Haemoptysis due to pulmonary venous stenosis

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ABSTRACT Haemoptysis is a potentially life-threatening condition with the need for prompt diagnosis. In about 10–20% of all cases the bleeding source remains unexplained with the standard diagnostic approach. The aim of this article is to show the necessity of widening the diagnostic approach to haemoptysis with consideration of pulmonary venous stenosis as a possible cause of even severe haemoptysis and haemoptoe.

A review of the literature was performed using the Medline/PubMed database with the terms: "pulmonary venous stenosis", "pulmonary venous infarction" and "haemoptysis". Further references from the case reports were considered.

58 case reports and case collections about patients with haemoptysis due to pulmonary venous stenosis were detected. This review gives an overview about the case reports and discusses the underlying pathophysiology and the pros and cons of different imaging techniques for the detection of pulmonary venous stenosis.

Several conditions predispose to the obstruction of the mediastinal pulmonary veins. Clinical findings are unspecific and may be misleading. Pulmonary venous stenosis can be detected using several imaging techniques, yet three-dimensional magnetic resonance-angiography and three-dimensional contrast-enhanced computed tomography are the most appropriate. Pulmonary venous stenosis should be considered in patients with haemoptysis.

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Pulmonary venous stenosis should be considered in haemoptysis and is best diagnosed using CT or MRI venography http://ow.ly/tMPFP

Introduction

This article gives an overview about pulmonary venous stenosis as a possible cause of haemoptysis. Inflammatory and malignant pulmonary diseases may cause haemoptysis, and diagnostic algorithms as management principles for haemoptysis are well described. However, with the standard diagnostic approach, including bronchoscopy, computed tomography (CT) and bronchial angiography, in about 10–20% of cases the bleeding source remains unexplained [1]. Although many cases were reported of patients with severe haemoptysis due to pulmonary venous obstruction [2–59] (online supplementary table S1), the pulmonary veins are only infrequently mentioned in the literature about the management of

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haemoptysis [60–65]. Besides the rare condition of congenital pulmonary venous stenosis, there are several clinical conditions predisposing to the obstruction of the central pulmonary veins, like mediastinal masses such as solid neoplasms or bulky lymphoma, fibrosing mediastinitis and mediastinal granulomatous diseases. In addition, lung transplantation [66, 67] and lobectomy or bilobectomy [24] may result in pulmonary venous stenosis (table 1). Furthermore, cor triatriatum [53], left atrial myxoma and post-pneumonectomy syndrome may cause functional pulmonary venous stenosis. Since the interventional ablation strategies for atrial fibrillation target the veno-atrial junctions of the pulmonary veins, plenty of cases with haemoptysis due to post-procedural pulmonary vein stenosis were reported. Due to thermal injury at the veno-atrial junctions [68, 69], pulmonary venous stenosis has become a well-recognised complication of these ablation procedures, with sometimes even fatal peri-procedural haemoptoe [41]. Because of this potentially life-threatening complication, ablation technology has changed from the intra-ostial radiofrequency ablation technique to the antral cryoballoon isolation technique during the past decade. With the radiofrequency procedures, pulmonary vein stenosis rates of up to 30–40% in scheduled surveillances were reported. With the cryoballoon technique, the official pulmonary vein stenosis rate is about 1–3% [70]. In the USA alone, about 40 000–50 000 atrial fibrillation ablation procedures are performed each year. This review focuses on haemoptysis due to the obstruction of the central mediastinal pulmonary veins.

Anatomy of the mediastinal pulmonary veins

The embryological formation of the pulmonary veins is quite complex and there is a remarkable diversity of pulmonary vein connections into the left atrium [71–74]. The classical description of two left-sided (left superior (LSPV) and left inferior (LIPV)) and two right-sided (right superior (RSPV) and right inferior (RIPV)) separately ending pulmonary veins accounts for only ~70% of the normal population. Approximately 28% of people have three to five ostia at the right side and 14% of the population have a single ostium at the left side. At the right side an accessory right pulmonary vein is common. The right-sided middle lobe vein (RMLV) may drain *via* the superior pulmonary vein, the inferior pulmonary vein or separately. The variant of RMLV drainage *via* the RIPV may result in life-threatening post-operative haemoptysis and respiratory distress in case of right lower lobectomy. Therefore, careful pre-operative assessment of the pulmonary venous return is crucial in patients undergoing pulmonary surgery [24, 75, 76]. In addition to congenital stenosis of pulmonary veins with normal connection, the varying forms of partial anomalous venous return may be combined with a pulmonary venous stenosis.

Pathophysiology

To understand the pathophysiology of haemoptysis in cases of pulmonary venous stenosis, it is important to know that both the pulmonary and the bronchial circulation drain *via* the pulmonary veins into the left atrium. Thus, in pulmonary venous stenosis the drainage systems of both lung circulations are blocked. Typical consequences include distended pleural-hilar bronchial veins, alveolar haemorrhage, a friable endobronchial mucosa, a reduced lymphatic drainage, interstitial pulmonary oedema, enlarged hilar lymph nodes, enlarged lymph vessels and sometimes pleural effusions [77–82]. To keep the lung an optimal

TABLE 1 Factors causing morphological or functional pulmonary venous stenosis

Congenital pulmonary venous stenosis
Circumscript pulmonary venous stenosis at the veno-atrial junctions of one or more pulmonary veins
Congenital hypoplasia of one or more pulmonary veins
Partial anomalous venous connection with stenosis of the aberrant veins
Cor triatriatum
Acquired pulmonary vein stenosis
Mediastinal or pulmonary neoplasms resulting in extrinsic compression of the pulmonary veins in their run through the mediastinum
Fibrosing mediastinitis due to mediastinal granulomatous diseases
Circumscript pulmonary venous stenosis as a complication of catheter-guided therapy for atrial fibrillation
Post-operative pulmonary vein thrombosis after lung transplantation
Right-sided lower lobectomy in case of drainage of the right middle lobe vein into the right inferior pulmonary vein with subsequent right middle lobe venous occlusion
Intraluminal growth of neoplasms in the pulmonary veins or in the left atrium
Post-operative stenosis after surgical correction of partial or total anomalous venous return
Restenosis or stent-thrombosis after interventional dilatation of pulmonary venous-stenosis
Functional pulmonary venous stenosis
Post-pneumonectomy syndrome after right-sided pneumonectomy with compression of the left pulmonary veins between the aorta and left ventricle in case of a cardiac shift into the right hemithorax

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TABLE 2 Histological changes in pulmonary venous stenosis

Pre-capillary	Typical vascular remodelling of pulmonary hypertension with hypertrophy of the media of the pulmonary arteries, resulting in reduced arborisation of the pulmonary arterial tree
Parenchymal	Accumulation of intraparenchymal siderophages
	Septal thickening
	Mild interstitial fibrosis
	Pleural plaques owing to organisation of fibrinous exudates
Lymphatic	Enlarged hilar lymph nodes
	Lymphangiectasis
	Pleural effusion
Post-capillary	"Arterialisation" of the pulmonary veins with intimal fibrosis and medial thickening
	Venous varices mimicking arteriovenous malformations
Bronchovascular	Remodelling of the bronchial arteries and bronchial veins with bronchovascular ectasis
Endobronchial	Friable endobronchial mucosa predisposed for haemoptysis and recurrent airway infection

gas-exchanging system, the pulmonary arterial blood flow is also affected, with redistribution of the pulmonary arterial blood flow towards regions with lower vascular resistance [83–87]. In severe stenosis even a reversal flow in the pulmonary arteries with development of pulmonary venous hypertension, pulmonary arterial remodelling and a decreased arborisation of the pulmonary arterial tree may develop [88, 89] (table 2).

Haemoptysis and other clinical symptoms and signs caused by pulmonary venous stenosis

Depending on the acuity of the pulmonary venous obstruction and the development of venous collaterals the venous parenchymal and mucosal bleeding may vary from even asymptomatic courses with occult alveolar haemorrhage to acute fatal haemoptoe. In cases of haemoptysis due to pulmonary venous stenosis the expectorated blood is deoxygenated and, therefore, usually darker compared to haemoptysis with offspring of the systemic bronchial arteries. As in other cases with massive haemoptysis, clinical management includes early endotracheal intubation with large-bore tubes in an intensive care unit setting, early bronchoscopy for localisation of the bleeding side and early endobronchial therapy to protect the nonbleeding side. The endobronchial changes with dilatation of the dense submucosal venous plexus can often be seen in bronchoscopy and the alveolar haemorrhage will result in a bloody bronchoalveolar lavage or, if occult, in an increased number of siderophages in the cell differentiation [82]. Due to the dense network between the pulmonary and bronchial circulation, extensive collaterals between both circulations may develop, with the possible occurrence of secondary bronchial and pulmonary venous varices in the long run. Misinterpretation of these varices and collaterals as pulmonary arteriovenous malformations has been reported. Bronchial artery embolisation may be deleterious in cases of hindered pulmonary venous drainage.

Besides haemoptysis, the typical clinical symptoms of pulmonary venous stenosis are tussive irritation, exertional dyspnoea, recurrent pulmonary infections and signs of pulmonary venous hypertension. Mimicking of primarily pulmonary diseases, such as recurrent pneumonia, interstitial pneumonitis, lung cancer and pulmonary embolism, has been reported in animal studies, as in many case reports [19, 90–93]. Mild interstitial fibrosis is thought to originate from the organisation of haemorrhagic oedema in the alveolar walls. The resulting clinical signs of pulmonary venous stenosis are highly unspecific and may, therefore, be misleading. Unilateral pleural effusions, haemoptysis in combination with enlarged hilar lymph nodes and pulmonary infiltrates in combination with positive blood cultures are only a few examples of the consequences of pulmonary venous stenosis. Figure 1 demonstrates different clinical signs caused by pulmonary venous stenosis in a patient with life-threatening haemoptysis. Haemoptysis in combination with the history of mediastinal masses, granulomatous diseases, interventional procedures for atrial fibrillation therapy, lobectomy or right-sided pneumonectomy, pulmonary hypertension, recurrent respiratory infections or after lung transplantation should prompt the suspicion of pulmonary venous stenosis (table 1). Yet the diagnostic workup of pulmonary venous stenosis is elusive, which is why the different diagnostic procedures to detect pulmonary venous stenosis are discussed here.

Diagnostic imaging

Accurate imaging of the anatomical and functional properties of the pulmonary veins is challenging. For example, a pathologic perfusion scan in combination with haemoptysis may be misinterpreted as acute pulmonary embolism [94, 95]. Various imaging techniques have been investigated to explore the mediastinal pulmonary veins, such as transoesophageal echocardiography (TOE), ventilation/perfusion scan,

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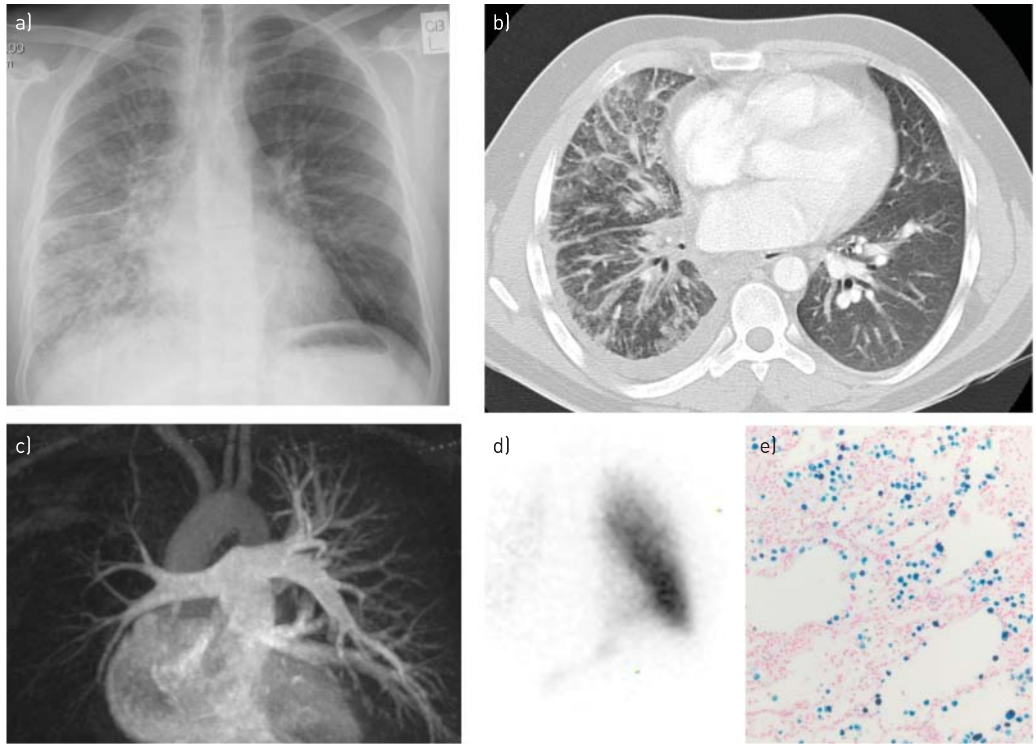

FIGURE 1 a) Chest radiograph, b) multislice computed tomography angiography, c) three-dimensional magnetic resonance angiography, d) perfusion scintigraphy and e) iron staining of a lung biopsy of a patient with severe haemoptysis due to occlusion of the right-sided pulmonary veins. Note the right-sided interstitial infiltrates, the hilar lymphadenopathy, the pleural effusion, the perfusion shift to the left lung and the siderophages in the specimen (a–e, respectively).

contrast-enhanced multisclice CT, magnetic resonance angiography and direct pulmonary venography. Wood *et al.* [96] compared CT, TOE and direct pulmonary venography to assess the number of detectable pulmonary veins and their diameters at the veno-atrial junctions in 24 patients. In contrast to CT, which detected 98 pulmonary veins, TOE detected only 80 and direct venography detected only 71 pulmonary veins. Thus, direct angiography missed 27% and TOE missed 18% of the pulmonary veins. With TOE in particular, the inferior and the right middle lobe veins will be missed. Depending on which imaging technique is used, the ostial diameters vary significantly from 1.6 ± 0.3 cm using direct venography to 1.1 ± 0.25 cm using TOE. Therefore, neither TOE nor direct pulmonary venography can be recommended for the exclusion of pulmonary venous stenosis. Depending on which imaging technique is used, the ostial diameters vary significantly from 1.6 ± 0.3 cm using direct venography to1.1 ± 0.25 cm using TOE.

A brief discussion of the pros and cons of these imaging techniques referring to pulmonary venous stenosis is shown in table 3 and discussed below.

Ventilation/perfusion scan

The ventilation/perfusion scan usually is performed for the detection of pulmonary embolism, but is also reported to serve as an effective screening tool for the detection of haemodynamically relevant pulmonary venous stenosis [84–87]. To maintain the lung, an optimal gas exchanging system, backward transmission of elevated venous pressures will immediately induce a local increase of vascular resistance with a subsequent shift of the pulmonary arterial blood flow towards regions with lower resistance. This shift explains the perfusion deficits in lung perfusion scans of patients with haemodynamically relevant pulmonary venous stenosis. Lepadat *et al.* [87] demonstrated an immediate shift of the pulmonary perfusion after pulmonary arterial as well as pulmonary venous ligation. Nanthakumar *et al.* [84] demonstrated pathological perfusion scans with a resting pressure gradient >5 mmHg between the pulmonary vein and the left atrium, or with a $\geqslant 80\%$ luminal stenosis. To minimise false-positive pulmonary embolism results, lung perfusion scans are best performed using the technique of single photon emission computed tomography (SPECT) and should be interpreted in conjunction with the corresponding ventilation scan. However, in case of alveolar haemorrhage and endobronchial thrombus formation,

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TABLE 3 Comparison of different imaging techniques for the detection of pulmonary venous stenosis

Imaging techniques	Pros	Cons
Perfusion scintigraphy	Perfusion deficits likely in pressure gradients left atrium/pulmonary vein >5 mmHg and/or >80% stenosis	Low specificity, perfusion deficits in cases with pulmonary embolism
Transoesophageal echocardiography	Information about left and right heart function Consider relevant stenosis if: pulmonary vein flow velocity >100 $cm \cdot s^{-1}$ pulmonary vein diameter <5 mm	Inferior pulmonary vein difficult to visualise Anomalies like accessory pulmonary veins, common left trunk or hypoplasia are often missed Underestimates pulmonary vein diameter
3D-MRA venography	Simultaneous visualisation of: mediastinal structures left and right heart function partial anomalous venous return Flow quantification with phase contrast	Limited post-processing Limited visualisation of the pulmonary parenchyma
3D-CT venography	Data acquisition within a few seconds Simultaneous visualisation of: pulmonary parenchyma mediastinal structures left and right heart Post-processing possible in all planes	Iodine contrast media and radiation exposure
Direct venography	Can be used in combination with therapeutic interventions Retrograde pulmonary vein detection in near-total occlusion Assessment pressure gradient from pulmonary vein pressure to left atrium pressure	Most invasive Lowest sensitivity for the detection of pulmonary veins in comparison with the other techniques Overestimates diameter of pulmonary veins Restricted to luminography

3D: three-dimensional; MRA: magnetic resonance angiography; CT: computed tomography.

pulmonary venous stenosis may also result in a combined ventilation/perfusion deficit. Perfusion deficits may be missed if the stenosis is <50%.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) offers multiple advantages such as noninvasiveness, freedom from radiation exposure and visualisation of the circumadjacent mediastinal structures. Furthermore, it provides information about blood flow and left and right ventricular function. For the assessment of pulmonary venous stenosis different MRI techniques are available, such as noncontrast white-blood imaging, three-dimensional (3D) steady-state free precession magnetic resonance angiography, four-dimensional flow MRI, phase-contrast velocity mapping and contrast-enhanced gadolinium magnetic resonance angiography [88, 89, 97–101]. Magnetic resonance-perfusion imaging has 95% sensitivity and 100% specificity to detect perfusion deficits in cases of haemodynamically relevant pulmonary venous stenosis, compared to the scintigraphic SPECT technique [97]. With phase-contrast MRI, the pulmonary venous flow and mean flow velocities in the mediastinal veins can be quantified. Signs of venous obstruction include flow acceleration downstream from the stenotic lesion and a loss of the normal phasic changes. Normal systolic and diastolic peaks of the pulmonary venous blood flow were reported at 51 ± 16 $cm \cdot s^{-1}$ and 47 ± 11 $cm \cdot s^{-1}$. There is a significant variability in pulmonary vein diameter and cross-sectional area over the cardiac cycle, with greatest diameters in ventricular diastole and a mean difference in diameter of ~15% and 27% for the cross-sectional area. For optimal imaging of the pulmonary veins, the authors suggest a gadolinium-enhanced, bolus-tracking technique with the region of interest in the left atrium to match the imaging sequences with the maximum contrast media peak into the left atrium.

Computed tomography

The advantage of multislice CT-venography compared to MRI is the simultaneous visualisation of the pulmonary parenchyma and that 3D-reconstructions of the pulmonary veins can easily be performed. CT scanning provides additional information about the functional consequences of pulmonary venous stenosis, because the morphological parenchymal alterations, such as thickening of the septal walls, mosaic pattern

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due to inhomogeneous aeration and perfusion, may not be detected with MRI. As with MRI, the scanning delay time should be defined by a bolus-tracking technique focusing the bolus arrival into the left atrium for optimal visualisation of the veno-atrial junctions. Mean pulmonary vein diameters were reported as follows: RSPV 13–15 mm, LSPV 16–17 mm, RIPV 16–17 mm, LIPV 14–15 mm and middle lobe vein 8.2–8.9 mm. Up-to-date (64-row or 128-row) multislice-detector CT scans are able to visualise the veno-atrial junctions with excellent spatial resolution [102–107].

Echocardiography

The transthoracic echo window usually is unsatisfactory for the evaluation of the pulmonary venous flow in adults. TOE, with the use of colour- and Doppler-mode at a Nyquist limit of ~40 $\text{cm}\cdot\text{s}^{-1}$, offers a much better ultrasound window. For the pulsed-wave Doppler analysis the standard position of the sample volume is about 1–2 cm upstream from the pulmonary vein orifices, where normally a triphasic flow pattern can be delineated. This flow profile is hooked to the left atrial pressure with mean velocities of ~0.5 $\text{m}\cdot\text{s}^{-1}$ in systole and 0.4 $\text{m}\cdot\text{s}^{-1}$ in diastole [108]. Pulmonary venous stenosis is suspected if peak flow velocities exceeds 1.0 $\text{m}\cdot\text{s}^{-1}$ and/or if pulmonary vein diameter is <5 mm. The inferior pulmonary veins and accessory right pulmonary veins are often difficult to view because Doppler imaging is highly angle dependent. Visualisation of the pulmonary veins with TOE is much poorer compared to the newer generations of multislice imaging techniques [96].

Direct venography

Direct venography is the most invasive and time-consuming method and is restricted to a planar luminography. Furthermore, a trans-septal puncture is required. However, in the case of a near-total pulmonary vein occlusion, a flow-through pulmonary angiogram sometimes demonstrates a residual pulmonary vein lumen, which then facilitates a retrograde recanalisation of the pulmonary vein [10]. Except in the case of a near-total occlusion, the multislice techniques have a much higher diagnostic accuracy, which is why the direct pulmonary venous angiography is performed in the context of therapeutic procedures rather than for diagnostic reasons.

Therapeutic options to restore pulmonary venous drainage in the case of central pulmonary venous stenosis

If pulmonary venous stenosis is diagnosed, catheter-guided and surgical procedures are established for therapy, depending on the aetiology of the stenosis. Pulmonary venous stenosis is usually a progressive disease resulting in a kind of functional lobectomy due to the perfusion shift, which is why symptomatic higher stenosis should be treated. In the case of pulmonary venous stenosis at the veno-atrial junctions due to interventional therapy of atrial fibrillation, a percutaneous catheter-guided dilatation is recommended. After puncture of the vena femoralis using the Seldinger technique and subsequent atrial transseptal

TABLE 4 Diagnostic approach to haemoptysis and therapeutic options to restore the pulmonary venous drainage

History	Standard approach	Pulmonary venous stenosis?	Therapeutic options
Mediastinal masses	Clinical stabilisation	Contrast-enhanced multislice computed tomography-venography with three-dimensional reconstruction of the pulmonary veins	Catheter-guided balloon dilatation in case of restenosis with bare-metal or drug-eluting stent implantation post-intervention anticoagulation
Granulomatous diseases	Coagulation tests	Or	Or
Interventional procedures for AF	Radiography	Contrast-enhanced magnetic resonance venography with three-dimensional reconstruction of the pulmonary veins	Surgical procedures
Lobectomy or bilobectomy	Computed tomography-angiography		Conventional venoplasty
Right-sided pneumonectomy	Bronchoscopy		Sutureless venoplasty
Pulmonary hypertension	Optional bronchial angiography		Post-operative anticoagulation
Recurrent pulmonary infections			Or
Lung transplantation			Emergency lobectomy in case of persistent life-threatening haemoptysis

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puncture, a guiding catheter is placed in the left atrium under fluoroscopy. Then, the interventionalist places a guidewire into the stenosed pulmonary vein and dilates the venous stenosis with a balloon catheter. Surgical procedures are commonly used in cases of congenital stenosis of the veno-atrial junctions either with conventional or with sutureless venoplasty or a pericardial patchplasty [109]. For aquired pulmonary venous stenosis due to mediastinal masses, the therapeutic decision is usually made subject to individual aspects. Both surgical techniques, as with catheter-guided techniques, have the problem of an extremely high proportion (up to 50%) of restenosis. Catheter-guided stent implantation with bare-metal stents or drug-eluting stents may be an alternative if restenosis develops [110]. If massive bleeding persists, an urgent surgical lobectomy or pneumonectomy can be life saving. Anticoagulation is mandatory after successful recanalisation of pulmonary venous stenosis; however, in the acute setting with haemoptysis anti-coagulation may be detrimental. Table 4 suggests a diagnostic algorithm for patients with unexplained haemoptysis, to exclude pulmonary venous stenosis of the mediastinal pulmonary veins and the veno-atrial junctions, and it describes the therapeutic options to restore the pulmonary venous drainage.

Conclusions

Pulmonary venous stenosis should be considered in the differential diagnosis of patients with haemoptysis. In particular, patients with a history of mediastinal masses, interventional therapy for atrial fibrillation or right lower lobectomy are predisposed to pulmonary venous obstruction. TOE, ventilation/perfusion scans and direct venoography may detect pulmonary venous stenosis, but cannot be recommended for the exclusion of pulmonary venous stenosis. Gadolinium-enhanced magnetic resonance venography and contrast-enhanced multislice CT with 3D reconstruction of the veno-atrial junctions are the most appropriate methods for the detection of pulmonary venous stenosis. For optimal visualisation of the veno-atrial junctions, the correct scanning delay time is important.

References

1 Herth F, Ernst A, Becker H. Long-term outcome and lung cancer incidence in patients with hemoptysis of unknown origin. *Chest* 2001; 120: 1592–1594.

2 Calero Acuña C, Elías Hernández T. Haemoptysis as a first sign of pulmonary venous stenosis secondary to radiofrequency ablation of atrial fibrillation. *Arch Bronchopneumol* 2011; 47: 162–163.

3 Aguilar-Cabello M, Martín-Bermúdez R, Jiménez-Jiménez J, *et al.* Hemoptisis amenazante y estenosis de venas pulmonares tras ablación por fibrilación auricular [Threatening hemoptysis and pulmonary vein stenosis after ablation due to atrial fibrillation]. *Med Intensiva* 2012; 36: 56–72.

4 Alexander G, Reddi A, Reddy D. Idiopathic pulmonary vein thrombosis: a rare cause of massive hemoptysis. *Ann Thorac Surg* 2009; 88: 281–283.

5 Beerman LB, Oh K, Park SC, *et al.* Unilateral pulmonary vein atresia: clinical and radiographic spectrum. *Pediatr Cardiol* 1983; 4: 105–112.

6 Berry DF, Buccigrossi D, Peabody J, *et al.* Pulmonary vascular occlusion and fibrosing mediastinitis. *Chest* 1986; 89: 296–301.

7 Bhagwandien R, Van Belle Y, de Groot N, *et al.* Hemoptysis after pulmonary vein isolation with a cryoballon: an analysis of the potential etiology. *J Cardiovasc Electrophysiol* 2011; 22: 1067–1069.

8 Botticelli J, Schlueter D, Lange R. Pulmonary venous and arterial hypertension due to chronic fibrous mediastinitis. *Circulation* 1966; 33: 862–871.

9 Braun S, Platzek I, Kolditz M, *et al.* Belastungsdyspnoe, Husten und Hämoptysen mit pathologischer Perfusionsszintigraphie [Dyspnea, cough and hemoptysis with pathologic perfusion scintigraphy]. *Pneumologe* 2012; 9: 465–469.

10 Braun S, Kolditz M, Halank M, *et al.* Hämoptysen infolge Pulmonalvenenstenose und -verschluss nach Pulmonalvenen-Isolation bei Vorhofflimmern [Hemoptysis because of pulmonary vein stenosis and occlusion after pulmonary vein isolation for atrial fibrillation]. *Dtsch Med Wochenschr* 2011; 136: 626–630.

11 Burri E, Duwe J, Kull C, *et al.* Pulmonary vein thrombosis after lower lobectomy of the left lung. *J Cardiovasc Surg* 2006; 47: 609–612.

12 Cabrera A, Vazquez C, Lekuona I. Isolated atresia of the left pulmonary veins. *Int J Cardiol* 1985; 7: 298–302.

13 Cho YK, Kim YO, Choi WY, *et al.* Bilateral congenital pulmonary vein stenosis with a normal connection. *J Cardiovasc Ultrasound* 2008; 16: 54–58.

14 Conte G, Gian-Battista C, Casado-Arroyo R, *et al.* Pulmonary vein intramural hematoma as a complication of cryoballoon ablation of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2013; 24: 930–931.

15 Cullen S, Deasy PF, Tempany E, *et al.* Isolated pulmonary vein atresia. *Br Heart J* 1990; 63: 350–354.

16 den Bakker M, Thomeer M, Maat A, *et al.* Life-threatening hemoptysis caused by chronic idiopathic pulmonary hilar fibrosis with unilateral pulmonary vein occlusion. *Ann Diagn Pathol* 2005; 9: 319–322.

17 Di Biase L, Fahmy TS, Wazni OM, *et al.* Pulmonary vein total occlusion following catheter ablation for atrial fibrillation. *J Am Coll Cardiol* 2006; 48: 2493–2499.

18 Dupuis C, Remy J, Remy-Jardin M, *et al.* Le syndrome du cimeterre avec absence anatomique ou fonctionnelle de l'artère pulmonaire droite. À propos de quatre observations [Scimitar syndrome with anatomical or functional absence of the right pulmonary artery. Apropos of 4 cases]. *Arch Pediatr* 1995; 2: 347–352.

19 Ernst S, Ouyang F, Goya M, *et al.* Total pulmonary vein occlusion as a consequence of catheter ablation for atrial fibrillation mimicking primary lung disease. *J Cardiovasc Electrophysiol* 2003; 14: 366–370.

20 Guzzi M, Bouza G, Rodríguez R, *et al.* Estenosis de vanos pulmonares post ablaction por radiofrecuencia [Pulmonary vein stenosis after radio frequency ablation]. *Medicina (B Aires)* 2011; 71: 251–253.

 DOI: 10.1183/09059180.00003713

21 Harrison JK, Hearne SE, Baker SE, *et al.* Esophageal varices in association with unilateral pulmonary vein atresia. *Cathet Cardiovasc Diagn* 1996; 38: 387–392.

22 Heyneman L, Nolan R, Harrison K, *et al.* Congenital unilateral pulmonary vein atresia: radiologic findings in three adult patients. *AJR Am J Roentgenol* 2001; 177: 681–685.

23 Holmes D, Monahan K, Packer D. Pulmonary vein stenosis complicating ablation for atrial fibrillation: clinical spectrum and interventional considerations. *JACC Cardiovasc Interv* 2009; 2: 267–276.

24 Hovaguimian H, Morris J, Gately H, *et al.* Pulmonary vein thrombosis following bilobectomy. *Chest* 1991; 99: 1515–1516.

25 Hull J, Menzies-Gow A, Nicholson A, *et al.* Exercise-induced haemoptyis: a thoroughbred cause? *Thorax* 2013; 68: 599–600.

26 Jaitovich A, Harmath C, Cuttica M. Pulmonary vein stenosis and hemoptysis. *Am J Respir Crit Care Med* 2012; 185: 1023.

27 Jones R, Dawson A, Jenkins GH, *et al.* Sarcoidosis-related pulmonary veno-occlusive disease presenting with recurrent haemoptysis. *Eur Respir J* 2009; 34: 517–520.

28 Karlsson SE, Kidron P. Radiofrekvensablation av formaksflimmer inducerade lungvensstenos. Ett fall visar ny orsak till hemoptys [Radiofrequency ablation for atrial fibrillation induced pulmonary vein stenosis. A case shows new cause of hemoptysis]. *Lakartidningen* 2008; 105: 998–999.

29 Kojodjojo P, Wong T, Wright AR, *et al.* Pulmonary venous stenosis after treatment for atrial fibrillation. *BMJ* 2008; 336: 830–832.

30 Kovach A, Cheng G, Channick C, *et al.* Postradiofrequency ablation inflammatory pseudotumor associated with pulmonary venoocclusive disease: case report and review of the literature. *Ann Diagn Pathol* 2013; 17: 466–469.

31 Laboux L, Michaud JL, Cornet E. Atresie unilateral des veins pulmonaires. Signes cliniques, hemodynamiques et angiographiques a propos d'une observation [Unilateral atresia of the pulmonary veins. Clinical, hemodynamic and angiographic signs apropos of a case]. *Arch Mal Coeur Vaiss* 1972; 65: 1155–1158.

32 Lange T, Luchner A, Endemann D, *et al.* A 46-year-old man with dyspnea and hemoptysis 3 years following mitral valve repair. *Chest* 2007; 132: 704–707.

33 Lee HN, Kim YT, Cho S. Individual pulmonary vein atresia in adults: report of two cases. *Korean J Radiol* 2011; 12: 395–399.

34 Lee J, Lee J, Kang C, *et al.* Unilateral pulmonary vein stenosis with life-threatening hemoptysis: a case report. *Korean J Thorac Cardiovasc Surg* 2005; 38: 725–728.

35 Loyd JE, Tillma B, Atkinson JB, *et al.* Mediastinal fibrosis complicating histoplasmosis. *Medicine* 1988; 67: 295–310.

36 Matsuyama K, Matsumoto M, Ogino H, *et al.* Pulmonary venous obstruction requiring lobectomy for hemoptysis after a Glenn operation. *Jpn J Thorac Cardiovasc Surg* 2001; 49: 629–631.

37 Mendelson E, Mintzer R, Hidvegi D. Venoocclusive pulmonary infarct: an unusual complication of fibrosing mediastinitis. *AJR Am J Roentgenol* 1983; 141: 175–176.

38 Morcos KH, Roditi G, Craig S. Life-threatening haemoptysis due to tracheal varices secondary to pulmonary vein obstruction. *Thorax* 2013; 68: 894–895.

39 Artero Muñoz I, Serrano Puche F, Padín Marín MI, *et al.* Atresia congénita unilateral de las venas pulmonares: hallazgos radiológicos [Congenital unilateral pulmonary vein atresia: imaging findings]. *Radiologia* 2008; 50: 82–85.

40 Nehra D, Liberman M, Vagefi PA, *et al.* Complete pulmonary venous occlusion after radiofrequency ablation for atrial fibrillation. *Ann Thorac Surg* 2009; 87: 292–295.

41 Nilsson B, Chen X, Pehrson S, *et al.* Acute fatal pulmonary vein occlusion after catheter ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2004; 11: 127–130.

42 Otto D, von Falkenhausen U, Schellong S, *et al.* Unilaterale Pulmonalveneratresie im fruhen Erwachsenenalter [Unilateral pulmonary vein atresia in early adulthood]. *Pneumologie* 1998; 52: 135–139.

43 Packer DL, Keelan P, Munger TM, *et al.* Clinical presentation, investigation, and management of pulmonary vein stenosis complicating ablation for atrial fibrillation. *Circulation* 2005; 111: 546–554.

44 Patel N, Petterson G, Murat Tuzcu E, *et al.* Sucessful surgical repair of iatrogenic pulmonary vein stenosis. *J Cardiovasc Electrophysiol* 2012; 23: 656–658.

45 Prieto L, Schoenhagen P, Arruda M, *et al.* Comparison of stent *versus* balloon angioplasty for pulmonary vein stenosis complicating pulmonary vein isolation. *J Cardiovasc Electrophysiol*, 19: 673–678.

46 Pürerfellner H, Aichinger J, Martinek M, *et al.* Incidence, management, and outcome in significant pulmonary vein stenosis complicating ablation for atrial fibrillation. *Am J Cardiol* 2004; 93: 1428–1431.

47 Qureshi AM, Prieto LR, Latson LA, *et al.* Transcatheter angioplasty for acquired pulmonary vein stenosis after radiofrequency ablation. *Circulation* 2003; 108: 1336–1342.

48 Ravenel J, McAdams HP. Pulmonary venous infarction after radiofrequency ablation for atrial fibrillation. *AJR Am J Roentgenol* 2002; 178: 664–666.

49 Reid J, Jamieson M, Cowan M. Unilateral pulmonary vein stenosis. *Br Heart J* 1986; 55: 599–601.

50 Routsi C, Charitos C, Rontogianni D, *et al.* Unilateral pulmonary edema due to pulmonary venous obstruction from fibrosing mediastinitis. *Int J Cardiol* 2006; 108: 418–421.

51 Saad EB, Marrouche NF, Saad CP, *et al.* Pulmonary vein stenosis after catheter ablation of atrial fibrillation: emergence of a new clinical syndrome. *Ann Intern Med* 2003; 138: 634–638.

52 Spragg DD, Dalal D, Cheema A, *et al.* Complications of catheter ablation for atrial fibrillation: incidence and predictors. *J Cardiovasc Electrophysiol* 2008; 19: 627–631.

53 Sritippayawan S, Margetis M, MacLaughlin E, *et al.* Cor triatriatum: a cause of hemoptysis. *Pediatr Pulmonol* 2002; 34: 405–408.

54 Swischuk L, L'Heureux P. Unilateral pulmonary vein atresia. *AJR Am J Roentgenol* 1980; 135: 667–672.

55 van der Werf TS, Mannes G, Hew JM, *et al.* Improved gas exchange after pneumonectomy in an adult with incomplete pulmonary vein atresia. *Thorax* 1994; 49: 723–725.

56 Walsh A, Canny G, McMahon CJ, *et al.* Hemoptysis from bronchial varices associated with pulmonary vein stenosis: role of surgical repair. *Pediatr Pulmonol* 2013; 48: 838–840.

57 Wiebe S, Maclusky I, Manson D, *et al.* Hemoptysis: a rare cause can be related to a bronchial varix due to pulmonary venous obstruction. *Pediatr Radiol* 2003; 33: 884–886.

58 Yacoub M, Thompson V. Chronic idiopathic pulmonary hilar fibrosis. A clinicopathological entity. *Thorax* 1971; 26: 365–375.

59 Yang HM, Lai C, Patel J, *et al.* Irreversible intrapulmonary vascular changes after pulmonary vein stenosis complicating catheter ablation for atrial fibrillation. *Cardiovasc Pathol* 2007; 16: 51–55.
60 Haponik E, Fein A, Chin R. Managing life-threatening hemoptysis: has anything really changed? *Chest* 2000; 118: 1431–1435.
61 Bidwell J, Pachner R. Hemoptysis: diagnosis and management. *Am Fam Physician* 2005; 72: 1253–1260.
62 Garwood S, Strange C, Sahn S. Massive hemoptysis. *In:* Parrillo JE, Dellinger RP, eds. Critical Care Medicine: Principles of Diagnosis and Management in the Adult. 3rd Edn. St Louis, Mosby Elsevier, 2008.
63 Jeudy J, Khan AR, Mohammed TL, *et al.* ACR Appropriateness Criteria hemoptysis. *J Thorac Imaging* 2010; 25: W67–W69.
64 Andersen PE. Imaging and interventional radiological treatment of hemoptysis. *Acta Radiol* 2006; 47: 780–792.
65 Sakr L, Dutau H. Massive hemoptysis: an update on the role of bronchoscopy in diagnosis and management. *Respiration* 2010; 80: 38–58.
66 McIlroy DR, Sesto AC, Buckland MR. Pulmonary vein thrombosis, lung transplantation, and intraoperative transoesophageal echocardiography. *J Cardiothorac Vasc Anesth* 2006; 20: 712–715.
67 Leibowitz DW, Smith CR, Michler RE, *et al.* Incidence of pulmonary vein complications after lung transplantation: a prospective transesophageal echocardiographic study. *J Am Coll Cardiol* 1994; 24: 671–675.
68 Kowalski M, Grimes M, Perez F, *et al.* Histopathologic characterization of chronic radiofrequency ablation lesions for pulmonary vein isolation. *J Am Coll Cardiol* 2012; 59: 930–938.
69 Taylor G, Kay N, Zheng X, *et al.* Pathological effects of extensive radiofrequency energy applications in the pulmonary veins in dogs. *Circulation* 2000; 101: 1736–1742.
70 Calkins H, Kuck KH, Cappato R, *et al.* 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trail design. *Europace* 2012; 14: 528–606.
71 Tekbas G, Gumus H, Onder H, *et al.* Evaluation of pulmonary vein variations and anomalies with 64 slice multi detector computed tomography. *Wien Klin Wochenschr* 2012; 124: 3–10.
72 Dillman J, Yarram S, Hernandez R. Imaging of pulmonary venous developmental anomalies. *AJR Am J Roentgenol* 2009; 192: 1272–1285.
73 Marom EM, Herndon JE, Kim YH, *et al.* Variations in pulmonary venous drainage to the left atrium: implications for radiofrequency ablation. *Radiology* 2004; 230: 824–829.
74 Snellen HA, van Ingen HC, Hoefsmit C. Patterns of anomalous pulmonary venous drainage. *Circulation* 1968; 38: 45–63.
75 Sugimoto S, Izumiyama O, Yamashita A, *et al.* Anatomy of inferior pulmonary vein should be clarified in lower lobectomy. *Ann Thorac Surg* 1998; 66: 1799–1800.
76 Yamada S, Suga A, Inoue Y, *et al.* Importance of preoperative assessment of pulmonary venous anomaly for safe video-assisted lobectomy. *Interact Cardiovasc Thorac Surg* 2010; 10: 851–854.
77 Heath D, Edwards J. Histological changes in the lung in diseases associated with pulmonary venous hypertension. *Br J Dis Chest* 1959; 53: 8–18.
78 Pietra G, Capron F, Stewart S, *et al.* Pathologic assessment of vasculopathies in pulmonary hypertension. *J Am Coll Cardiol* 2004; 43: Suppl. 12, 25S–32S.
79 Pietra G, Edwards W, Kay J, *et al.* Histopathology of primary pulmonary hypertension. A qualitative and quantitative study of pulmonary blood vessels from 58 patients in the National Heart, Lung, and Blood Institute, Primary Pulmonary Hypertension Registry. *Circulation* 1989; 80: 1198–1206.
80 Frazier A, Galvin J, Franks T, *et al.* From the archives of the AFIP: pulmonary vasculature: hypertension and infarction. *Radiographics* 2000; 20: 491–524.
81 Chazova I, Robbins I, Loyd J, *et al.* Venous and arterial changes in pulmonary veno-occlusive disease, mitral stenosis and fibrosing mediastinitis. *Eur Respir J* 2000; 15: 116–122.
82 Ohmichi M, Tagaki S, Nomura N, *et al.* Endobronchial changes in chronic pulmonary venous hypertension. *Chest* 1988; 94: 1127–1132.
83 Williamson W, Tronic B, Levitan N, *et al.* Pulmonary venous infarction. *Chest* 1992; 102: 937–940.
84 Nanthakumar K, Mountz J, Plumb JV, *et al.* Functional assessment of pulmonary vein stenosis using radionuclide ventilation/perfusion imaging. *Chest* 2004; 126: 645–651.
85 Mendelson D, Train J, Goldsmith S, *et al.* Ventilation-perfusion mismatch due to obstruction of pulmonary vein. *J Nucl Med* 1981; 22: 1062–1063.
86 Aghaji MC. Radionuclide evaluation of unilateral pulmonary vein stenosis. Correlation with chest roentgenogram and clinical profiles. *J Nucl Med Allied Sci* 1986; 30: 225–229.
87 Lepădat P, Burnea D, Stăncioiu G, *et al.* Modificari scintigrafice si electrocardiografice dupa ligature la clini a arterei pulmonare, a venelar pulmonare si mixta [Scintigraphic and electrocardiographic changes after ligation of the pulmonary artery, pulmonary veins and mixed ligation in dogs]. *Rev Chir Oncol Radiol ORL Oftalmol Stomatol Chir* 1977; 26: 207–215.
88 Kluge A, Dill T, Ekinci O, *et al.* Decreased pulmonary perfusion in pulmonary vein stenosis after radiofrequency ablation: assessment with dynamic magnetic resonance perfusion imaging. *Chest* 2004; 126: 428–437.
89 Roman K, Kellenberger C, Macgowan C, *et al.* How is pulmonary arterial blood flow affected by pulmonary venous obstruction in children? A phase-contrast magnetic resonance study. *Pediatr Radiol* 2005; 35: 580–586.
90 Wyatt J, Burke D, Hanlon R. Morphological study of canine lungs after ligation of the pulmonary veins. *Am J Pathol* 1953; 29: 291–303.
91 Cavaco R, Kaul S, Chapman T, *et al.* Idiopathic pulmonary fibrosis associated with pulmonary vein thrombosis: a case report. *Cases J* 2009; 2: 9156.
92 Sacco O, Fregonese B, Fregonese L, *et al.* Recurrent unilateral bacterial pneumonias and interstitial fibrosis associated with pulmonary vein atresia: successful treatment with endovascular stent implantation. *Pediatr Pulmonol* 2002; 34: 324–328.
93 Palazzini M, Manes A. Pulmonary veno-occlusive disease misdiagnosed as idiopathic pulmonary arterial hypertension. *Eur Respir Rev* 2009; 18: 177–180.
94 Abikhzer G, Zand K, Stern J, *et al.* False positive high probability V/Q scan due to malignant obstruction of both pulmonary vein and artery. *Clin Nucl Med* 2009; 34: 367–370.

 DOI: 10.1183/09059180.00003713

95 Bailey C, Channick R, Auger W, *et al.* "High probability" perfusion lung scans in pulmonary venoocclusive disease. *Am J Respir Crit Care Med* 2000; 162: 1974–1978.
96 Wood M, Wittkamp M, Henry D, *et al.* A comparison of pulmonary vein ostial anatomy by computerized tomography, echocardiography, and venography in patients with atrial fibrillation having radiofrequency catheter ablation. *Am J Cardiol* 2004; 93: 49–53.
97 Roman K, Kellenberger C, Farooq S, *et al.* Comparative imaging of differential pulmonary blood flow in patients with congenital heart disease: magnetic resonance imaging *versus* lung perfusion scintigraphy. *Pediatr Radiol* 2005; 35: 295–301.
98 Valsangiacomo E, Barrea C, Macgowan C, *et al.* Phase-contrast MR assessment of pulmonary venous blood flow in children with surgically repaired pulmonary veins. *Pediatr Radiol* 2003; 33: 607–613.
99 Valverde I, Miller O, Beerbaum P, *et al.* Imaging of pulmonary vein stenosis using multidimensional phase contrast magnetic resonance imaging (4-dimensional flow). *J Am Coll Cardiol* 2011; 58: e3.
100 Greil G, Powell A, Gildein H, *et al.* Gadolinium-enhanced threee-dimensional magnetic resonance angiography of pulmonary and systemic venous anomalies. *J Am Coll Cardiol* 2002; 39: 335–341.
101 Grosse-Wortmann L, Al-Otay A, Goo HW, *et al.* Anatomical and functional evaluation of pulmonary veins in children by magnetic resonance imaging. *J Am Coll Cardiol* 2007; 49: 993–1002.
102 Stanford W, Breen J. CT evaluation of left atrial pulmonary venous anatomy. *Int J Cardiovasc Imaging* 2005; 21: 133–139.
103 Burgstahler C, Trabold T, Kuettner A, *et al.* Visualization of pulmonary vein stenosis after radio frequency ablation using multi-slice computed tomography: initial clinical experience in 33 patients. *Int J Cardiol* 2005; 102: 287–291.
104 Kim Y, Marom E, Herndon J, *et al.* Pulmonary vein diameter, cross-sectional area, and shape: CT analysis. *Radiology* 2005; 235: 43–49.
105 Cronin P, Kelly AM, Desjardins B, *et al.* Normative analysis of pulmonary vein drainage patterns on multidetector CT with measurements of pulmonary vein ostial diameter and distance to first bifurcation. *Acad Radiol* 2007; 14: 178–188.
106 Hauser T, Yeon S, Kissinger K, *et al.* Variation in pulmonary vein size during the cardiac cycle: implications for non-electrocardiogram-gated imaging. *Am Heart J* 2006; 152: 974.
107 Thai W, Wai B, Lin K, *et al.* Pulmonary venous anatomy imaging with low-dose, prospectively ECG-triggered, high-pitch 128-slice dual-source computed tomography. *Circ Arrhythm Electrophysiol* 2012; 5: 521–530.
108 de Marchi S, Bodenmüller M, Lai D, *et al.* Pulmonary venous flow velocity patterns in 404 individuals without cardiovascular disease. *Heart* 2001; 85: 23–29.
109 Devaney E, Chang A, Ohye R, *et al.* Management of congenital and acquired pulmonary vein stenosis. *Ann Thorac Surg* 2006; 81: 992–995.
110 De Potter TJ, Schmidt B, Chun KR, *et al.* Drug-eluting stents for the treatment of pulmonary vein stenosis after atrial fibrillation ablation. *Europace* 2011; 13: 57–61.