Radiologic review of acquired pulmonary vein stenosis in adults

Mauricio Galizia\textsuperscript{1,2}, Rahul Renapurkar\textsuperscript{1,3}, Lourdes Prieto\textsuperscript{4}, Michael Bolen\textsuperscript{1,3}, Joseph Azok\textsuperscript{1}, Charles T. Lau\textsuperscript{1,5,6}, Ahmed H. El-Sherief\textsuperscript{1,7,8}

\textsuperscript{1}Division of Thoracic Imaging, Cleveland Clinic, Cleveland, OH, USA; \textsuperscript{2}Division of Thoracic Imaging, The Ohio State University Wexner Medical Center, Columbus, OH, USA; \textsuperscript{3}Division of Cardiovascular Imaging, \textsuperscript{4}Division of Pediatric Cardiology, Cleveland Clinic, Cleveland, OH, USA; \textsuperscript{5}Division of Thoracic Imaging, Palo Alto Veterans Administration Medical Center, Los Angeles, CA, USA; \textsuperscript{6}Stanford University School of Medicine, Stanford, CA, USA; \textsuperscript{7}Division of Thoracic Imaging, Veterans Administration Greater Los Angeles Healthcare System, Los Angeles, CA, USA; \textsuperscript{8}David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ahmed H. El-Sherief, MD. Division of Thoracic Imaging, Veterans Administration Greater Los Angeles Healthcare System, 11301 Wilshire Boulevard, Los Angeles, CA 90073, USA. Email: ahelsherief@gmail.com.

Abstract: Acquired pulmonary vein stenosis (PVS) is an uncommon occurrence in adults, but one that carries significant morbidity/mortality. PVS can be secondary to neoplastic infiltration/extrinsic compression, non-neoplastic infiltration/extrinsic compression, or iatrogenic intervention. This article: (I) reviews the common causes of acquired PVS; (II) illustrates direct and indirect cross-sectional imaging findings in acquired PVS (in order to avoid misinterpretation of these imaging findings); and (III) details the role of imaging before and after the treatment of acquired PVS.

Keywords: Pulmonary vein stenosis (PVS); pulmonary vein isolation (PVI); pulmonary vein ablation; imaging; radiology; computed tomography (CT); magnetic resonance imaging (MRI)

Submitted Feb 05, 2018. Accepted for publication May 16, 2018.
doi: 10.21037/cdt.2018.05.05
View this article at: http://dx.doi.org/10.21037/cdt.2018.05.05

Introduction

Pulmonary vein stenosis (PVS), though a relatively uncommon occurrence (1,2), is associated with significant morbidity and mortality if not recognized and treated promptly. In adults PVS is often secondary to infiltration/extrinsic compression by a mediastinal or lung process. More recently, the increased use of catheter-based ablation therapy for treatment of atrial fibrillation has led to a new cohort of patients with PVS. Radiologists play an important role in the identification and evaluation of PVS, however this requires an understanding of the patient population at risk, the direct and indirect imaging findings of PVS on cross-sectional imaging, as well as relevant information in the treatment of this condition.

This article: (I) reviews the common causes of secondary PVS in adults; (II) illustrates direct and indirect cross-sectional imaging findings in secondary PVS; and (III) details the role of imaging before and after the treatment of secondary PVS in adults.

Embryology and anatomy

In early gestation, the veins draining the primitive lung buds do not connect to the primitive left atrium, but rather connect to various systemic venous systems (e.g., cardinal venous system, umbilical venous system) through the pulmonary venous plexus. An outpouching of the primordial left atrium develops and connects to the pulmonary venous plexus at around 30 days of gestation. At the same time, in normal development, the connections between the pulmonary venous plexus and the systemic venous systems atrophy, and the primitive pulmonary vein starts draining oxygenated blood from the lungs into the
left atrium through a common confluence of the pulmonary veins. This common confluence of the pulmonary veins then integrates with the primordial left atrium, forming the posterior wall of the completed left atrium and generating the usual pattern of four separate ostia for the pulmonary veins (2,3) (Figure 1A,B).

Although the pulmonary veins usually drain into four separate ostia, many different anatomic variants have been described (4). The most common pattern is that of two separate ostia on the left, one superiorly, draining the left upper lobe, and one inferiorly, draining the left lower lobe; and two separate ostia on the right, one superiorly, draining the right upper and middle lobes, and one inferiorly, draining the right lower lobe (Figure 2). Radiologists should be familiar with the other anatomic variants so that they can differentiate between a naturally occurring reduced number of ostia and a pulmonary vein occlusion.

Causes of acquired PVS

Causes of PVS in adults can be grouped in three categories: neoplastic infiltration/extrinsic compression, non-neoplastic infiltration/extrinsic compression, and iatrogenic intervention.

Any neoplastic disease occurring in the mediastinum and lungs can cause PVS by either infiltration or extrinsic compression of a pulmonary vein. Common neoplastic diseases that can cause PVS include primary lung cancer (5-9) and lymphoma (10) (Figure 3A). Non-thoracic primary neoplasms can also metastasize to the mediastinum and lungs and cause PVS (11). Non-neoplastic causes of PVS include fibrosing mediastinitis (12-16) (Figure 3B), sarcoidosis, and mediastinal cysts (17-19) (Figure 3C).

Iatrogenic causes of PVS include complications of percutaneous radiofrequency catheter ablation for atrial fibrillation, known as pulmonary vein isolation (PVI), and cardiothoracic surgery for repair of congenital heart disease. Even though the incidence of complications after PVI is low, the increasing use of this procedure makes it currently the most common iatrogenic cause of PVS in adults (2) (Figure 3D).

Imaging evaluation of the pulmonary veins

The pulmonary veins are typically well depicted by noninvasive imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI), even when aforementioned imaging modalities are performed for other reasons. Although transthoracic echocardiography can be successfully used to visualize the pulmonary veins in children (2), its use in adults is not as sensitive as the other available noninvasive imaging modalities (20).

Although a routine chest CT scan with contrast typically depicts the pulmonary veins, more detailed anatomic depiction is achieved with the use of electrocardiogram (ECG)-gating for patients in normal sinus rhythm. CT has the advantage of providing good spatial resolution and a three-dimensional (3D) data set within a short scanning time. However, this imaging modality is associated with
ionizing radiation, which can be a concern, especially in young patients (2).

MRI can be used to image the pulmonary veins (21,22). Many different techniques have been used, including traditional contrast-enhanced MRI (23) and, more recently, time-resolved magnetic resonance venography (MRV) (24). MRI, like CT, can provide a 3D data set, but has the advantage of not using ionizing radiation. However, its spatial resolution is slightly inferior to that of CT, it requires a longer scanning time, and it may be contraindicated in patients with metal implants (2).

For assessment of the pulmonary veins, CT and MR are typically performed with an intravenous contrast material, which should not be used in patients with significantly decreased renal function. The iodine-based contrast material used for CT is potentially nephrotoxic (25), whereas the gadolinium-based contrast material used for MRI is a risk factor for nephrogenic systemic fibrosis in patients with a very low glomerular filtration rate (26). Noncontrast MRV techniques have been used to visualize the pulmonary veins (27,28), but they are not regularly employed in the clinical setting, and our own experience has shown contrast techniques to be, on the whole, more reliable in depiction of the pulmonary vein anatomy.

As reference, the following is an example of a MRI specific protocol to evaluate the pulmonary veins: axial HASTE (half-Fourier acquisition single-shot turbo spin echo) and SSFP (steady state free precession) images/injection of gadolinium followed by 3D contrast enhanced MR angiography (MRA) in the coronal plane timed to the left atrium/in patients referred for evaluation of the pulmonary veins post ablation, fat suppressed delayed

Figure 2 Diagram demonstrating the normal anatomic variants of the pulmonary veins. L1, two separate ostia for the left pulmonary veins that are not separated by atrial wall; L2, two separate ostia for the left pulmonary veins that are separated by atrial wall; L3, the left lower PV drains into the left upper PV with a short (<1 cm) common segment; L4, the left lower PV drains into the left upper PV with a long (>1 cm) common segment; R1, two separate ostia for the right pulmonary veins, with the vein draining the RML joining the right upper PV and forming a short (<1 cm) common segment; R2, three separate ostia for the right-sided pulmonary veins; R3, two separate ostia for the right pulmonary veins, with the vein draining the RML joining the right upper PV and forming a long (>1 cm) common segment; R4, two separate ostia for the right pulmonary veins, with the vein draining the RML joining the right lower PV; R5, four separate ostia for the right-sided pulmonary veins, with two veins draining the RML; R6, common ostium for the right-sided pulmonary veins; R7, four separate ostia for the right-sided pulmonary veins, with a separate ostium for the vein draining the RML and an accessory right top PV that drains the apical segment of the RUL. The most common anatomic pattern is L1/R1, with a total of four pulmonary veins draining into the left atrium. LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; RTPV, right top pulmonary vein; PV, pulmonary vein.
gadolinium enhancement images are obtained in the axial plane approximately 20 minutes post injection of gadolinium to evaluate for pulmonary vein ostial and left atrial scar.

**Direct cross-sectional imaging findings in secondary PVS**

Direct cross-sectional imaging findings in patients with PVS include absence, abrupt cut off, and narrowing of a pulmonary vein (29,30) *(Figure 4A,B)*. It is important to note that sometimes the left inferior pulmonary vein can occasionally become physiologically compressed between the left atrium and the descending thoracic aorta, mimicking a true stenosis (30). Because of the many described variations in pulmonary vein anatomy, comparison with old studies is important to confirm PVS.

**Indirect cross-sectional imaging findings and imaging pitfalls in secondary PVS**

Indirect cross-sectional imaging findings in patients with PVS include regional lung edema, lung opacities that wax and wane, lung infarct, lung fibrosis, decreased lung perfusion, and longer blood/contrast transit time in the lung that is drained by the stenosed pulmonary vein. All of aforementioned indirect cross-sectional imaging findings may be mistaken for other conditions.
PVS causes an increase in the pulmonary venous pressure, which may lead to lung edema in the lung that is drained by the stenosed vein. CT imaging findings in lung edema include bronchial wall thickening, interlobular septal thickening, intralobular interstitial thickening, ground-glass opacity, and consolidative opacity (Figure 5A).

Indirect CT imaging findings can wax and wane depending on factors that transiently alter pulmonary venous pressures (Figure 5B). Because indirect cross-sectional imaging findings are often constrained to one or two lobes, they may be mistaken for entities such as lung infection (leading to inappropriate use of antibiotic therapy), lung infarction from pulmonary embolism (leading to inappropriate use of anti-coagulation therapy), lung fibrosis (leading to inappropriate lung biopsy), or lung cancer (leading to inappropriate lung biopsy) depending on the acuteness or chronicity of the cross-sectional imaging findings.

Due to the increase in pulmonary venous pressure, PVS leads to a longer blood/contrast transit time in the lung that is drained by the stenosed vein resulting in decreased perfusion to the lung that is drained by the stenosed vein (Figure 5C), non-opacification of segmental and subsegmental veins in the lung lobe drained by the stenosed vein (Figure 5D), and mixing artifact in the left atrium adjacent to the pulmonary vein orifice (Figure 5E). Non-opacification of lobar, segmental, and subsegmental pulmonary veins can be mistaken for pulmonary arterial thromboembolic disease if the non-opacified veins are mistaken for the pulmonary arteries; and mixing artifact in the left atrium adjacent to the pulmonary vein orifice can be mistaken for thrombus.

**Screening for PVS after PVI**

Although the incidence of PVS after PVI is low, the consequences of this condition can be life threatening. Therefore, early detection of PVS is essential to prevent irreversible lung vasculature changes.

Symptoms caused by PVS commonly arise weeks to months after PVI (30), although there are reports of symptoms developing up to a year after PVI (20). Symptoms include shortness of breath, dry cough, and recurrent hemoptysis (2), and in some instances chest pain.

Every patient who presents with respiratory symptoms after having undergone an ablation procedure should be considered for PVS screening. At this time, there is no consensus on how to screen asymptomatic patients after PVI. At our institution, screening is performed at 3 months by tailored CT or MRI examination. If a significant stenosis is found, another imaging study is performed 3 months later (20).

**Percutaneous intervention for PVS after PVI**

**Confirmation of occlusion**

CT, the noninvasive exam with the best spatial resolution, has been shown in some instances to overestimate the
severity of PVS after PVI. In many cases, what appears to be an occluded pulmonary vein is shown on angiography to be a pulmonary vein with a tiny opening through which a stent can be placed when appropriate (2).

CT assessment of severely stenosed veins may be limited by slow or incomplete opacification. For confirmation of the degree of stenosis, further interrogation is obtained with a pulmonary artery wedge angiogram (Figure 6). In this procedure, a pulmonary arterial catheter is advanced into a pulmonary arterial segment that drains into the pulmonary vein of interest. Subsequently, the pulmonary arterial segment is occluded by a balloon wedge catheter, and a small amount of nonionic contrast material is injected under fluoroscopic observation. Very tiny openings in the severely stenosed vein can be demonstrated with this technique (2).

**Decision to treat**

PVS after PVI may be treated by percutaneous intervention. The decision to treat depends on the severity of stenosis and the presence of symptoms. Please note a discussion of treatment of PVS from extrinsic compression is limited to

---

**Figure 5** Indirect cross-sectional imaging findings of acquired pulmonary vein stenosis in an adult: lung edema, waxing and waning lung opacities, decreased perfusion to the lung that is drained by the stenosed vein, non-opacified peripheral pulmonary veins, and mixing artifact at the interface between the stenosed pulmonary vein and the left atrium. (A) Axial CT shows interlobular septal thickening, intralobular interstitial thickening, and ground-glass opacity in the left lower lobe; lung edema secondary to left inferior pulmonary vein stenosis (can be mistaken for lung infection or lung hemorrhage); (B) coronal CT images from serial CT scans demonstrate waxing and waning lung opacities in the right upper and right middle lobes secondary to right superior pulmonary vein stenosis (can be mistaken for lung infection or lung infarction from pulmonary embolism); (C) coronal dual-energy CT image in demonstrates decreased lung perfusion to the left upper, left lower, and right upper lobes secondary to left superior pulmonary vein stenosis, left inferior pulmonary vein stenosis, right superior pulmonary vein stenosis; (D) axial CT image shows non-opacification of the right upper lobe pulmonary veins secondary to right superior pulmonary vein stenosis (can be mistaken for pulmonary emboli); (E) axial CT image shows mixing artifact at the interface between the left superior pulmonary vein and the left atrium (arrow) secondary to left superior pulmonary vein stenosis (can be mistaken for thrombus).
Every symptomatic patient should be considered a potential candidate for percutaneous treatment. For symptoms to occur, at least 60% vessel diameter narrowing is usually necessary (20). As a normal pulmonary vein has an average diameter of 10 to 15 mm, a diameter of approximately 4 to 6 mm is usually necessary for symptoms to occur.

It is uncertain whether treatment is beneficial in asymptomatic patients with PVS. Most of this uncertainty arises from a lack of knowledge of the natural history of PVS. It is not known which patients will develop symptoms over time and which stenosis will progress to a complete occlusion, which could preclude the possibility of treatment. In our institution, the decision to treat asymptomatic patients is taken on a case-by-case basis in conjunction with the patient (20).

**Treatment planning**

There are two types of percutaneous procedures that can be used to treat PVS: ballooning and stenting. Ballooning, the first method used, has been associated with a rate of restenosis as high as 70% (31,32). Stenting is also associated with restenosis, but at a lower rate of around 10% for relatively large stents (20). Some studies have shown a decrease in the rate of restenosis when a stent with a diameter of at least 10 mm is used (31,33). However, not all stenotic veins can accommodate a large stent. In fact, some pulmonary veins demonstrate not just a focal stenosis but also diffuse hypoplasia. Placing a stent significantly larger than the vessel reference diameter (maximal diameter of the pulmonary vein just distal to the stenosis) can lead to a proliferative reaction at the edge of the stent that may cause restenosis at the edge with progression of the stenosis into the vessel (20). Therefore, at our institution, in the proper clinical setting, any pulmonary vein that can accommodate a stent of at least 8 mm in diameter is stented (20) (Figures 7, 8); for pulmonary veins that can only accommodate stents smaller than 7 mm in diameter, we perform ballooning with the knowledge that the restenosis rate will be high (20). Some veins increase their reference diameter after this procedure, enabling the placement of a larger stent in a second procedure (20).

To plan the stenting procedure, the interventionalist should know the minimal diameter at the stenosis, the maximal diameter of the pulmonary vein just distal to the stenosis (also called the reference diameter), and the distance from the stenosis site to the first distal branching point. The reference diameter is the theoretical normal diameter of the pulmonary vein and represents the diameter to which the stenosis can potentially be dilated. The distance from the stenosis site to the first branch is used to assess whether there is enough length to accommodate the stent in the central pulmonary vein proximal to the branching point. Although a distal branch can be crossed as long as a conventional, not covered, stent is often used, this typically means the stent will be dilated to a smaller diameter, namely that of the branch it is extending into. These measurements are derived from multiplanar reconstruction images, usually from a CT scan, although an MRI scan can also be used (Figure 9A,B,C).

When PVS progresses to complete occlusion, it is sometimes possible to cross the occluded segment and recanalize the vein, followed by either dilation or stenting depending on the reference diameter (34). However, if there is total obliteration of the vessel, percutaneous treatment is no longer possible. Chronic and complete obliteration of a pulmonary vein can result in lung infarction, which may manifest with cough, hemoptysis, wheeze, and pleuritic pain (35). If the patient’s quality of life is significantly impaired, an open thoracotomy and lobectomy may be necessary to alleviate the symptoms (35,36).

**Postprocedure complications**

Bleeding complications are the most frequent and serious
complications post venoplasty and stenting of PV. Usually, these are acute in presentation in a perioperative setting. Several other early and delayed complications have been discussed in multiple case series; these include pulmonary vein perforation, stent dislodgment, hemoptysis, pulmonary hemorrhage, ST-elevation and transient neurologic deficits. The complication rates range from 0% to 25%, but need to be kept in mind before considering intervention (37). In a series of 98 patients requiring 145 catheterizations, only two vein perforations were reported (20). In this same series, only one stent dislodgement was reported. Transient hemoptysis is a self-limited condition, usually resolving within 24 to 72 hours after the procedure (20).

A more delayed complication is in-stent restenosis (Figure 10). The risk of restenosis depends on the diameter of the stent that was placed, the reference diameter of the pulmonary vein, and the time interval between the PVI and the intervention for PVS (20).

A useful test for following up with patients who have undergone a percutaneous procedure for the treatment of PVS is radionuclide quantitative lung perfusion imaging. In quantitative flow imaging, regions of interest are drawn...
around each lung, and the relative blood flow is calculated (Figure 11).

At our institution, every patient undergoes quantitative lung perfusion imaging within a few days of the percutaneous procedure for the treatment of PVS to establish a baseline. For patients who have a stent placed that is smaller than 10 mm, the follow-up plan depends upon the immediate post-procedure lung perfusion scan. If this scan shows an increase in blood flow in the affected lung, another lung perfusion scan is performed after 3 to 4 months. If there is no significant increase in pulmonary flow after the procedure, a CT scan is performed after 3 to 4 months (20). For those patients who have stents placed that are 10 mm or larger, either a CT or a lung perfusion scan

is performed yearly for the first 3 to 4 years. After 4 years of follow-up, if no restenosis has been identified, a CT scan or a lung perfusion scan is performed every few years. As longer-term follow-up is gathered on these patients we may stop recommending further imaging after 4–5 years if in-stent restenosis for larger stents is not detected beyond that point.

**Conclusions**

PVS, though uncommon, is a condition with important clinical ramifications. Radiologists can play a crucial role in the identification and evaluation of PVS, however this requires an understanding of the patient population at risk,
the direct and indirect imaging findings of PVS on imaging, and what information is relevant in the treatment of this condition.

Acknowledgements

The authors thank Megan M. Griffiths, MA, for her editing contribution to the manuscript.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

9. Hamzeh I, Rashid A, Shaib F, et al. Pulmonary vein stenosis due to a compressive malignant tumor detected...


