Progress in Cardiovascular Diseases 60 (2018) 613–621

Contents lists available at ScienceDirect

Progress in Cardiovascular Diseases

journal homepage: www.onlinepcd.com

Pulmonary embolism: Care standards in 2018☆

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ARTICLE INFO

Keywords:
Pulmonary embolism
Deep venous thrombosis
Venous thromboembolism

ABSTRACT

Pulmonary embolism (PE) is a leading cause of cardiovascular mortality worldwide. Clinical presentation can be diverse, and clinicians should have a high index of suspicion regarding the diagnosis. Evaluation should include detailed history of possible risk factors, physical examination and laboratory tests that would support the diagnosis and help risk-stratify patients. Finally, a dedicated imaging study should be performed in order to make a definitive diagnosis. Decisions regarding short-term, immediate, treatment are dictated by PE risk category. Treatment of low and high-risk PE is relatively straightforward. But treating moderate risk PE is challenging since aggressive treatment is not devoid of potential harm. This review focuses on the acute and chronic treatment of PE. We present risk stratification, guidance as to treatment choice and insights into chronic treatment with available anticoagulants.

Contents

Abbreviations and acronyms: CDT, Catheter Directed Thrombolysis; CT, Computed tomography; CTA, CT angiography; DOAC, direct oral anticoagulant; DUS, Doppler ultrasound; DVT, deep vein thrombosis; ECMO, Extra Corporeal Membrane Oxygenation; ICH, intracranial hemorrhage; ICU, intensive care unit; INR, international normalized ratio; IVCF, Inferior Vena Cava Filter; L, liter; LMWH, low molecular weight heparin; Mg, milligram; Ng, nanogram; NT-BNP, N Terminal Pro Blood Natriuretic Peptide; O2, oxygen; PE, pulmonary embolism; PERT, pulmonary embolism response team; PESI, Pulmonary Embolism Severity Index; Pg, picogram; RV, right ventricle; SSPE, sub segmental pulmonary embolism; TT, thrombolytic therapy; TTE, Trans-Thoracic Echocardiography; UFH, unfractionated heparin; VKA, vitamin K antagonist; V\Q, ventilation perfusion scan; VTE, venous thromboembolism.

☆ Statement of Conflict of Interest: see page 619.

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https://doi.org/10.1016/j.pcad.2017.12.005
0033-0620/

A 67-year-old male presents to the emergency department complaining of increasing left pleuritic chest pain and effort intolerance for the past 13 days and a single episode of blood tinged sputum the day prior to presentation. The patient denies recent surgery, trauma or immobility and does not have a personal or family history of thrombosis or known hypercoagulable state.

Past medical history includes hypertension, hyperlipidemia, chronic obstructive pulmonary disease and newly diagnosed multiple myeloma.

Upon presentation abnormal vital signs include: heart rate 130 beats per minute and, O2 saturation of 89% while breathing room air.

Examination reveals tachypnea and increased respiratory effort and is otherwise normal.

Laboratory tests reveal a d-dimer of 3.3 mg/L (normal value below 0.5 mg/L), NT-BNP of 730 pg/mL (normal value below 125 pg/mL), and Troponin of 450 ng/L (normal value below 50 ng/L).

The patient underwent a dedicated computed tomographic (CT) scan and was found to have a pulmonary embolism (PE) involving the left main pulmonary artery.

How should this patient be further evaluated and treated?

Background

PE is common, affecting as many as 112 patients per 100,000 every year in the United States alone.[1] Furthermore, it is a leading cause of cardiovascular death.[2] Pulmonary emboli represent an extended spectrum of disease; they can be found incidentally or present with sudden death.[3] Thus, clinicians treating patients presenting with PE must be able to identify PE severity appropriately and tailor treatment accordingly.

Most PE originate from lower limb deep veins. Deep vein thrombi (DVT) dislodge from its site of origin and pass through the right side of the heart into the pulmonary vasculature. It is much more common for a DVT to cause PE if it is proximal, whereas distal (to the popliteal fossa) DVT rarely cause PE and usually resolve spontaneously. PE arising from upper extremity or aortic branch DVT are rare.

Key risk factors for PE [and DVT/venous thromboembolism(VTE) as well] include recent surgery, trauma, immobilization and active cancer. Heavy smoking, obesity and congestive heart failure are also associated with increased risk. Medications which have potential to cause PE are mainly oral contraceptives and hormone replacement therapy.[4] PE may also be encountered when all of the above are lacking. These are known as unprovoked. While uncommon, these may be associated with inherited thrombophilia.

PE severity is assessed through physical examination, echocardiographic imaging of the heart and cardiac biomarkers. A patient seen in a state of hypotension or shock is suffering from a life threatening condition and if PE is suspected it is immediately classified as a high-risk. This patient will require prompt diagnosis and rapid initiation of treatment with a thrombolytic agent. On the other end of the spectrum are asymptomatic patients discovered to have PE while undergoing imaging for unrelated reasons. In contrast to high-risk PE patients, the question of benefits of treatment (versus potential harm) is often relevant to this low-risk patient population. Thus, clinicians caring for PE patients should be well aware of the versatility of this condition and the need to tailor care according to specific patient needs.

Evaluation

Patient evaluation for PE should be geared towards both acute and long-term treatment goals. Thus, evaluation will include a focused history, specific laboratory indices and tailored imaging (Fig 1). While a thorough discussion of a comprehensive PE-related history is beyond the scope of this review, some examples can be found in Table 1.

As there are many mimickers of PE (e.g. myocardial infarction and sepsis-associated hypotension and Right ventricle (RV) dysfunction), PE related imaging should include a dedicated study such as computed tomographic (CT) angiogram (CTA). If, however, CTA is unavailable or contraindicated, a Ventilation Perfusion (V/Q) scan can be performed. PE can be classified by location into saddle, lobar, segmental and subsegmental. A saddle PE lodges at the bifurcation of the aorta and extends into the right and left main pulmonary arteries. Contrary to widespread practice, proximal emboli, including saddle emboli, are not necessarily associated with higher mortality[5–7] In this context, clot burden also has not been consistently associated with increased mortality.[8]

In contrast, RV enlargement does correlate with a higher incidence of adverse outcomes including mortality. This is true both in hemodynamically stable and unstable patients[9–11] Notably, as will be elaborated below, this does not offer direct insight into best management practices. However, it is well accepted that a patient with RV dilatation on CT should be treated as an inpatient. Such a patient will likely benefit from close monitoring in an intensive care unit. It is less clear whether early aggressive treatment, without observed clinical deterioration, benefits these patients in clinically meaningful ways.[12]

Next, a transthoracic echocardiogram (TTE) should be obtained, either acutely at the bedside (for sicker patients) or later on for purposes of risk stratification.[13] Parameters such as RV dilatation or hypokinesia of the RV free wall are indicators of RV dysfunction and are associated with an elevated risk of short term mortality even in the stable, non-hypotensive patient.[14,15] Nonetheless, clinicians should be knowledgeable of the fact that interpretation of RV function on TTE is less standardized and more subject to opinion than left ventricular analysis.[16]

Some have used signs of RV dysfunction in hypotensive patients, too unstable to transport to the CT machine, to support a diagnosis of PE. As mentioned above, this practice has the potential to result in false diagnoses and in errors in care and thus should be used sparsely and carefully. Other findings on TTE that have potential relevance to the treatment of PE patients include a patent foramen ovale and clot in transit.

The majority of PE arises from the lower extremity. In fact, DVT has been reported in as many as 50% of PE patients.[17] Furthermore, in an otherwise stable patient suspected of having PE who is found to have a proximal DVT, clinicians should initiate anticoagulation even before a definitive diagnosis of PE is obtained, since the same treatment is warranted. Thus, a lower extremity venous Doppler ultrasound (DUS) may be a reasonable preliminary diagnostic solution when CTA is contraindicated (e.g. renal failure, dye allergy or pregnancy) and V/Q scan is also not available or is inconclusive. Also, lower extremity DUS should be considered as an ancillary bedside test in the unstable patient as diagnosis will support (but not prove) venous thromboembolism as a mechanism for instability.

Standard laboratory tests that should be sent as part of the evaluation for PE include complete blood count, basic metabolic panel, N-terminal B Natriuretic peptide (NT-BNP) and Troponin (Table 2). D-dimer should be