A 31-year-old, married female was admitted with complaints of sudden-onset shortness of breath and dry cough since that morning. It was not associated with chest tightness, wheezing or pleuritic chest pain. There was no history of fever, running nose or haemoptysis. The patient had undergone lower-segment caesarean section 2 weeks previously and had reduced mobility since then. She was known to have hypothyroidism for the past 3 years, which was well controlled on thyroxine. On admission, the patient had a respiratory rate of 30 per min, pulse rate of 130 per min, blood pressure of 110/70 mmHg and oxygen saturation by finger pulse oximetry of 89% on room air. Arterial blood gases on ambient air revealed pH of 7.48, carbon dioxide tension of 30 mmHg, oxygen tension of 58 mmHg and bicarbonate of 22 mEq·L⁻¹. Chest radiography did not reveal any significant abnormality. ECG revealed sinus tachycardia, right-axis deviation and T-wave inversion in leads V1–V4.

Assessment of pre-test probability assumes importance as the post-test probability of pulmonary embolism depends upon the pre-test probability and the diagnostic test used. Pre-test probability of pulmonary embolism is assessed by taking into consideration clinical symptoms and signs of pulmonary embolism along with presence of predisposing factors for venous thromboembolism. Pre-test probability can be predicted by clinical judgement or by using prediction rules like the Wells score or revised Geneva score. Patients with low or intermediate clinical probability should undergo D-dimer testing as it has a high negative predictive value and helps to exclude pulmonary embolism in 30% of patients. Computed tomography–pulmonary angiography (CTPA) is the investigation of choice in patients with high clinical probability of pulmonary embolism. D-dimer has low negative predictive value in these patients and, hence, testing is not recommended [1, 2].

The patient’s Wells score was 6 and revised Geneva score was 5. High-sensitivity D-dimer was 4050 ng·mL⁻¹. CTPA was performed, which revealed a thrombus in both the right and left pulmonary arteries, and infarction involving the right middle lobe and posterior basal segment of the left lower lobe. Two-dimensional (2D) echocardiography revealed dilatation of the right atrium and ventricle, akinesia of right ventricular...
mid-free wall with preserved wall motion at the apex and raised pulmonary artery systolic pressure of 60 mmHg. A cardiac troponin test was positive and N-terminal brain natriuretic peptide concentration was 8054 pg·mL−1. Compression venous ultrasonography of the bilateral lower limbs revealed deep vein thrombosis of the right saphenous-femoral vein and popliteal vein. Her simplified Pulmonary Embolism Severity Index score was 2.

As the patient had an intermediate to high early mortality risk from pulmonary embolism, the best management strategy would be to initiate parenteral anticoagulation and to closely observe for any signs of haemodynamic instability. Thrombolysis is indicated in patients with high early mortality risk, i.e. those with haemodynamic instability. Surgical pulmonary embolectomy is indicated in patients with high early mortality risk in whom thrombolysis is contraindicated [1].

**Task 2**
What is the optimal management strategy for the patient?

a. Thrombolysis  
b. Anticoagulation  
c. Observation  
d. Surgical pulmonary embolectomy

**Answer 2**  
b. Anticoagulation

Considering that our patient was breastfeeding her baby, which of the following drugs should be avoided for parenteral anticoagulation?

a. Unfractionated heparin (UFH)  
b. Low molecular weight heparin (LMWH)  
c. Fondaparinux  
d. All the above
UFH and LMWH are secreted in breast milk in small amounts [3]. However, oral bioavailability of heparin is low [4]. Therefore, orally ingested heparin via breast milk does not produce any clinically significant effects in the baby. UFH and LMWH can be safely given in breastfeeding mothers [5–8]. There are no data regarding excretion of fondaparinux in human milk. It is known to be excreted in the milk of rats. As per the manufacturers prescribing information, caution is to be exercised while prescribing fondaparinux to breastfeeding mothers [9].

The patient was started on initial parenteral anticoagulation with unfractionated heparin. However, after a few hours, she developed hypotension that was unresponsive to crystalloid bolus infusion. Noradrenaline was initiated. Repeat 2D echocardiography revealed bowing of interventricular septum to the left in addition to previous findings.

Pulmonary embolism patients with intermediate–high mortality risk must be closely observed for any signs of haemodynamic instability. Rescue thrombolysis is indicated if haemodynamic decompensation occurs [1]. In our case, systemic thrombolysis was indicated as the patient developed hypotension due to obstructive shock. However, she had undergone lower-segment caesarean section 2 weeks previously, which is a major surgery. Recent major surgery within 3 weeks is an absolute contraindication to systemic thrombolysis [1]. So, in such cases, catheter-directed thrombolysis is the next best option.

Catheter-directed thrombolysis was not immediately available. After multidisciplinary discussion with a cardiologist and cardiovascular surgeon, and after discussion with the patient and her relatives, thrombolysis with streptokinase was performed. The patient showed signs of improvement 24 h post-thrombolysis. Her tachycardia and tachypnoea resolved, she became normotensive, and she was weaned off oxygen. 2D echocardiography was repeated after 48 h. The right atrium and ventricle were of normal size with no regional wall motion abnormality. Pulmonary artery systolic pressure was 30 mmHg. The patient did not develop any bleeding complications.

**Task 4**
What is the next step in management of the patient?
- a. Systemic thrombolysis
- b. Continue only anticoagulation
- c. Catheter-directed thrombolysis
- d. Surgical pulmonary embolectomy

**Task 5**
Which is the oral anticoagulant of choice in lactating mothers?
- a. Warfarin
- b. Edoxaban
- c. Dabigatran
- d. Rivaroxaban
Answer 5

a. Warfarin

Warfarin is not excreted in breast milk. Hence, is safe to use in breastfeeding mothers [4–7]. There are no data available regarding the clinical effect of direct thrombin inhibitors (dabigatran) and oral factor Xa inhibitors (rivaroxaban, edoxaban and apixaban) on breastfed infants. They are therefore avoided in breastfeeding mothers [10–14].

The patient received initial anticoagulation with UFH overlapped with warfarin. UFH was discontinued after 5 days as an international normalised ratio (INR) of 2.3 was achieved, and warfarin was continued on day 7 post-admission.

Discussion

The post partum period is one of increased risk for pulmonary embolism. Venous thromboembolism is common in all trimesters of pregnancy while pulmonary embolism is particularly common in post partum period [15]. This increased risk is due to formation of Virchow’s triad. Virchow’s triad consists of venous stasis, increased coagulability and endothelial injury. During pregnancy, venous stasis in the lower limbs is due to the vasodilatory effect of progesterone, obstruction of venous flow by the enlarged uterus, and due to compression of the left iliac vein by the left iliac artery and ovarian artery. Endothelial damage occurs due to venous hypertension [16]. Concentrations of clotting factors like VIII, IX, X and fibrinogen are increased while fibrinolytic activity is decreased to prevent massive blood loss during delivery [17]. Our patient was in the post partum period and was at high risk of pulmonary embolism.

Management of pulmonary embolism depends upon early mortality risk. Patients at high early mortality risk should be started on parenteral anticoagulation and should undergo systemic thrombolysis within 48 h of symptom onset. Even though the efficacy of thrombolysis decreases with each additional day from system onset, substantial benefit has been observed up to the 14th day from pulmonary embolism symptom onset [18]. Thrombolysis can be performed with alteplase, streptokinase or urokinase. Absolute contraindications to thrombolysis are history of haemorrhagic stroke or stroke of unknown origin, ischaemic stroke in past 6 months, major trauma, head injury or surgery in past 3 weeks, brain or spinal cord neoplasm, active bleeding, or bleeding diathesis. However, depending on the risk/benefit ratio, an absolute contraindication may become a relative contraindication [1]. The relative merits of thrombolysis are to be judged by the treating physician on a case-by-case basis. In our case, as the patient developed hypotension and right ventricular failure, the risk of mortality increased significantly. Also, even though the risk of bleeding due to thrombolysis is greater in patients who have undergone recent major surgery in the past 3 weeks, it is in surgery involving the brain and spinal cord where the risk of bleeding is substantial [19, 20]. So in our case, the benefit of thrombolysis far outweighed the risk of bleeding. Relative contraindications include transient ischaemic attack in past 6 months, advanced liver disease, active peptic ulcer, refractory hypertension, noncompressible puncture sites, pregnancy and first post partum week. Patients who have intermediate early mortality risk are initiated on parenteral anticoagulation. Rescue thrombolysis should be considered in these patients if clinical signs of haemodynamic decompensation appear [1]. Percutaneous catheter directed interventions or surgical embolectomy are recommended if systemic thrombolysis is contraindicated or has failed. Percutaneous catheter-based interventions include catheter-directed thrombolysis or fragmentation and aspiration. Fragmentation can be performed mechanically or via ultrasound. The efficacy of catheter-directed therapy has been reported to be 85.7% in patients with massive pulmonary embolism and 97.3% in submassive pulmonary embolism, and it was not associated with any major complications [21]. Primary systemic thrombolysis is not recommended as the risk of life-threatening bleeding far outweighs any potential benefits in these patients. Parenteral anticoagulation in patients with high and intermediate risk pulmonary embolism is initiated using UFH, LMWH or fondaparinux. UFH is preferred over LMWH or fondaparinux in patients with high early mortality risk, those with renal failure and the severely obese, and as initial anticoagulation in patients in whom thrombolysis is contraindicated and who are awaiting surgery or catheter-based interventions. Patients with low early mortality risk are started on anticoagulation and can be discharged early if there are no comorbidities. Maintenance anticoagulation can be performed using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants (NOACs). If vitamin K antagonists are used, they are to be overlapped with UFH, LMWH or fondaparinux for 3–5 days till an INR between 2 and 3 is achieved [1]. As far as NOACs are concerned, dabigatran and edoxaban require overlap, while rivaroxaban and apixaban do not require overlap with parenteral anticoagulants [22].

Practices regarding follow-up of patients with pulmonary embolism vary widely and there are no standard international guidelines addressing the issue of duration and intensity of follow-up of these patients. All diagnosed cases of pulmonary embolism should receive ≥ 3 months of anticoagulation. During follow-up, patients should be monitored for adequacy of anticoagulation, pulmonary embolism recurrence, development of chronic thromboembolic pulmonary hypertension.
(CTEPH) and any complications resulting from therapy. Monitoring is not required if NOACs are used. If vitamin K antagonists are used, the INR should be kept between 2 and 3. Patients with active cancer or antiphospholipid syndrome, those with confirmed deficiency of antithrombin, protein C or protein S, those with homozygous factor V Leiden or homozygous prothrombin G20210A mutations, and those without any major transient or reversible factor are candidates for indefinite anticoagulation [1]. Persistence of dyspnoea and functional impairment even after 3 months of anticoagulation may be due to development of CTEPH. Ventilation/perfusion (V/Q) scanning is the first-line investigation for CTEPH. Diagnosis of CTEPH requires a mean pulmonary artery pressure >25 mmHg along with mismatched perfusion defects on V/Q scan [1]. Certain patients have functional impairment and persistent perfusion defects but do not have pulmonary hypertension. These patients are classified as having post-pulmonary embolism syndrome [23]. The results of the ongoing FOCUS and InSHAPE II studies will provide more insights into follow-up of patients with pulmonary embolism [24, 25].

### Conclusion

The post partum period is one of increased risk of pulmonary embolism. Catheter-directed thrombolysis or surgical pulmonary embolectomy can be considered in patients of pulmonary embolism who present within 3 weeks of major surgery. UFH, LMWH and warfarin are safe to use in breastfeeding mothers. Currently, the evidence regarding use of NOAC in breast feeding mothers is insufficient.

### Affiliations

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### Conflict of interest

None declared.

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