Functional Assessment of Pulmonary Vein Stenosis with Magnetic Resonance

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Pulmonary vein stenosis is rare but may have a lethal outcome with development of severe pulmonary hypertension. Early diagnosis is crucial to improve outcome. MR is an excellent imaging modality that provides complete information regarding anatomical findings and hemodynamic / functional consequences of pulmonary vein stenosis. The anatomical assessment can quickly and easily be made with contrast MR angiography. The hemodynamic consequences of pulmonary vein stenosis can be assessed using ECG-gated phase-contrast velocity imaging. Potential effects on ventricular function is evaluated using ECG-gated cine imaging in multiple short-axis planes.

The hemodynamic and functional consequences of pulmonary vein stenosis seen at MR include:

- **Direct effects on pulmonary venous flow:**
  - Increased flow velocity and turbulence within and downstream from the stenotic segment
  - Decreased flow velocity in the pulmonary vein upstream from the stenosis
  - Loss of phasic changes of velocity over the course of the cardiac cycle
  - Reduced blood flow rate

- **Redistribution of pulmonary blood flow between the right and left lung as well as within the lung**
  - Reduced systolic flow to the affected lung or a part of the lung and increased systolic flow to the unaffected lung or parts of the lung
  - Retrograde flow in diastole in the pulmonary artery to the affected lung or lung parts. This retrograde flow is directed towards the pulmonary artery to the unaffected lung or lung parts.
  - Reduced and delayed uptake of contrast medium in the affected lung or parts of the lung at contrast angiography
  - Diminished size of the pulmonary artery supplying the affected lung

- **Decompression through pulmonary vein-to-pulmonary venous or pulmonary vein-to-systemic venous collaterals**

- **Development of systemic-to-pulmonary collateral arteries**
  - Recruitment of systemic arterial blood supply to the affected lung may cause retrograde flow in the ipsilateral pulmonary artery towards the unaffected lung

- **Secondary pulmonary hypertension**
  - Right ventricular hypertrophy with flattened ventricular septum in systole that bows toward the left ventricle in severe cases
  - Shortened ejection time of the pulmonary blood flow with early arrival of systolic peak and rapid deceleration
  - Reduced systolic peak velocity
  - Multiple additional minor waves in deceleration phase of the systolic curve of the pulmonary arterial flow

Key words: pulmonary vein stenosis, magnetic resonance, pulmonary venous flow pattern, venous collaterals, systemic arterial collaterals
General consideration

Pulmonary vein stenosis is a rare condition with a bimodal age distribution.\(^1\) In pediatric patients it occurs as a primary lesion or develops after a surgical procedure involving an incision of one or more of the pulmonary veins or the left atrium, such as repair of anomalous pulmonary venous connection. Although primary pulmonary vein stenosis may be present at birth as a congenital lesion, it is more often acquired and progressive in the first few months of life. It can manifest either as diffuse hypoplasia or localized stenosis, typically at the junction with the left atrium.\(^1\)–\(^5\) Any number of pulmonary veins may be involved. Prematurity with chronic lung disease is a risk factor for postnatal development of pulmonary vein stenosis.\(^3\), \(^5\) Increased flow in the pulmonary venous system due to a left-to-right shunt or contralateral pulmonary arterial stenosis is an additional risk factor for acquired venous stenosis.\(^2\), \(^3\), \(^5\) Approximately half of the patients with primary pulmonary vein stenosis have associated congenital heart disease. Total or partial anomalous pulmonary venous connection can be complicated by stenosis of the individual veins or, more commonly, the anomalous draining route. Pulmonary vein stenosis may also occur due to mechanical compression by an enlarged heart or adjacent neoplasm or secondary to fibrosing mediastinitis or sarcoidosis.\(^6\) Recently, an increasing number of adult patients have been reported to develop pulmonary vein stenosis as a complication of radiofrequency ablation procedures around the pulmonary veins.\(^7\), \(^8\) The presentation and outcome of pulmonary vein stenosis are contingent on several factors, including the number of stenosed pulmonary veins. Management options include surgical repair, balloon angioplasty, intravascular stenting and, in select cases, administration of chemotherapeutic agents and lung transplantation.\(^7\)

Recently, the technique of sutureless pericardial marsupialization has been embraced by most pediatric surgical centers.\(^9\) Balloon angioplasty with or without stenting is commonly performed in adults. It should be noted, however, that the longterm success of these interventions is often disappointing. Therefore, despite the simple anatomical nature of the disease and various management options, pulmonary vein stenosis remains associated with guarded prognosis, especially when more than two veins are involved and when it occurs in early childhood.\(^1\), \(^2\) For improved outcome of treatment, pulmonary vein stenosis should be recognized in its early stage before severe pulmonary hypertension develops.

Echocardiography with color and spectral Doppler is usually performed as the initial screening test in patients with suspected pulmonary vein stenosis.\(^10\)–\(^14\) However, echocardiography is not able to visualize the pulmonary veins within the lungs.\(^7\), \(^15\), \(^16\) Although catheterization with x-ray angiography has been regarded as the final diagnostic modality in this disease, it is invasive and can be dangerous especially when the disease is complicated by severe pulmonary hypertension. Anatomic assessment of pulmonary vein stenosis can now be made accurately and easily with computed tomography (CT) or magnetic resonance (MR).\(^8\), \(^15\), \(^17\), \(^18\) MR is preferred to CT as it is able to provide information regarding the hemodynamic consequences as well as anatomical detail of obstructed pulmonary veins without radiation.\(^15\), \(^18\)–\(^20\) Contrast-enhanced MR angiography is now recognized as the accurate diagnostic tool for anatomical evaluation of the pulmonary veins.\(^15\), \(^18\) Phase-contrast cine MR allows evaluation of velocity, volume and pattern of blood flow. It is advantageous over Doppler ultrasound techniques in at least two respects.\(^19\)–\(^22\) Firstly, phase-contrast MR provides the information on flow velocity as well as on volume. Secondly, any vessel in any anatomical location and orientation can be imaged. This paper summarizes contemporary utilization of MR in functional assessment of pulmonary vein stenosis. For better understanding of abnormal pulmonary venous flow patterns seen in MR, a brief review of normal pulmonary venous flow will precede.

Normal pulmonary venous flow pattern

Pulmonary venous flow is regulated by both upstream (right heart) and downstream (left heart) events during the cardiac cycle.\(^13\), \(^23\)–\(^25\) It consists of four phases that can be linked to the driving forces and mechanisms behind them (Figs. 1 and 2, Table 1). They are:

- Early systolic forward flow (S1 peak of the time-velocity curve): Pulmonary venous blood flow is pulled by the pressure drop within the left atrium (x descent) due to left atrial relaxation and descent of the mitral valve in early systole.
- Late systolic forward flow (S2): Pulmonary blood flow is pushed across the lungs by the driving force of right ventricular contraction. The left atrial pressure rises in this phase (v wave).
- Diastolic forward flow (D): Pulmonary venous blood is pulled by the declining left atrial pressure (y descent) with left ventricular relaxation in early diastole.
Late diastolic nadir (A): Pulmonary venous blood is pushed backward by the force of left atrial contraction. A retrograde flow is seen with a slow heart rate. The left atrial pressure rises in this phase (a wave).

Normal pulmonary venous flow is laminar with a peak velocity in a wide range from 40 to 90 cm/s at both echocardiographic and phase-contrast MR studies. Pulmonary vein velocities greater than 100 cm/s are generally regarded elevated. The peak velocities and durations of the components of the normal pulmonary venous flow are affected by age, respiration, heart rate and loading conditions. The ratio between the peak systolic and peak diastolic velocities (S/D) increases with age, which reflects both an increase in systolic flow and a decrease in diastolic flow. In the early neonatal period, the pulmonary veins show a continuous and high velocity waveform that resembles the pattern of the waveform seen in pulmonary vein stenosis. This finding reflects a sudden increase in pulmonary blood flow.

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**Table 1** Phases of normal pulmonary venous blood flow

<table>
<thead>
<tr>
<th>Phase</th>
<th>Primary mechanism</th>
<th>Force</th>
<th>Left atrial pressure</th>
<th>Major confounding factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early systolic forward flow (S1)</td>
<td>Left atrial relaxation</td>
<td>Forward pulling</td>
<td>Falls</td>
<td>Left atrial compliance and pressure</td>
</tr>
<tr>
<td>Late systolic forward flow (S2)</td>
<td>Right ventricular contraction</td>
<td>Forward pushing</td>
<td>Rises</td>
<td>Left atrial compliance and pressure</td>
</tr>
<tr>
<td>Early diastolic forward flow (D)</td>
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flow volume due to left-to-right shunt through the patent ductus arteriosus and disappears with ductal closure. Respiration has significant effects on the components of normal pulmonary venous flow. In general, all peak velocities and velocity–time integrals of the pulmonary venous flow components, especially of the ‘A’ wave, fall during inspiration and increase during expiration. The effect of the heart rate on pulmonary venous flow occurs mainly in diastole. At a slower heart rate with a longer diastole, the ‘D’ wave has enough time to return to baseline during the diastatic period. Left atrial contraction results in a retrograde ‘A’ wave in the pulmonary vein. At a higher heart rate (with a shorter diastole), there is insufficient time for the ‘D’ wave to decline and the left atrial contraction merely results in a downward deflection without actual reversal of flow. As the diastolic period shortens, the early systolic fraction of pulmonary vein flow (S1) increases resulting in increased S/D ratio. Volume loading increases peak velocities and velocity-time integrals of all pulmonary venous flow components, with the largest effect on the ‘A’ wave.

**MR protocol for pulmonary vein stenosis**

The purposes of MR are: 1) to assess the pulmonary arterial and venous anatomy, 2) to evaluate the hemodynamic consequences of pulmonary vein stenosis; and 3) to evaluate the ventricular function, either qualitatively or quantitatively. For anatomic evaluation, contrast angiography is preferred to non-contrast techniques such as static or cine imaging with balanced steady-state free precession (SSFP) sequences and static imaging with fast spin-echo sequence. As contrast angiography provides full anatomic information regarding pulmonary arteries and pulmonary veins within one or two minutes, it is advised to be performed as the initial sequence. Therefore, the following MR protocol is suggested:

1. Static white blood imaging in axial, coronal and sagittal planes using ECG-gated balanced steady state free precession (SSFP) sequences.
2. Contrast angiography: spatial resolution 1–1.2 mm (isotropic voxels), intravenous injection of 0.1–0.2 mmol / kg of body weight of gadolinium compound for a period of half of total scan time, scan started at arrival of contrast medium in the pulmonary veins using real-time imaging, acquisition of two sets of 3D-volume data. Dynamic angiography can be performed with a lower spatial resolution and a smaller dose of contrast medium (0.05–0.1 mmol / kg).
3. Phase-contrast imaging of individual pulmonary veins, right and left pulmonary arteries, ascending aorta and superior vena cava: Through-plane imaging plane is prescribed perpendicular to the target vessel by referring to the static white blood images or contrast angiograms that have been obtained previously. In-plane imaging along the pulmonary vein can be performed to visualize turbulent blood flow jet but is less reproducible. When the pulmonary vein stenosis involves the veno-atrial junction, it is difficult to target the downstream jet as its direction in the atrium is unpredictable. In these cases, the pre-stenotic segment is easier to target and more reproducible than the downstream post-stenotic jet.
4. Cine imaging using ECG-gated balanced SSFP sequence. Coverage of the whole heart in short-axis planes for quantification of ventricular function or a four-chamber plane for qualitative assessment.

**Anatomic findings in pulmonary vein stenosis at MR**

Stenosis of the pulmonary veins occurs most commonly at the junction with the left atrium. A narrowing of this region can be readily appreciated using MR angiography or gradient echo sequences. Longstanding pulmonary vein stenosis will lead to redistribution of blood flow to portions of the lung with unobstructed venous outlets. As a consequence, the stenotic pulmonary vein carries less blood flow and becomes diffusely hypoplastic. Conversely, a pulmonary venous narrowing in the presence of a preserved flow volume and a good caliper is thought to be less than severe. MR also identifies any neighboring structures that compress the pulmonary veins, most often the descending aorta and an enlarged cardiac mass. Compression is easily missed by X-ray angiography in the anterior-posterior projection, since the compression occurs typically in that direction, while the cranio-caudal dimension is maintained. Axial imaging or reformattting is suitable to identify compression with MR. The same criteria as for intrinsic stenosis apply with regards to the severity of the obstruction.

**Hemodynamic consequences of pulmonary vein stenosis seen with MR**

**Direct effects of the stenosis on pulmonary venous flow:** Pulmonary vein stenosis causes reduced flow rate, increased flow velocity in and downstream from the stenotic segment...
and decreased velocity upstream (Fig. 3). As neither the backward nor the forward force underlying the normal pulmonary blood flow is transmitted across the stenosis, the pulmonary blood flow looses its normal phasic changes during the cardiac cycle. It should be kept in mind that minor flow acceleration or turbulence does not necessarily indicate pulmonary vein stenosis. Valsangiaccomo, et al showed that echocardiographic suspicion of pulmonary vein stenosis based on presence of turbulent flow was dismissed in almost 50% of the pulmonary veins studied by subsequent contrast MR angiography. Jander, et al also showed echocardiographically that minor flow acceleration with normal phasic changes during a cardiac cycle does not indicate stenosis. The pressure gradient across the stenosis can be calculated by using the simplified Bernoulli’s equation, \( \Delta P = 4V^2 \) where \( \Delta P \) is the pressure gradient in mmHg and \( V \) is the maximal velocity of blood flow in the stenosis in m/sec.

**Redistribution of pulmonary blood flow:** Pulmonary vein stenosis results in redistribution of the pulmonary blood flow from the affected to the unaffected or less severely affected parts of the lung. Redistribution of blood flow is easily appreciated in the first pass contrast angiograms. Contrast uptake is reduced and delayed in the lung parts drained by the obstructed pulmonary vein (Fig. 4). Redistribution of blood flow occurs in both systole and diastole (Fig. 5). The systolic redistribution is characterized by decreased velocity and duration of forward flow in the pulmonary artery supplying the affected lung and increased systolic flow in the contralateral pulmonary artery. In addition, the pulmonary artery to the affected lung shows retrograde flow throughout diastole, further decreasing net flow into the affected lung. In severe cases, the redistribution can be to a degree where net forward flow to the affected lung is negligible. These hemodynamic changes are well reflected in the caliber of the branch pulmonary arteries. Roman, et al showed that the cross-sectional area ratio between the right and left pulmonary arteries correlated well with the ratio of net forward flow volumes. Blood flow redistribution can also be observed within the affected lung when the stenosed and normal pulmonary veins coexist on the same side. Radionuclide perfusion scan can be a simple test for following pulmonary blood flow distribution in patients with known pulmonary vein stenosis.

**Development of decompressing venous collateral channels:** In rare cases, the obstructed pulmonary vein is decompressed to the unobstructed pulmonary veins or the systemic veins through collateral venous channels. Pulmonary venovenous collaterals are seen as tortuous channels in the peripheral parts of the lungs (Fig. 6). The systemic venous drainage is via bronchial or intercostals veins (Fig. 4D). Dilated bronchial veins draining the obstructed pulmonary vein may rupture to cause hemoptysis. In contrast to other causes of hemoptysis, bleeding from bronchial varices due to pulmonary vein stenosis is characterized by the pink color of
Fig. 4 Postoperative obstruction of the re-routed scimitar vein in a 15-year old boy. Preoperative contrast-enhanced MR angiogram (A) shows unobstructed scimitar vein connecting to the lower part of the right atrium (RA). An aberrant systemic artery supplies the right lower lung. At 10-month follow-up, the patient complained of shortness of breath on exercise. A source image of the first-pass contrast-enhanced MR angiogram (B) shows decreased perfusion of the entire right lung. The reformatted image from the second acquisition contrast-enhanced MR angiogram (C) demonstrates the collapsed scimitar vein filled with non-enhancing material that is considered a thrombus. The pleural layer of the right thorax shows contrast enhancement. Reformat image from the third set angiograms (D) show anastomoses between the dilated peripheral pulmonary veins and the chest wall veins (arrows).

IVC: inferior vena cava, LA: left atrium, LLPV: left lower pulmonary vein
Development of systemic-to-pulmonary arterial collaterals: Pulmonary vein stenosis is sometimes associated with development of systemic-to-pulmonary arterial collaterals in the affected lung (Fig. 7). This phenomenon is particularly common in patients with prior surgical intervention in the thorax. Those with passive blood flow as a result of a bidirectional cavopulmonary anastomosis or Fontan procedure appear to be at greatest risk for this complication. Recurrent pulmonary or pleural infections may also play a role. The collateral arteries usually arise from bronchial, intercostal, internal mammary and lateral thoracic arteries but can also be recruited from the arteries in the neck or upper abdomen. Adhesions between the parietal and visceral pleurae due to prior surgery or infection appear to be favor-
able access routes for the development of collateral channels. The collateral arteries usually connect to the pulmonary arterioles. Because of distal venous obstruction, the collateral arterial blood flow typically fills the pulmonary artery to the affected lung in a retrograde fashion. As the pulmonary valve is closed in diastole, this retrograde flow from the affected lung in diastole flows into the contralateral pulmonary artery to be drained by the unobstructed pulmonary veins. The amount of collateral arterial flow to the affected lung can be quantified simply by subtracting the pulmonary arterial flow volume from the pulmonary venous flow volume.\(^{34,35}\) When there is a retrograde flow in the pulmonary artery, the pulmonary arterial flow volume should be added to the pulmonary venous flow volume.

**Secondary pulmonary hypertension:** The findings of pulmonary hypertension at phase-contrast imaging of the pulmonary artery include early systolic peak with reduced peak velocity, early cessation of the systolic forward flow with shortened ejection time and multiple minor waves in the deceleration phase of the systolic curve (Fig. 8).\(^{39}\) A degree of right ventricular hypertrophy is seen with increasing pulmonary arterial pressure secondary to pulmonary vein stenosis. Severe pulmonary hypertension is characterized by marked hypertrophy of the right ventricle and flattening of the ventricular septum that may bow towards the left ventricle.

In summary, MR is an excellent imaging modality that provides complete information regarding anatomical find-
ings and hemodynamic/functional consequences of pulmonary vein stenosis. The anatomical assessment can be readily made with contrast MR angiography. The hemodynamic consequences of pulmonary MR angiography can be assessed using ECG-gated phase-contrast velocity imaging. Potential effects on ventricular function is evaluated using ECG-gated cine imaging in short-axis planes.

[REFERENCES]