Pulmonary vascular disease: pulmonary thromboembolism and pulmonary hypertension

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Abstract

The pulmonary circulation is a high-flow, low-pressure circuit that is highly adapted for efficient gas exchange. Pathological events in the pulmonary circulation either seriously impair ventilation–perfusion matching, resulting in increased dead space, or increase pulmonary vascular resistance, putting extra load on the right ventricle that ultimately leads to right heart failure. This article explores the pathophysiology, clinical presentation, diagnosis and treatment of two major diseases affecting the pulmonary circulation – pulmonary thromboembolism and pulmonary hypertension.

Keywords Chronic thromboembolic pulmonary hypertension; pulmonary arterial hypertension; pulmonary circulation; pulmonary embolism; pulmonary vascular resistance

Key points

- Outpatient treatment of pulmonary embolism should be considered only in line with local policy
- Patients with acute pulmonary embolism should be reviewed for the development of pulmonary hypertension
- Patients with pulmonary hypertension require a detailed work-up including cardiac catheterization with or without a vasodilator study to define the aetiology and appropriate treatment
- Patients with suspected pulmonary arterial hypertension (PAH) and chronic thromboembolic hypertension should be referred promptly to a specialist centre
- All patients with chronic thromboembolic pulmonary hypertension should be referred for consideration of endarterectomy
- Early recognition of PAH is key to improving survival

Introduction

The pulmonary circulation is highly adapted to ensure efficient gas exchange at the alveolar membrane. The larger, more proximal vessels are conduit vessels; therefore, they have thick medial walls to cope with the relatively high transmural pressures. However, as the pulmonary arteries divide, the structure of the vessel network changes to facilitate efficient gas exchange. The vessels become much greater in number, and the vessel walls are no longer muscularized. These small, peripheral vessels form a high-volume, low-pressure network to maximize the efficiency of gas exchange.

Any change in vessel tone in this region leads to a dramatic increase in pulmonary vascular resistance. This has a significant impact on the ease with which oxygen diffuses across the vessel wall and also leads to an increase in pulmonary arterial pressure. The resulting strain on the right ventricle eventually causes right ventricular failure. There are many causes of pulmonary vascular disease that adversely affect the ability of the pulmonary circulation to maintain efficient gas exchange at the alveolar membrane. The two discussed here are pulmonary thromboembolic disease and pulmonary arterial hypertension (PAH).

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Pulmonary thromboembolic disease

Pulmonary thromboembolic disease, defined by the presence of a thrombosis in the pulmonary arterial circulation, is a major cause of morbidity and mortality. A primary care-based series in the UK reported an incidence of 57 per 100,000 population, and it is widely accepted that 50% of thromboembolic events develop in patients while they are in hospital or long-term care. With mortality rates ranging from 7% to 11%, careful risk analysis and prophylaxis for at-risk populations are hugely important.

Pathophysiology of pulmonary thromboembolism

Most pulmonary emboli are thought to occur following transition of a thrombus from the deep venous system of the lower limbs into the pulmonary circulation. In one series, 70% of patients presenting with a pulmonary embolus were found to have a concomitant deep venous thrombosis and 50% of patients presenting with a deep venous thrombosis were found to have an asymptomatic pulmonary embolus.

The presence of a thrombus in the pulmonary circulation greatly affects gas exchange by leading to an area of lung that is ventilated but not perfused, thereby increasing the dead space of the lung. Furthermore, obstruction of the vessel lumen by thrombus increases the pulmonary vascular resistance, reduces flow through the vasculature and leads to increased strain on the right ventricle; ultimately, there is reduced cardiac output. The area of parenchyma that is not perfused is at risk of infarction, but this is usually counteracted by the dual supply of the lung parenchyma via the bronchial arteries from the systemic circulation.

Risk factors

Although 20% of patients have an unprovoked event, most patients presenting with thromboembolic disease have an identifiable risk factor (Table 1). The additional risk of travel often attracts considerable concern. Travelling for more than 4 hours in the 8 weeks preceding presentation was found to increase the

Risk factors leading to the development of pulmonary embolism

Major risk: OR >10	Moderate risk: OR 2–9	Minor risk: OR <2
Hip or leg fracture	Malignancy	Immobility[a]
Hip or knee replacement	Drug therapy – OCP, HRT, chemotherapy	Increasing age
Major general surgery	Chronic heart or respiratory failure	Laparoscopic surgery
Major trauma	Postpartum	Obesity
Spinal cord injury	Previous VTE or thrombophilia	Varicose veins

HRT, hormone replacement therapy; OCP, oral contraceptive pill; OR, odds ratio, VTE, venous thromboembolic event.
[a] Immobility – bed rest >3 days; flight or other long journey.

Table 1

risk of developing venous thromboembolic disease twofold. The risk was significantly greater in individuals with a factor V Leiden mutation, taking the oral contraceptive pill, with a body mass index greater than 30 kg/m^2 or taller than 1.9 m. The risk was similar regardless of the mode of transport. However, there was an additional risk in individuals of less than 1.6 m tall when flying that was not present for other modes of transport.

Definition

Pulmonary embolism can be defined according to the clinical presentation as high risk, intermediate-high, intermediate-low and low risk.[1] This is crucial as it determines the order of investigation and also the treatment required.

High-risk pulmonary embolism is defined by the presence of circulatory shock or significant systemic hypotension (systolic arterial pressure <90 mmHg or a drop in systolic arterial pressure of at least 40 mmHg for at least 15 minutes) with no other identifiable cause. It carries a 15% in-hospital mortality and requires prompt treatment. **Intermediate-risk** patients are haemodynamically stable yet have a Pulmonary Embolism Severity Index (PESI) class III or above or a simplified PESI (sPESI) score greater than 0 (Table 2). They also have either right ventricular dysfunction (on CT imaging or echocardiography) or positive biomarkers (troponin I/T or natriuretic peptides) in the case of intermediate-low risk, or both of these in the case of intermediate-high risk. A **low-risk** presentation occurs when there is no systemic hypotension and the patient is in PESI class I or II or has a sPESI of 0. The risk stratification is summarized in Table 3.

Diagnosis

The diagnosis of massive pulmonary embolism is usually overt, with patients reporting syncope, chest pain and sometimes shortness of breath in the presence of circulatory compromise. These patients should undergo urgent imaging in the form of computed tomography pulmonary angiography (CTPA) or echocardiography looking for right ventricular dilatation.

However, most patients found to have pulmonary embolism present with non-specific symptoms of chest pain, dyspnoea, cough, haemoptysis or syncope, and clinical examination often adds little to the diagnosis. Chest radiographic changes (band atelectasis, pleural effusion) are suggestive but again non-specific, and although a widened arterial–alveolar oxygen gradient is predictive, it is normal in 20% of patients at rest with confirmed pulmonary embolism. Furthermore, screening investigations have a significant false-negative rate and must be interpreted with knowledge of the pre-test probability to increase the sensitivity of the test. Several probability scoring systems have been developed, the currently recommended score being the simplified Wells' Score (Table 4).

The simplified Wells' Score is used to help interpret further investigations (Table 4). If pulmonary embolism is deemed unlikely on the basis of a score of 0–1, a D-dimer test can be performed. If the D-dimer result is negative, no further imaging is required. A D-dimer test should not be requested when pulmonary embolism is deemed likely (simplified Wells' Score ≥2) as the test has a significant false-negative rate, which can mislead the practitioner in the context of a high clinical pre-test probability of pulmonary embolism.

If the D-dimer result is positive, the recommended imaging modality in the majority of patients is CTPA. It has a high sensitivity and specificity for segmental and subsegmental pulmonary emboli. However, if there is no prior history of cardiopulmonary disease and the patient has a normal chest radiograph, a nuclear medicine ventilation/perfusion (V/Q) scan can be performed. The V/Q scan should be confirmed with a further imaging modality, usually CTPA, if it is non-diagnostic (intermediate probability) (Figure 1).

Treatment

The treatment of massive pulmonary embolism is summarized in Figure 2; thrombolysis is the treatment of choice. If thrombolysis is contraindicated, surgical embolectomy should be considered. Thrombolysis can be considered for patients with intermediate-high-risk pulmonary embolism, but the evidence remains unclear; the major concern is major bleeding. Consultation with a physician specializing in the management of pulmonary embolism is advised in this circumstance.

Patients with suspected intermediate or low-risk pulmonary embolism should be treated with an anticoagulant if imaging cannot be undertaken within the hour. Anticoagulation usually involves a therapeutic dosage of low molecular weight heparin. If a pulmonary embolus is confirmed, oral anticoagulation can be commenced with either a vitamin K antagonist, warfarin (overlapping with low molecular weight heparin and continuing until a therapeutic international normalized ratio has been achieved) or a direct oral anticoagulant.[1] Rivaroxaban and apixaban can be commenced without a heparin lead-in, starting at higher doses