three-dimensional reconstruction (3D-SSD) segmentation for a better understanding of the anatomy of the abnormal systemic arteries. However, as shown in case 2, three-dimensional imaging dedicated to the venous drainage can also be made.[8]

Spiral CT angiography is a minimally invasive technique for vascular imaging that is made possible by combining slip ring CT scanning and computerised three-dimensional reconstruction.[9] Spiral CT angiography has several advantages over other non-invasive vascular imaging techniques.[4 10] CT scanning, with its superior spatial resolution, yields the most information about the bronchial anatomy and the pulmonary parenchymal lesion. Sonography and MRI cannot evaluate lung abnormalities accurately although MRI can reveal the cystic nature of many intralobar sequestrations as well as the variable solid, fluid, haemorrhagic, and mucus-containing components. MR angiography is hampered by artefacts caused by respiratory motion whereas this problem is generally avoided in helical CT scanning. CT angiography is less expensive than MR angiography and can be used on patients with a metallic device or who do not tolerate the MR examination. Furthermore, helical CT scanning is faster resulting in less sedation and reduced amount of contrast medium. The disadvantages of helical CT scanning are minor and arise from exposure of the patient to ionising radiation and the administration of intravenous contrast material.

In summary, we report four cases of pulmonary sequestration successfully diagnosed using spiral CT angiography. By allowing simultaneous imaging of anomalous vessels and parenchymal lesions in a single examination, spiral CT angiography is a particularly efficacious technique and has the potential to become the procedure of choice in the diagnosis and assessment of pulmonary sequestration.

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Interventricular septal shift due to massive pulmonary embolism shown by CT pulmonary angiography: an old sign revisited

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Abstract
The computed tomographic (CT) pulmonary angiogram appearances of acute right ventricular dysfunction due to massive pulmonary embolus in a patient are described. Abnormal findings comprised right ventricular dilatation, interventricular septal shift, and compression of the left ventricle. These changes resolved following thrombolysis. Use of CT pulmonary angiography to diagnose pulmonary emboli is increasing. Secondary cardiac effects are established diagnostic features shown by echocardiography. These have not been previously described but are important to recognise as they may carry important prognostic and therapeutic implications.
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Keywords: pulmonary embolism; right ventricular dysfunction; spiral computed tomography; pulmonary angiography

A 43 year old man collapsed while out walking. On admission to hospital he was dyspnoeic and cyanosed. On direct questioning he admitted to right leg pain. Examination showed that his heart rate was 105 beats/min, respiratory rate was 28 breaths/min, and blood pressure was 100/60 mm Hg. His jugular venous pressure was raised but examination was otherwise normal. Electrocardiography demonstrated sinus tachycardia; the chest radiograph was normal. Measurement of arterial blood gas tensions confirmed hypoxaemia with hypocapnia (P_{O_2} 8 kPa on 6 l/min oxygen, P_{CO_2} 4 kPa). An echocardiogram demonstrated dilatation of the right ventricle. The clinical features of syncope, cyanosis and dyspnoea with engorged neck veins in a patient with a normal chest radiograph and clinical suspicion of deep venous thrombosis led to a presumptive diagnosis of pulmonary embolus.

A computed tomographic (CT) pulmonary angiogram was performed. A 3 mm spiral scan, reconstructed at 1.5 mm intervals, was undertaken on a Hi Speed Advantage scanner (General Electric Medical Systems, Milwaukee, Wisconsin, USA) using 150 ml of contrast (200 mg I/ml) at 4 ml/s. This showed multiple pulmonary emboli within the main and segmental pulmonary arteries. In addition there was dilatation of the right ventricle and atrium with normal wall thicknesses, the interven-

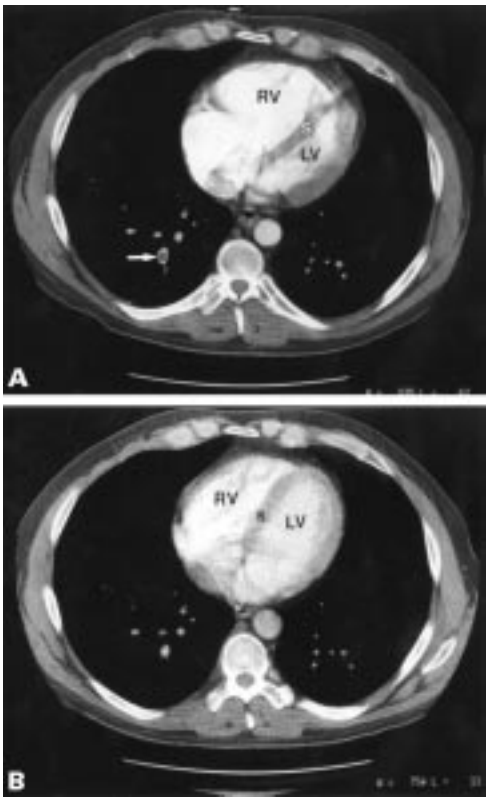

Figure 1 Computed tomographic (CT) pulmonary angiograms at the level of the interventricular septum in a patient with massive pulmonary embolism. (A) The scan at presentation shows right ventricular dilatation and septal displacement which results in compression of the left ventricle. A filling defect due to an embolus is seen within a segmental branch of the descending right pulmonary artery (arrow). (B) Five days after thrombolysis the pulmonary embolus has resolved. The associated reduction in pulmonary artery pressure has allowed normal septal and ventricular appearances to return. The long axis of the heart now occupies a more normal position. RV = right ventricle, LV = left ventricle, S = interventricular septum.

tricular septum was displaced to the left, and there was compression of the left ventricle (fig 1A). These features persisted throughout the cardiac cycle. A central venous catheter was placed and tissue plasminogen activator was infused into the central pulmonary arteries. Immediately before treatment the central venous pressure was 22 mm Hg, right atrial pressure was 30 mm Hg, right ventricular pressure was 33/13 mm Hg, and pulmonary artery pressure was 33/20 mm Hg. Five hours after treatment the pulmonary artery pressure had reduced to 20/10 mm Hg and systemic blood pressure had increased to 160/70 mm Hg. A continuing anticoagulation regime was commenced. A venogram showed thrombus within the right popliteal vein. A repeat CT angiogram five days after treatment showed considerable reduction in the load of embolic material within the pulmonary arteries together with a return of the interventricular septum to its normal position and resumption of normal right and left ventricular morphologies (fig 1B).

Discussion

Massive pulmonary embolism sets in sequence a chain of physiological events that ultimately lead to reduced systemic cardiac output.[1] The initial abrupt rise in pulmonary artery pressure causes increased right ventricular afterload which results in right ventricular dilatation and dyskinesia. Secondary effects of this are tricuspid regurgitation, right atrial enlargement, and loss of respiratory variation in calibre of the great veins. Increased right ventricular wall tension may reduce local coronary blood flow, resulting in ischaemia which impairs right ventricular function further. As the right ventricle dilates, the interventricular septum is displaced towards the left ventricle, the right ventricle assuming a circular axial configuration and the left ventricle a crescentic appearance more typical of the normal right ventricle. This septal shift, combined with the constraining influence of the pericardium, results in reduced left ventricular filling which is already compromised by reduced preload. The cardiac output falls.

Signs documenting this sequence such as right ventricular dilatation and hypokinesis (which may spare the apex), abnormal interventricular septal motion, pulmonary artery dilatation, tricuspid regurgitation, and loss in respiratory variation in inferior vena caval diameter can be detected at echocardiography. Echocardiographic assessment of the right ventricle has been recommended as an integral part of the investigative algorithm for suspected acute pulmonary embolus published recently by the British Thoracic Society working party.[2] "Right ventricular dysfunction" is an umbrella term which also includes more subjective echocardiographic findings such as abnormalities of the motion of the right ventricular wall. These findings are often encountered in lesser degrees of pulmonary embolus and have led to debate over the significance of the more objective signs. Acute right ventricular dilatation and interventricular septal shift have been associated specifically with massive pulmonary embolism[3 4] and reversible septal displacement has been described in a series of patients requiring aggressive treatment for circulatory failure due to massive pulmonary embolism.[3] Thrombolysis is an accepted treatment in massive life threatening pulmonary embolus and its administration in the case described here was associated with a rapid return of pulmonary and systemic arterial pressures towards normal. Recognition of the signs presented by CT scanning or echocardiography allows more aggressive therapy to be targeted to individuals at greatest risk.

CT pulmonary angiography is increasingly used to diagnose pulmonary embolus. It is non-invasive and quick to perform. In the case described the patient was imaged directly after initial assessment in the emergency room and spent less than 15 minutes in the imaging suite. Comparative studies have shown excellent correlation between CT and conventional pulmonary angiography in the detection of emboli in segmental or larger vessels and in many centres the technique has largely replaced conventional pulmonary angiography.[5 6] Secondary signs of pulmonary embolus have not, to our knowledge, been described at CT pulmonary angiography. The interventricular septum is usually

clearly visualised by thoracic CT scanning following intravenous contrast. We have observed interventricular septal shift in several patients with acute pulmonary embolus. Septal shift may also be identified by CT scanning or MRI in patients with chronic pulmonary hypertension due to a variety of causes; however, an important distinguishing feature in such cases is co-existing thickening of the right ventricular wall, which is not observed in acute pulmonary embolus and was not apparent in the case presented here. A typical CT pulmonary angiogram will include in its acquisition time two or three cardiac cycles and some normal variation in the appearance of the cardiac chambers is to be anticipated over the length of the scan. Nevertheless, the constellation of CT findings of proximal emboli, enlargement of the right ventricle with normal wall thickness, interventricular septal shift, and crescentic axial left ventricular morphology which persists throughout the CT scan is likely to be a reliable indication that an embolus of major proportions has occurred.

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LETTERS TO THE EDITOR

Cardiac risks with β agonists

Martin *et al*[1] suggest that caution should be exercised when prescribing long acting oral β agonists to patients at risk of cardiac failure, based on results from a prescription event monitoring (PEM) study.

Firstly, all β_2 agonists (short and long acting, oral and inhaled) should be used with caution in patients with severe cardiovascular disease, as is pointed out in the package insert for all drugs of this class.

Secondly, the study does not provide any evidence on this issue. PEM studies are not designed to study causal relations but to generate new hypotheses. Although the authors have made an attempt to consider several potential biases in the analyses, the study design is inappropriate compared with, for example, a prospective randomised controlled trial, and the results must be interpreted with great caution.

Thirdly, no support for an association between bambuterol and an increased risk for cardiac failure has been found in our review of preclinical studies, clinical studies (including >3000 patients/healthy volunteers), or post-marketing surveillance (based on >130 million treatment days).

Fourthly, according to the authors there have been no spontaneous reports of cardiac failure with bambuterol to the Committee on Safety of Medicines. This is in agreement with the WHO database Intdis, with no reports of cardiac failure for bambuterol.

Finally, the paper suggests a doubled asthma mortality in patients receiving salmeterol. In our opinion the reported higher relative risk for non-fatal cardiac failure for bambuterol and the doubled asthma mortality for salmeterol both appear equally explicable by factors other than direct causality, such as confounding by concomitant diseases and disease severity.

Thus, PEM data may be of help in identifying signals with new drugs, but there is little if any merit in comparing drugs used in different populations and introduced to the market at different times.

Table 1 Rates of cardiac failure during the first month of exposure to bambuterol or a cardiovascular drug studied by prescription event monitoring (PEM)

Drug (ranked by rate)*	*No. of patients with reported cardiac failure during month 1*	*No. of patient-months of exposure during month 1*	*Rate (events per 1000 months of exposure)*	*Mean (SD) age*	*Males (%)*
Xamoterol	97	4 463	21.7	70.8 (13.9)	53.0
Nicorandil	73	11 578	6.3	66.9 (11.2)	61.1
Bambuterol	29	5 891	4.9	58.5 (18.6)	44.8
Losartan	53	12 990	4.1	63.5 (12.1)	40.2
Diltiazem	24	8 808	2.7	62.3 (13.9)	59.3
Enalapril	33	13 544	2.4	61.2 (14.9)	46.1
Perindopril	17	8 368	2.0	61.8 (12.7)	45.0
Nicardipine	17	9 517	1.8	62.9 (13.9)	48.4
Lisinopril	18	11 574	1.6	60.9 (14.3)	44.0
Ramipril	2	1 277	1.6	60.5 (12.4)	45.1
Amlodipine	12	12 085	1.0	61.8 (14.7)	46.9

*Betaxolol, doxazosin, isradipine not shown as number of patients with event was <2, or rate was <1.0 per 1000 patient-months of exposure.

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1 Martin RM, Dunn NR, Freemantle SN, *et al*. The risk of non-fatal cardiac failure and ischemic heart disease with long acting β_2 agonists. *Thorax* 1998;**53**:558–62.

AUTHORS' REPLY Bertil Lindmark of Astra Draco makes five points about our study on the risk of non-fatal cardiac failure and ischaemic heart disease with long acting β_2 agonists. Firstly, he points out that all β_2 agonists should be used with caution in patients with severe cardiovascular disease. The cardiac effects of β_2 agonists are well described,[1] but there is limited evidence available on whether or not the risks of adverse cardiac effects differ depending on the dose and method of administration of the drug. Clearly, these are important questions for prescribing doctors faced with treating asthmatic patients with concomitant cardiac disease. An observational cohort study formed from health insurance databases from the Province of Saskatchewan, Canada found an increased relative risk of death from cardiovascular disease in users of β_2 agonists taken orally or by nebuliser, but not in users of β_2 agonists administered by metered dose inhaler.[2] The deaths occurred in patients with significant cardiac disease, suggesting that β_2 agonists taken orally or by nebuliser should be avoided in patients at high risk of cardiovascular events. We found that the oral β_2 agonist bambuterol, but not the inhaled β_2 agonist salmeterol, was associated with an increased risk of non-fatal cardiac failure. The results from both these studies are plausible as oral β agonists provide a greater systemic dose than that achieved with metered dose inhalers[1] and tachycardia and prolonged Q-T interval have been reported principally with nebulised or oral β agonists.[2] The advised total daily dose of oral bambuterol