Diagnosing pulmonary embolism in a rural setting

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Introduction

The paradox in the diagnosis of pulmonary embolism (PE) is that it tends to be both under-diagnosed and over-investigated.[1] Seventy percent of emboli are diagnosed at autopsy.[2] Even today, guidelines to investigations are variable and not always evidence-based. In the rural setting many of these investigations are delayed or simply unavailable, yet a timely decision for or against anticoagulation needs to be made. Rural physicians have the advantage of knowing the patient better and can therefore better assess probability of disease prior to testing. D-dimer tests, now available in most rural centres, have proved to be useful in patients with low probability of embolism and, if results are negative, can exclude the diagnosis. Additional studies such as chest x-ray, other laboratory tests, or ECG can support an alternate diagnosis. The rest of the investigation sometimes becomes less evidence-based, but, given the following checklist, we should be able to pursue the diagnosis appropriately with the help of our imaging colleagues in our referral centres.

Step 1

Think of the diagnosis.

Avoiding under-diagnosis involves including PE in the differential. There are 5 identifiable syndromes.

1. Isolated dyspnea and tachypnea
2. Pneumonic syndrome of pleuritic chest pain, cough, râles or hemoptysis
3. Central catastrophe of shock, hypotension, right heart failure or sudden death. Fortunately this is uncommon. Timely diagnosis is unlikely in a rural facility.
4. Chronic recurring emboli leading to pulmonary hypertension and right heart failure.
5. Septic emboli (e.g., IV drug abuse or infected central catheter).

The first 2 syndromes are the most common and produce the findings that are most characteristic. Ninety-seven percent of patients with PE have either dyspnea, tachypnea or pleuritic pain.[2] Other symptoms or signs can include cough, fever, râles, leg pain and hemoptysis. If pneumonia or chronic obstructive pulmonary disease with exacerbation is the diagnosis, PE should usually be thought of in the differential.

Step 2

Assess patient risk factors.

Avoiding under-diagnosis involves considering at higher risk any patient with features of Virchow's triad (stasis, endothelial injury or hypercoagulability). This would include patients in the following scenarios:

1. within 4 weeks of surgery;
2. pregnancy and puerperium;
3. lower limb fracture or paralysis;
4. malignancy;
5. reduced mobility;
6. previous PE, or previous or current deep venous thrombosis (DVT);
7. cardiovascular or pulmonary disease;
8. use of oral contraceptives or estrogen therapy;

9. thrombophilias such as protein C and S deficiency, antiphospholipid antibodies and Factor V Leiden mutation.

Step 3

Apply locally available, less specific investigations.

The following investigations may provide an alternate diagnosis and avoid over-investigation.

1. Chest x-ray. Only 12% of patients with PE have a normal chest radiograph.[3] Atalectasis, parenchymal abnormality, pleural effusion, cardiomegaly or raised hemidiaphragm may be found, but these findings are neither sensitive nor specific. Lobar consolidation, however, suggests a diagnosis of pneumonia. Pneumothorax or pneumomediastinum can suggest an alternative diagnosis.
2. ECG. This is commonly abnormal in PE, but never diagnostic. Common changes such as sinus tachycardia, supraventricular arrhythmias, right bundle branch block, and right axis deviation are neither specific nor sensitive. ST changes suggesting pericarditis or infarction are helpful in providing an alternative diagnosis.
3. Blood gases. Often there is hypoxia with respiratory alkalosis. Gases can be normal 15% of the time. In PE this may indicate severity of illness, but it is unlikely to help with diagnosis. A finding of metabolic acidosis may suggest an alternative reason for dyspnea and tachypnea.
4. Pulmonary function tests. Often abnormal, but not specific or sensitive. Not recommended.
5. Echocardiography. Often abnormal in PE and may be prognostic, but never diagnostic.[4] Seldom easily available in rural practice. Not recommended.

Step 4

Apply Steps 1 to 3 to determine pre-test probability.

This takes into consideration physical findings, risk factors and more probable diagnoses to yield the Wells Score.[5] Wells Score points values are calculated as follows.

- Clinical signs of DVT: 3.0
- Alternative diagnosis less probable than PE: 3.0
- Heart rate >100 beats/min: 1.5
- Immobilization or surgery <4 weeks ago: 1.5
- Previous DVT or PE: 1.5
- Hemoptysis: 1.0
- Cancer: 1.0

Total points score:[6]
<2 = low probability with ≤10% risk of PE;
2–6 = moderate probability with 25% risk of PE;
>6 = high probability with ≥60% risk of PE.

Moderate- and high-probability patients should be administed a low-molecular-weight heparin (LMWH) anticoagulant while awaiting further investigation.

Step 5

Consider more specific testing and imaging.

1. D-dimer

- The latex fixation test is not sensitive enough. The whole blood assay (SimpliRED™; AGEN Biomedical Limited, Brisband, Australia) is recommended in patients with low pre-test probability, to rule out the possibilty of PE in these patients. More highly sensitive ELISA [enzyme-linked immunosorbent assay] tests are available, but have a higher false-positive rate.[6] Most rural areas should have access to the SimpliRED™ assay in-house.
- False-positive D-dimer tests are more common in the elderly, in patients with a history of recent surgery, or in those with cancer. Such patients are more likely to have higher pre-test probability and therefore PE could not be excluded by D-dimer. **This test has no predictive value in patients of intermediate or high pre-test probability.**
- **A negative SimpliRED™ D-dimer is sufficient to exclude diagnosis of PE in a low pre-test probability patient. A patient with a positive SimpliRED™ D-dimer should be administered a LMWH anticoagulant while awaiting further investigation.**[4]

2. Ventilation perfusion (VQ) scan

- Indicated **only if chest x-ray is normal and there is no cardiovascular or pulmonary disease.**
- **High probability scan makes the diagnosis of PE in the context of reasonable pre-test probability of PE.**[7] False-positives can occur.

- **Normal scan effectively excludes PE.**[7]
- 65% of scans are non-diagnostic and require another test for exclusion.[6] Proximal leg ultrasonography, weekly for 2 weeks, is usually recommended, but difficult to schedule on time. It often does not get done, leading to unnecessary or prolonged anticoagulation or missed diagnosis. Rural patients are at a particular disadvantage in having to travel for multiple tests.
- More limited availability, especially out of hours.
- Investigation of choice in pregnancy, having 10% of the radiation dose of CT studies.

3. **Computerized tomography (CT) pulmonary angiography and proximal leg venography.** This is not the same as chest CT or pulmonary angiography. Helical CT is done with rapid high-pressure contrast injection and imaging within a few seconds.
- **Used if there is an abnormal chest x-ray, cardiovascular or respiratory disease.**
- **Some sources recommend this as initial imaging for non-massive PE.**[8] Good evidence for this approach may have to wait for the results of the PIOPED II Study [Prospective Investigation of Pulmonary Embolism Diagnosis], expected to be available in 2005.[9] Advances in CT imaging are expected to steadily improve reliability.
- **A positive study confirms PE.**
- **A negative scan is not equivalent to a normal VQ scan and does not exclude PE.**[10] An additional study is required, such as CT venography or proximal leg ultrasonography. Ideally the latter study is repeated twice, at weekly intervals.[8]
- **Useful to obtain another diagnosis that would explain symptoms and exclude PE.**
- **CT venography done at the same time as CT pulmonary angiography takes little additional time and adds to sensitivity. It also identifies pelvic or abdominal thrombi that would otherwise be missed. There is larger exposure to both radiation and contrast. This combination is probably a good "one stop" resource for the rural patient who has to travel for each investigation and has faint hope of access to weekly leg ultrasonography as recommended in many guidelines.**[1] The evidence for accuracy of this approach awaits the publication of the PIOPED II data. Meanwhile, there are guidelines from the British Thoracic Society that suggest that CT pulmonary angiography is the best initial imaging modality.[8]
- Occurrence of venous thromboembolism in patients with negative CT pulmonary angiography and negative leg ultrasonography taken the same day and repeated in 1 week is as low as 1.5%.[11] Study follow-up, however, was only for 3 months, and more robust data are needed. There are still no good outcome studies assessing CT venography with CT pulmonary angiography.
- Sometimes more available in centres taking rural referrals and more accessible out of hours. Timely imaging is always desirable.
- Caution is advised in renal failure, contrast allergy and pregnancy, where VQ scanning is usually preferred.

4. **Ultrasound of proximal leg veins**
- **If clinical DVT is present, leg ultrasonography can be the initial investigation. If positive, it is sufficient to confirm PE.**[8]
- In absence of clinical DVT, proximal clot is found in only 23%–52% of patients with confirmed PE when ultrasonography is used. It is known that 60% of patients with PE have proximal DVT when venography is done. Compression ultrasonography therefore has limited clinical usefulness as an initial test in absence of leg symptoms.[8]
- This is a useful and non-invasive test, but it is often difficult to obtain a study at an appropriate time — especially for a rural patient.
- This is a recommended additional test for the patient with a non-diagnostic VQ scan or a negative CT angiogram. If negative, a repeat is suggested at 1 and 2 weeks if pre-test probability is intermediate or high.

5. **Pulmonary angiography**
- Still considered the "gold standard" for PE diagnosis, this study is reserved for patients at very high pre-test probability who have otherwise negative imaging and in whom suspicion for PE remains very high. This is the province of the consultant.
- Mortality as a result of the study can be up to 0.5%.

Step 6

Apply Steps 4 and 5 to the algorithm to confirm or exclude a diagnosis of pulmonary embolism in your patient.

See Figure 1 for the diagnostic algorithm.

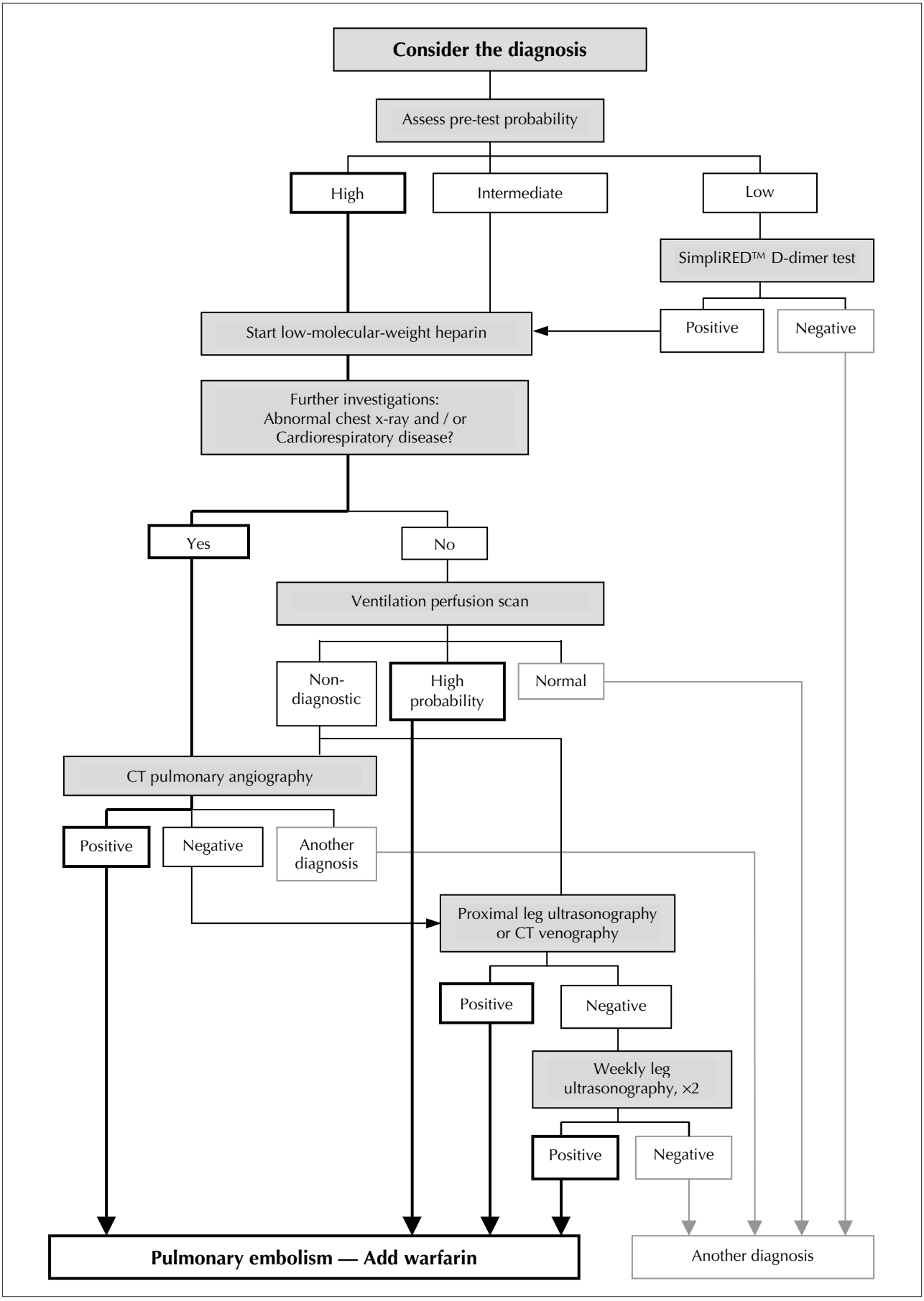

Fig. 1. Diagnostic algorithm for diagnosis of pulmonary embolism

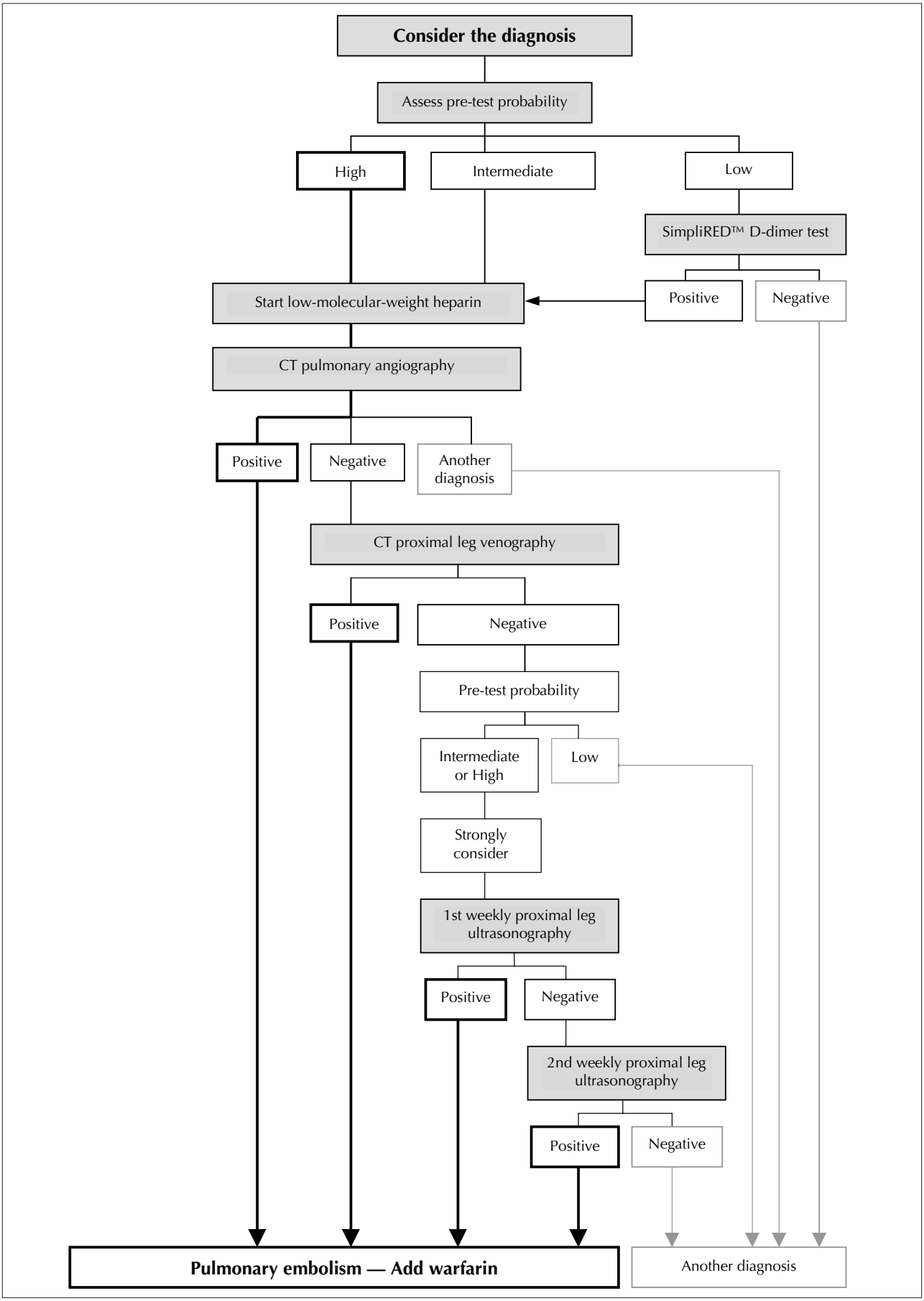

Fig. 2. Streamlined diagnostic strategy for the rural patient

Step 7

Treat the patient.

The difficult work has been done. Apart from the rare unstable patient, all patients can be managed in a rural setting. **The unstable patient needs rapid anticoagulation with unfractionated heparin and rapid transport for specialty evaluation and possible thrombolysis.**

1. Patients with low pre-test probability and negative SimpliRED™ D-dimer should have another diagnosis pursued and have no treatment for PE.
2. Patients with a negative VQ scan should have another diagnosis pursued and no treatment for PE.
3. Patients with intermediate or high pre-test probability need to have LMWH started prior to any further imaging. If a thrombophilia is suspected, consider drawing blood for studies prior to anticoagulation.
4. Patients with confirmed PE (through high probability VQ scan, positive CT pulmonary angiography/venography or positive proximal leg ultrasonography) should have warfarin added. Once INR [international normalized ratio] is in the 2–3 range, heparin can be discontinued. Recommended duration of warfarin use appears in Table 1.[12,13]
5. For unstable patients, anticoagulation is achieved more quickly with unfractionated heparin. It would require high pre-test probability with reasonable exclusion of alternate diagnoses (such as dissecting aneurysm) before consideration of anticoagulation in this event. Thrombolysis can be considered, but must await further imaging for diagnosis and will need to be considered in a referral centre.
6. Patients with another diagnosis receive alternative treatment.

Table 1. Recommended duration of anticoagulant (warfarin) use in patients with confirmed* pulmonary embolism (PE)

Description of event	Duration of anticoagulation
First event, if there is a temporary or reversible risk factor (e.g., trauma or surgery)	at least 3 mo
First event, if the cause of PE is not identified	at least 6 mo
Recurrent idiopathic PE or continuing risk factor (e.g., thrombophilia)	at least 12 mo
Symptomatic isolated calf-vein thrombosis	6 to 12 wk

*PE confirmed by high-probability ventilation perfusion scan, positive CT pulmonary angiography/venography or positive proximal leg ultrasonography.
Note: For the full American College of Chest Physicians recommendations visit:
www.chestjournal.org/cgi/content/full/119/1_suppl/176S176S#SEC9

Considerations for rural physicians

Figure 2 illustrates a streamlined diagnostic strategy for the rural patient.

1. Exclude PE in a low-probability patient with a negative SimpliRED™ D-dimer. All other patients need further work-up.
2. Consider VQ scanning in otherwise healthy patients with normal chest x-ray, pregnancy, renal failure or contrast allergy, but remember that 65% of these will be non-diagnostic and will need leg ultrasonography concurrently, perhaps at 1 and 2 weeks. Scanning takes 4–5 hours, and ultrasonography is difficult to schedule.
3. Strongly consider CT pulmonary angiography with proximal leg venography as your initial imaging investigation. It is more widely and immediately available, and the initial venous imaging can be done at the same time. It is occasionally going to provide an alternate diagnosis. Some current guidelines would support terminating investigation if this were negative,[1,8] however, intermediate- and high-risk patients are still going to need follow-up ultrasonography at 1 and 2 weeks, if we consider the best evidence at present.
4. Take the trouble to follow patients with negative CT studies with proximal leg ultrasonography at 1 and perhaps 2 weeks. This is often a scheduling nightmare, and primary physicians and consultants often overlook this step.
5. **In summary: Low probability patients with negative D-dimer can be excluded. All other patients can be managed more simply and quickly by CT pulmonary angiography and proximal leg venography. Low-risk patients, if this study is negative, can be excluded. All other patients should be considered for proximal leg ultrasonography up to twice, at weekly intervals.**

Competing interests: None declared.

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