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VASCULAR-INTERVENTIONAL

Percutaneous endovascular biopsy of intravascular masses: efficacy and safety in establishing pre-therapy diagnosis

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Abstract

Purpose To evaluate the efficacy and safety of percutaneous endovascular biopsy (PEB) in intravascular filling-defect lesions (IVLs) of the great vessels.

Material and methods We retrospectively reviewed 19 patients (age 65 ± 12 years), 11 men and eight women, who underwent PEB for IVLs, between March 2004 and November 2014. All PEBs were performed for early diagnosis and/or characterization of the IVL, or in case of reasonable doubt about the IVL nature. Pre-intervention imaging work-up included CT, MRI and/or PET-CT. PEBs were obtained with a 7F biopsy forceps device. Clinical profile, procedure technical success and safety, and clinical success were evaluated.

Results PEB was technically successful in all patients (mean of two samples per IVL). No intra- or post-procedural complications were reported. Histopathological analysis provided a diagnosis in all PEBs with a clinical success of 100%. Of the 19 IVLs, 14 were malignant (74%). The most frequent malignant lesion observed was leiomyosarcoma (29%). Benign lesions (26%) included three thrombi (pulmonary artery) and two myxomas.

Conclusion PEB is a safe and efficient procedure providing the most effective technique to obtain a tissue sample of high diagnostic quality, which serves to establish early diagnosis in patients with suspected malignant lesions.

Key Points

- *Intravascular filling-defect lesions are related to both benign conditions and malignant tumours.*
- *Endovascular biopsy is indicated in case of doubt about intravascular lesion nature.*
- *Percutaneous endovascular biopsy is a safe technique.*
- *Endovascular biopsy provides tissue samples leading to correct histopathological analysis.*
- *Percutaneous endovascular biopsy provides early diagnosis of malignant intravascular lesions.*

Keywords Angiography · Intravascular filling-defect · Endovascular biopsy · Early diagnosis · Sarcoma

Introduction

Intravascular filling-defect lesions (IVLs) occur from a myriad of underlying pathologies and include, but are not limited to, benign tumours, reactive changes, fibrinocruoric thrombosis, metastatic disease and primary malignant tumours. Primary tumours of the heart and the great vessels are extremely rare and are usually sarcomatous neoplasms [1] associated with a poor prognosis [2]. Most sarcomas are located in the pulmonary trunk or the right and left pulmonary arteries as well as in the superior and inferior vena cava. Even though local disease progression may be slow, associated thrombosis may progressively obstruct the vessel, causing few symptoms but nevertheless being mistaken for an acute pulmonary embolism [3–5]. A large percentage of these patients are treated for months with anticoagulant therapy before establishing the malignant nature of the mass. The duration between symptom onset and diagnosis has been reported to be as high as 12 months due to initial misdiagnosis [6–9]. Early diagnosis with histology confirmation is therefore crucial to plan the most appropriate treatment.

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Table 1 Patient characteristics, type of imaging and endovascular biopsy-related information

	Gender	Age	Main symptoms	Imaging	Localisation	Histology
1	M	73	Dyspnoea/chest pain/syncope	CTA	RPA	Pulmonary embolism
2	M	87	Syncope/dyspnoea	CTA	LPA	Rhabdomyosarcoma
3	F	80	Shortness of breath/syncope	CTA/PET/MRI	RPA	Pulmonary embolism
4	F	47	Dyspnoea/Abdominal pain	CTA	IVC	Myxoma
5	M	60	Chest pain/dyspnoea	CTA	IVC/Atrium	Mets HCC
6	F	70	Dyspnoea	CTA	PV	Myxoma
7	F	52	Chest pain/dyspnoea/weight loss	CTA	SVC	Undifferentiated sarcoma
8	M	72	Dyspnoea/weight loss	CTA/PET	SVC	Mets pulmonary cancer
9	F	47	Dyspnoea	CTA	RPA	Pulmonary embolism
10	F	72	Dyspnoea	CTA	MPA	Leiomyosarcoma
11	M	54	Chest pain/weight loss	CTA	RV	Lymphoma
12	M	78	Chest pain/syncope/dyspnoea	CTA/PET	RV	Lung cancer
13	M	80	Dypsnoea	CTA	MPA	Leiomyosarcoma
14	F	69	SVC syndrome	CTA/PET/MRI	SVC	Leiomyosarcoma
15	M	63	Weight loss	CTA	RV	Lymphoma
16	M	61	Abdominal pain	CTA	IVC	Leiomyosarcoma
17	M	56	Dyspnoea	CTA	LPA	Cancer thrombus by metastatic renal cancer
18	F	51	Abdominal pain	CTA	IVC	Cancer thrombus by metastatic caecal adenocarcinoma
19	M	62	Dyspnoea/Chest pain/weight loss	CTA/PET/MRI	RPA	Sarcoma of pulmonary artery

CTA computed tomography angiography, *PET* positron emission tomography, *MRI* magnetic resonance imaging, *RPA* right pulmonary artery, *LPA* left pulmonary artery, *IVC* inferior vena cava, *PV* pulmonary vein, *SVC* superior vena cava, *MPA* main pulmonary artery, *RV* right ventricle

While non-invasive imaging techniques remain non-conclusive in identifying the underlying pathology [6], the final diagnosis is frequently made after surgery.

Percutaneous endovascular biopsy (PEB) is a minimally invasive procedure that can be performed in an angiography suite by a trained interventional radiologist. The objective of this study was to report our 10-year experience with PEB in a patient cohort with specific regard to the feasibility, efficacy and safety of the procedure. Based on a comprehensive literature search, this is the first case series of PEB of IVLs.

Materials and methods

Study population

We retrospectively analysed data for all patients who had a PEB from March 2004 to November 2014 to establish the nature of the IVL. Medical records from 19 patients, 11 men and eight women, with a mean age of 65 ± 12 years were reviewed. Intravascular filling-defect masses were located in the superior vena cava (n = 3), inferior vena cava (n = 3), pulmonary arteries (n = 8), right ventricle (n = 3), and pulmonary vein (n = 1). Additionally, one patient (n = 1) had a mass in the proximal inferior vena cave extending to the right atrium. Two patients presented with superior vena cava syndrome due to an underlying pulmonary carcinoma and were subsequently sent for endovascular revascularisation. Moreover, a patient with a pelvic mass presenting with IVL in the inferior vena cava was sent for inferior vena cava filter placement before surgery. Symptoms described by patients at the time of presentation were not specific and included chest pain, dyspnoea, shortness of breath and weight loss. Three lesions presented in asymptomatic patients and thus were considered incidental findings. All patients underwent various non-invasive investigations before PEB including computed tomography (CT) (n = 19), MR imaging (n = 3) and PET CT (n = 5) to confirm the presence of an IVL, to characterise its nature and to assess its anatomical relationship to nearby structures. Table 1 summarizes patient characteristics prior to the PEB and histological findings.

Indication of the PEB was made on the basis of suspicion of malignancy in order to obtain a high quality tissue sample and corresponding histopathological analysis to optimise the treatment or in case of reasonable doubt on the benign nature of the IVL. At the time of the PEB, no patients had metastatic disease.

All patients were aware of the details of the procedure, and of its benefit and possible complications, and thus all provided informed consent was obtained prior to PEB. The Institutional Ethics Committee approved the study.

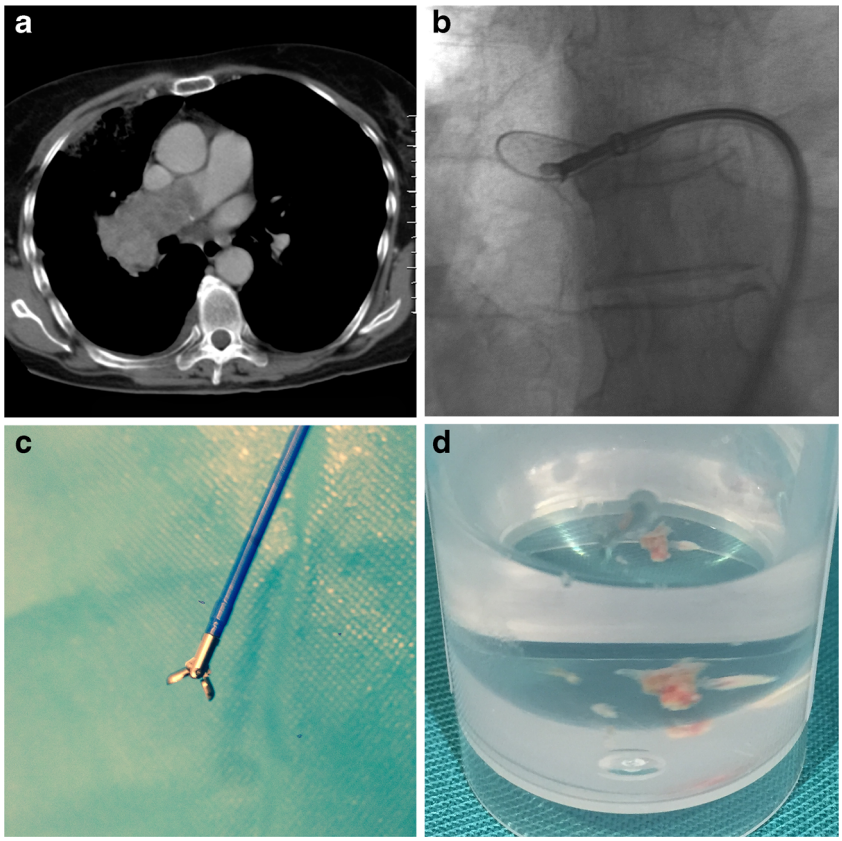

Fig. 1 A 62-year-old woman presented with dyspnoea, right lower thoracic pain and weight loss of 7 kg in the last 2 months. (**a**) Axial CT images showing enhancing heterogeneous intravascular mass in the right pulmonary artery and its proximal branches. (**b**) Fluoroscopy view demonstrating the introducer placed in the pulmonary trunk as well as a 0.035 guide wire (Radiofocus Glidewire Advantage, Terumo) advanced to the right lobar pulmonary artery in order to stabilise the introducer in the target position. (**c**) Magnified image of the tip of a 7-French biopsy forceps (Bi-Pal, Cordis Corporation, Miami, FL, USA) used for the biopsy of the right pulmonary artery. (**d**) Tissue sample obtained by the biopsy device. Histopathological analysis revealed an intimal sarcoma of the pulmonary artery

PEB procedure

The procedure was performed in an angiography suite using dedicated digital angiography equipment. Local anaesthesia was performed in 18 patients and one patient received general anaesthesia. Venous vascular access was obtained on all patients. The common femoral vein was used in 18 patients and the internal jugular vein in one patient. In the first six patients (n = 6), either a 65- or an 80-cm 7-French or 8-French vascular introducer sheath (Super Arrow-Flex, Arrow International Inc, Reading PA, USA) was used. In the subsequent 13 patients (n = 13), we opted to use larger vascular introducers (10 F, Super Arrow-Flex, Arrow). Prior to the PEB, an angiogram confirmed the IVL. For pulmonary arteries, after selective catheterization, the catheter was exchanged over a J-tip 0.035 guide wire (e.g. Amplatz Super Stiff, Boston Scientific, Heredia, Costa Rica). Under fluoroscopic guidance, the sheath tip, typically over a hybrid 0.035 guidewire (Radiofocus Glidewire Advantage, Terumo Europe NV, Leuven, Belgium), was cautiously positioned near to the mass. A 7-French biopsy forceps device (Bi-Pal, Cordis Corporation, Miami, FL, USA) was gently advanced up with both stainless steel hinged cutting jaws in the closed position. A test injection was then performed with iodinated contrast media in order to confirm that the tip of the sheath abutted the mass. The biopsy device was advanced under fluoroscopic guidance outside the introducer tip with the hinged jaws in the open position and subsequently gently placed into the mass, anchoring the jaws in the mass and then finally putting the hinged jaws into the closed position. Several tissue samples of the mass were obtained. A theoretical sample diameter specimen obtained with the 7-French devices is 5 mm^3. However, in some cases, the specimen obtained was larger than the jaws' volume. Two to four samples were usually obtained. The 10-French introducer sheaths were preferred as they allowed continuous aspiration with a 50-ml aspiration syringe during the biopsy manoeuvres. Simultaneous aspiration was used to prevent distal embolisation during the biopsy and device removal.

In order to achieve a biopsy material of optimal quality, the introducer sheath has to be positioned towards the surface of the mass and stabilised in this position when the biopsy device is advanced to the target lesion. Because of the rigidity of the biopsy device, this is not always feasible, especially in the pulmonary arteries where the trajectory of the introducer is the subject of multiple curvatures. As a result, additional manoeuvres are necessary. We used a parallel guidewire 0.035 (Radiofocus stiff or Radiofocus Glidewire Advantage, Terumo Europe NV) placed in a distal pulmonary artery branch to maintain the introducer in the desired position (facing the target lesion) when the device is travelling through and during the biopsy manoeuvers (Figs. 1 and 2). The specimens

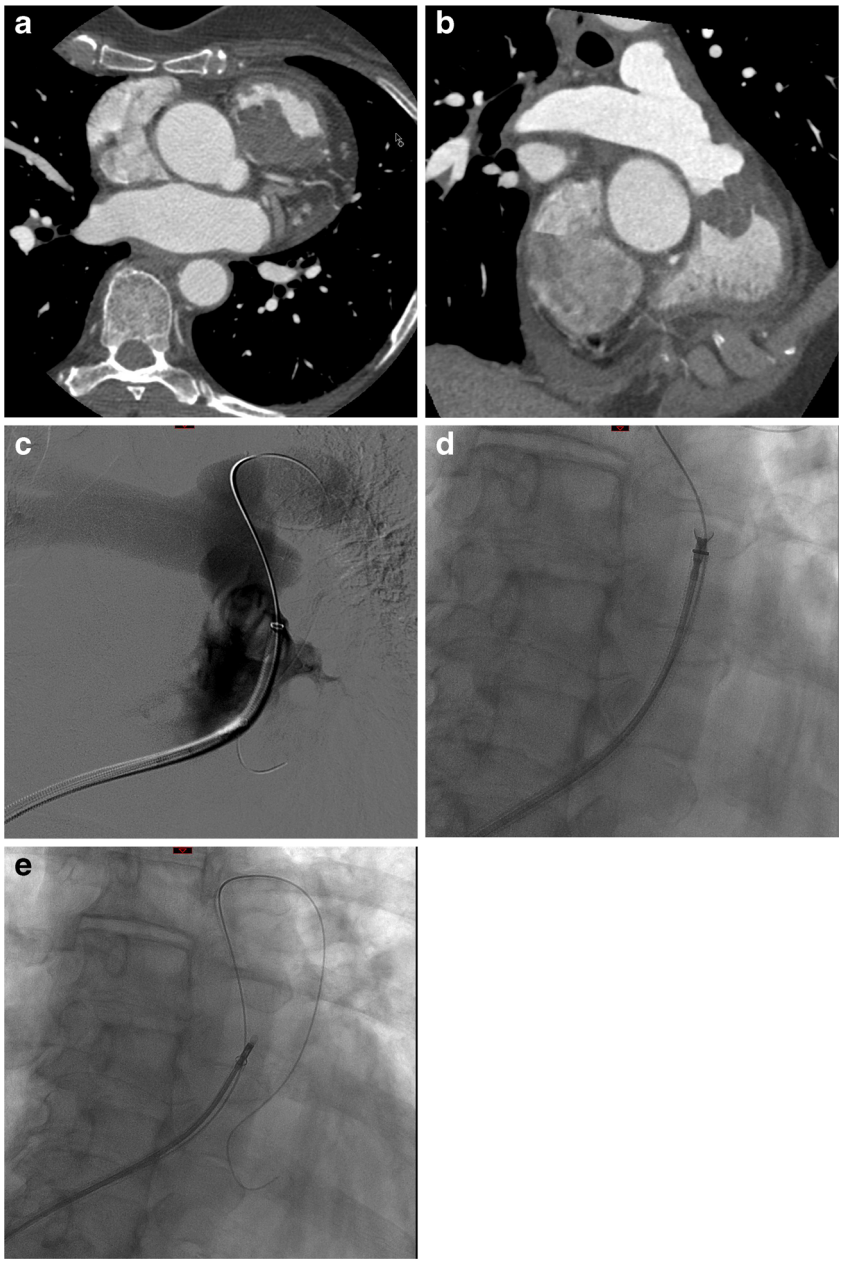

Fig. 2 A 70-year-old woman with a mass in the pulmonary valve, found during a routine control for renal cancer. (**a**, **b**) Axial and oblique CT images demonstrate a mass in the pulmonary valve. (**c**) Pulmonary angiogram confirms the filling defect of the pulmonary valve. (**d**, **e**) Due to the unstable position of the introducer sheath in the right ventricle, a 0.035 guide wire was positioned in the inferior left pulmonary lobar artery to stabilise the introducer in the target position. The biopsy device was advanced coaxially to the guidewire. Under fluoroscopy the jaws of the device were opened before anchoring in the mass and then closed to obtain the tissue sample. Histopathological analysis revealed a myxoma of the pulmonary valve

were fixed in both normal saline and formalin solutions and were sent for pathological evaluation.

For all procedures, 2,500 to 5,000 units of heparin were administered intravenously. At the end of the procedure, manual compression on the site of the venous puncture was performed over 5–10 min in order to achieve haemostasis. For seven patients, the procedure was performed on an ambulatory basis and they were observed in our day hospital unit for 4–6 h before discharge.

Data analysis

Technical success was defined as ability to obtain at least one sample tissue during the PEB. Clinical success was defined as biopsy material that could provide pathological diagnosis of the IVL. Clinical outcome was evaluated using institutional patient files. Continuous variables are presented as mean ± SD. Categorical variables are reported as percentages.

Results

Technical success was achieved in all of our procedures. A total of 19 intravascular filling-defect masses were evaluated, one in each patient, with the mean of two samples obtained per biopsy procedure (range 1–4). No intra- or post-procedure complications were reported.

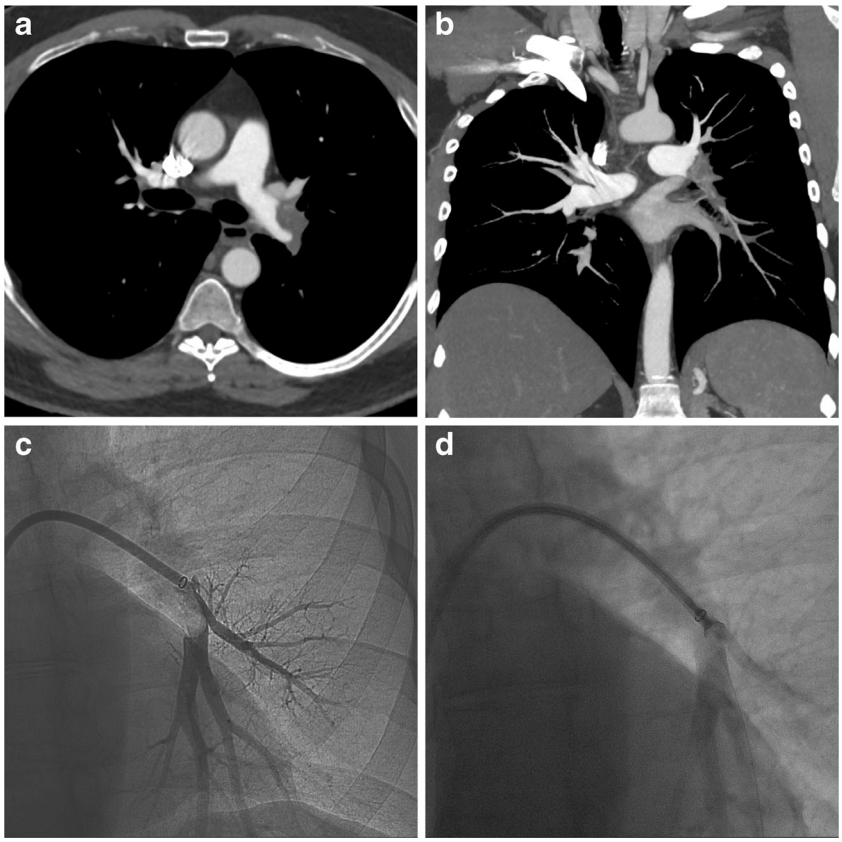

Fig. 3 A 56-year-old man who had previously been diagnosed with renal cell carcinoma. (**a,b**) Axial and coronal CT images demonstrate a 'thrombus-like' mass of the left pulmonary artery. (c) Angiographic view confirms the endoluminal defect of the left pulmonary artery. (**d**) Under fluoroscopic guidance the biopsy device was advanced into the left inferior lobar artery. Histopathological analysis revealed metastatic disease from the renal cell carcinoma

The quality of the tissue samples, as evaluated by pathologists, was sufficient to histologically confirm the diagnosis in all PEB materials. Thus, the clinical success was 100%. A malignant lesion was found in 14 cases (76%), three were thrombi of the right pulmonary artery, and two were myxomas, of which one was located in the inferior vena cava and the other one in the pulmonary valve (Fig. 2). In the patients with thrombi imaging findings were not clear, so biopsy was performed. The malignant lesions included two leiomyosarcomas of the pulmonary trunk, one leiomyosarcoma of the superior vena cava and one of the inferior vena cava, one undifferentiated intimal sarcoma of the superior vena cava, one rhabdomyosarcoma of the left pulmonary artery, two lymphomas of the right ventricle, one recurrence of lung cancer invading the superior vena cava, one metastasis of lung cancer in the right ventricle, one sarcoma of the right pulmonary artery (Fig. 1), one metastasis to the inferior vena cava from hepatocellular carcinoma, one metastasis of renal cancer (Fig. 3) and one metastasis of caecal adenocarcinoma (Fig. 4).

Two out of three patients that were diagnosed with pulmonary embolism died within approximately 10 days whereas the third patient received anticoagulant treatment. The majority of our patients underwent neo-adjuvant treatment and two patients received only surgical treatment. One patient refused any type of treatment and returned to the hospital with inoperable extensive malignancy 18 months later.

Discussion

Vascular tumours are often found incidentally. Most cases occur in patients presenting with non-specific symptoms and filling defect lesions may be mistaken for thrombo-embolic disease. These patients are treated for months with anticoagulant therapy before confirmation of a malignant nature of the vascular mass [4]. At the time of clinical suspicion of pulmonary artery sarcoma, metastases are present in 50–89% of the patients [10, 11]. Imaging techniques such as CT or MRI can demonstrate filling defect features and are useful in distinguishing a tumour from a thrombus. However, noninvasive imaging may not be able to optimally characterise the intravascular filling-defect mass in several cases, even with the modern advanced tools. Moreover, the final diagnosis is established only by the pathology.

Establishment of early diagnosis of a malignant IVL is critical for the outcome of the patient [12]. It is also crucial to plan the best treatment sequence option. Surgery with disease-free margins remains the only potentially curative treatment, and thus the therapy of choice. Obtaining a tissue sample of excellent quality is important in order to plan the best surgical treatment. In patients with unresectable masses, an adequate neo-adjuvant therapy can be considered. Radiation therapy may also be considered in incomplete resection to help local tumour control. Certainly, we do not

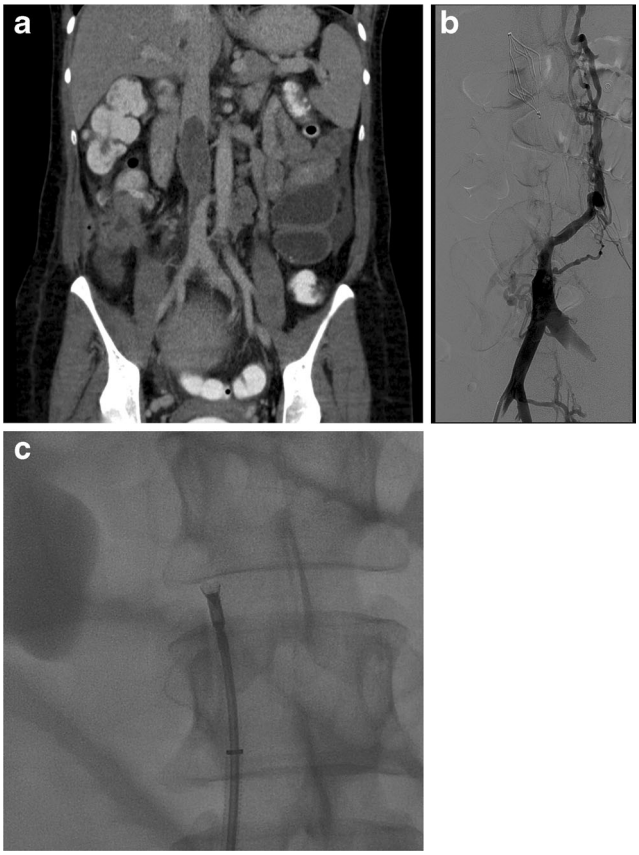

Fig. 4 A 51-year-old woman with abdominal pain without prior medical history. (**a**) Coronal CT images showing an enhancing, heterogeneous endovascular mass of the inferior vena cava as well as a mass in the caecum and a voluminous uterine mass. (**b**) Cavography through an introducer inserted via femoral access, demonstrating an irregular occlusion 6 cm above the confluence of iliac veins as well as a significant collateral venous network. (**c**) Biopsy device with jaws opened just before the biopsy. Histopathological analysis revealed a cancerogenous thrombus of a moderately differentiated adenocarcinoma originating from the caecum, confirmed by surgery

suggest biopsy of all patients with vena cava or pulmonary thrombus but only where there is high clinical and radiological suspicion of malignancy.

Due to their intravascular position these tumours are not easily accessed by direct percutaneous biopsy and the risk of haemorrhagic complication is elevated. Moreover, transbronchial access may not provide sufficient material for definite diagnosis [12]. Percutaneous endovascular biopsy is a safe and efficient alternative procedure that can be performed with a high rate of technical success associated with a low complication rate. Among the theoretical complications that may occur is the formation of a haematoma at the site of the puncture, the formation of a pseudoaneuryism or bleeding adjacent to the vessel due to the extravascular needle excursion inducing injury into contiguous structures. There is also a theoretical complication of seeding of tumour emboli, especially for tumours of the pulmonary artery, even though the real risk of these complications has yet to be established.

From a technical point of view, the device has the advantage of being flexible and able to follow even the most tortuous vascular paths up to the IVL. Under fluoroscopic and contrast-enhanced imaging, the precise position of the biopsy device can be evaluated in real time in order to avoid a non-targeted biopsy site, especially the normal vessel wall. In complex anatomy and in case of a marginal lesion, we propose the use of parallel guidewire to stabilise the introducer sheath and also the PEB device.

Primary vascular tumours are very rare [1] and still poorly understood. Malignant tumours are the most frequent. In our series, 14 patients had malignant tumours out of all tumoral causes. Primary pulmonary artery sarcoma (PAS) is the most well known malignant vascular tumour. However, since the first report in 1923 [5], the clinical experience in diagnosis and management of PAS is still limited, with less than 300 cases in the literature and most of them are reported as case reports [2, 13]. The tumours usually originate from the media of venous vessel walls, but sometimes they may originate from the arterial structures. Most sarcomas are frequently located in the pulmonary trunk as well as in the right and left pulmonary arteries with a considerable potential ability to grow locally as they tend to infiltrate the vessel leading to progressive obstruction. Various subtypes have been described, including rhabdomyosarcoma, osteogenic sarcoma, angiosarcoma, fibrosarcoma, myxosarcoma, liposarcoma and undifferentiated sarcoma [14, 15]. Although correlations between the clinical profile, imaging features and pathological findings in pulmonary sarcomas have been evaluated [16], the distinction between the different subtypes needs histological assessment. The prognosis of PAS is poor, with a significant difference between patients who had complete resection and patients with incomplete resection and/or multimodal treatment. In the review reported by Blackmon et al. [17], the median survival was 36 ± 20 months for patients undergoing an attempt of curative surgery and 11 ± 3 months for those undergoing incomplete surgery. Therefore, early diagnosis is the key for improving prognosis. Furthermore, some reports estimate longer survival in leiomyosarcoma and worse prognosis with rhabdomyosarcoma [16]. Less frequent are the primary vascular tumours of SVC and IVC [18]. Amongst them, leiomyosarcoma is the most frequent tumour, accounting for 2% of a vascular origin. The tumour is usually observed in the IVC with intraluminal and/or intramural development [19], and rarely metastases are encountered at the time of the diagnosis [20, 21]. Regarding the malignant mesenchymal tumours of the large arteries that originate from the intimal layer of the vessel wall, intimal sarcoma and angiosarcoma are considered in the differential diagnosis. In our series we did have two cases of lymphoma of the right ventricle as well as two benign myxomas of the inferior vena cava.

Although our study suggests a benefit of PEB, one of our major limitations is patient cohort size. Since the disease is

rare we were only able to enrol a small number of patients in a decade. Moreover, the retrospective design of the study makes it difficult to arrive at a firm conclusion.

In summary, malignant soft tumours of the heart and great vessels are rare tumours with an insidious, slow growth and with a clinical presentation that can be misleading when clinical symptoms do occur. Even though imaging modalities can most of the times lead to demonstration of the intravascular filling-defect mass, the diagnosis is based upon histopathological examination of specimens. Currently, PEB is a direct, safe and very efficient procedure that aims to obtain a tissue sample of high diagnostic quality in order to establish early diagnosis and appropriate treatment with the hope of offering the best chance of survival.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Prof. Salah D. Qanadli MD, PhD, FCIRSE.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap One patient's data have been previously reported in the European Journal of Cardiothoracic Surgery.

Methodology
• retrospective
• performed at one institution

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