheterization Only	3 (37.5%)	16 (21.9%)
CT Angiography Only (Cardiac Specific)	1 (12.5%)	7 (9.6%)
CT Angiography Only (Non-cardiac specific)	0	4 (5.5%)
Cardiac Catheterization and CT Angiography (Cardiac Specific)	3 (37.5%)	2 (2.7%)
Cardiac Catheterization and CT Angiography (Non-cardiac Specific)	0	5 (6.8%)
Cardiac Catheterization and Cardiac MRI	0	2 (2.7%)
No Cardiac Catheterization, CT Angiography, or MRI	1 (12.5%)	37 (50.7%)

## Conclusion

This study illustrates the importance of diagnostic investigation for trisomy 21 patients in the setting of PH and demonstrates that PV stenosis is a more common etiology of PH in trisomy 21 than previously understood. Given that PV stenosis is likely currently underreported and may be missed with standard diagnostic testing, such as echocardiogram, all trisomy 21 patients with pulmonary hypertension should undergo diagnostic cardiac catheterization to rule out isolated or segmental pulmonary vein stenosis which could go undetected without angiography. This step should be taken to further clarify the etiology of PH in these patients and to better guide surgical and medical management of the condition. Further study is needed in this area. To estimate the true incidence of PV stenosis in trisomy 21 patients with PH, a prospective study should be conducted. Additionally, a multi-center study should be undertaken to ensure a broad patient representation.

## References

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