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Ministry of Health

# Pulmonary Embolism (PE) Protocol for Adult Patient



N.B. Staff should be discouraged from printing this document.

This is to avoid the risk of out-of-date printed versions of the document.

The Intranet should be referred to for the current version of the document.

## Introduction:

Pulmonary Embolism (PE) is defined as the obstruction of one or more pulmonary arteries. In most cases, it is caused by blood clots that, most often, arise from deep vein thrombosis (DVT) of the lower extremities and reach the pulmonary arteries.

- Clinical signs of PE are nonspecific, such as dyspnea, chest pain, hemoptysis, and syncope or pre-syncope.
- If PE is suspected, it must be confirmed or ruled out to avoid the risk of overtreatment or under-treatment.

## Purpose:

This protocol is intended to be used by the physicians and other Health Care Providers working at MOH hospitals.

## Aim and scope:

support to the point of care and standardizes the clinical practice for PE to reduce morbidity and mortality.

## Targeted population:

All adult patients were admitted to MOH hospitals.

## Targeted end users:

This protocol is intended to be used by the physicians and other Health Care Providers working at MOH hospitals.

## Setup:

Hospitalized adult patients.

## Methodology:

Review of best practice and expert opinion.

## Conflict of interest:

The guideline was developed based on valid scientific evidence, critical evaluation of that evidence, and objective clinical judgment for practitioners and patients.

## Funding:

No fund was provided.

## Updating:

The first version of this guideline is created in 2022. The guideline will be updated annually if any changes or updates are released by international/national guidelines, pharmacotherapy references, or MOH formulary.

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PE diagnosis confirmed

Hemodynamically unstable

High risk PE (massive)

Shock

End organ

Hypoperfusion

Hypotension

Cardiac arrest

Thrombolysis

(reperfusion strategy)

Hestia score

Condition is hemodynamically unstable

High risk of bleeding

Oxygen supplementation indicated

IV analgesia indicated.

PE was diagnosed while patient was taking an anticoagulant

Other medical reason for admission

Inadequate social support to discharge

Heparin-induces thrombocytopenia

Pregnancy

Crcl<30ml\min

Sever hepatic impairment.

Hemodynamically stable

Intermediate risk PE

Signs of right heart strain on imaging, elevated troponin or BNP, or both

Admit, monitor vital signs, and administer anticoagulant

Low risk PE

All other patients

No Hestia criteria Or Simplified PESI score =0 Implicit assessment that patient's condition is stable without IV medication or oxygen

Patient not suitable for discharges Admit, DOAC (LMWH or VKA if indicated)

Patient suitable for discharge; Discharge from hospital while taking DOAC (LMWH or VKA if indicated

| PESI score | Points |
|---|---|
| Age >80 year. | 1 |
| History of cancer. | 1 |
| History of chronic. cardiopulmonary disease | 1 |
| Heart rate >=110 beats/minute | 1 |
| SBP<100mmHG | 1 |
| Oxygen<90 | 1 |

**The initial approach** to patients with suspected PE is to stabilize the patient and start anticoagulation before confirming the diagnosis of PE.

Most patients have low-risk pulmonary embolism and can be assessed for outpatient anticoagulant therapy according to their Hestia score, score on the simplified Pulmonary Embolism Severity Index (PESI), or the physician's implicit judgment.

**Respiratory support** — Supplemental oxygen should be administered to target an oxygen saturation ≥90 percent. Severe hypoxemia, hemodynamic collapse, or respiratory failure should prompt consideration of intubation and mechanical ventilation.

**Hemodynamic support**— The precise threshold that warrants hemodynamic support depends upon the patient's baseline blood pressure and whether there is clinical evidence of hypo perfusion (eg, change in mental status, diminished urine output). In general, we prefer small volumes of intravenous fluid (IVF), usually, 500 to 1000 mL of normal saline, followed by vasopressor therapy should perfusion fail to respond to IVF.

- **Intravenous fluid** – IVF is first-line therapy for patients with hypotension.
- **Vasopressors** – Intravenous vasopressors are administered when adequate perfusion is not restored with IVF. The optimal vasopressor for patients with shock due to acute PE is unknown, but norepinephrine is
- generally preferred.
    - **Norepinephrine** is the most frequently utilized agent in this population because it is effective and less likely to cause tachycardia.
    - **Dobutamine** is sometimes used to increase myocardial contractility in patients with circulatory shock from PE.

### Table1: Approaches to the treatment of VTE

| Treatment strategy | Anticoagulant choices |
|---|---|
| **Bridging therapy** | Injectable anticoagulant (UFH, LMWH, OR FONDAPARINUX) initiated with warfarin and overlapped for at least 5 days and until the INR IS > 2.0. Then discontinue injectable anticoagulant and continue warfarin for the appropriate duration |
| **Switching therapy** | Injectable anticoagulant (UFH, LMWH, OR FONDAPARINUX) for at least 5 days, then stop injectable anticoagulant therapy and initiate dabigatran for the appropriate duration |
| **Monotherapy** | Initiate apixaban at a higher initial dose and then convert the patient to a lower maintenance dose for the appropriate duration |

## Table 2. Dosing of Oral Anticoagulant Treatment for Pulmonary Embolism

| Initial Phase of Anticoagulation | Short-Term Phase of Anticoagulation (3–6 mo.) | Indefinite Phase of Anticoagulation > 6 mo) |
|---|---|---|
| **Apixaban,** administered orally, **10 mg** twice a day for **7 days** | **Apixaban**, administered orally, **5 mg twice a day** | Apixaban, administered orally, **5 mg twice a day or 2.5 mg twice** a day |
| **UFH** or **Enoxaparin** Administered subcutaneously for a **minimum of 5 days, plus** Warfarin, administered orally, with **INR ≥2 for 2 days** | **Warfarin was** administered orally, with a target **INR of (2-3)** | Warfarin was administered orally, with a target **INR of (2 – 3)** |

Direct oral anticoagulants and low-molecular-weight heparin are contraindicated in patients with severe renal impairment. Dosing of these medications in patients with renal impairment differs with the specific agent and among jurisdictions. With regard to the use of direct oral anticoagulants in patients with obesity, post hoc analyses of phase 3 trials, observational data, and pharmacokinetic and pharmacodynamic data suggest that direct oral anticoagulants and vitamin K antagonists have similar effectiveness and safety in patients with body weight up to 120 kg or a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of up to 40. For patients who weigh more than 120 kg or have a BMI higher than 40, standard doses of rivaroxaban or apixaban are among the appropriate anticoagulant options; fewer supportive data exist for apixaban than for rivaroxaban. Other options include vitamin K antagonists, weight-based low-molecular-weight heparin (administered according to manufacturer recommendations), and fondaparinux. (2) INR denotes the international normalized ratio.

## Table 3: Dosing of Injectable Anticoagulants for VTE

| Agent and Route | Dosing |
|---|---|
| **Unfractionated Heparin** | |
| IV UFH[a] | Weight adjusted with an initial bolus of 80 units/kg, followed by an initial infusion of 18 units/kg/hr. Subsequent doses should be adjusted to maintain the institution's goal aPTT |
| SC UFH | 17,500 units (250 units/kg) given q12hr[b]. Subsequent doses should be adjusted to maintain the institution's goal aPTT |
| SC UFH | 333 units/kg, followed by 250 units/kg given q12hr without aPTT monitoring. |
| **Low-Molecular-Weight Heparin (SC)** | |
| Enoxaparin | 1mg/kg q12hr or 1.5 mg/kg q24hr[d] ; if CrCl < 30 mL/min/1.73 m2, give 1 mg/kg q24hr |
| **Pentasaccharide (SC)** | |
| Fondaparinux | Weight < 50 kg – Give 5 mg q24hr<br>Weight 50–100 kg – Give 7.5 mg q24hr<br>Weight > 100 kg – Give 10 mg q24hr<br>CrCl < 30 mL/min/1.73 m2 – Contraindicated |

[a] IV administration is preferred because of improved dosing precision.
[b] An initial 5000-unit IV bolus is recommended to achieve rapid anticoagulation.
[c] Good regimen for outpatient treatment for patients who cannot afford LMWH. Not practical for patients weighing > 80 kg because of issues with injection volume.
[d] 1.5 mg/kg q24hr should be avoided in patients with a current or history of malignancy, weight > 120 kg, DVT with iliac vein involvement, or antiphospholipid syndrome.
aPTT = activated partial thromboplastin time.

## Table 4: Duration of Anticoagulation Therapy in Patients with VTE:

| Indication | Therapy Duration | Comments |
|---|---|---|
| The first episode of VTE secondary to a transient or reversible risk factor | 3 months | The recommendation applies to both proximal DVT and PE |
| The first episode of Unprovoked VTE | At least 3 months | Continue oral anticoagulant therapy if the patient is not at high risk of bleeding and is adherent to therapy<br>Risk-benefit of indefinite therapy should be reassessed at periodic intervals |
| The first episode of VTE with inherited or acquired thrombophilia [a] | At least 3 months | The first episode of VTE with inherited or acquired thrombophilia |
| The first episode of cancer-associated VTE | At least 3–6 mo and consider the extended duration until cancer resolves and cancer treatment is completed | LMWH or rivaroxaban are recommended over other anticoagulants |
| Second VTE (provoked or unprovoked) | Indefinite | This applies to patients, not at high risk of bleeding |

[a] Factor V Leiden; prothrombin G20210A; antiphospholipid antibody syndrome; excess factor VIII; deficiency in protein C, protein S, anti-thrombin deficiency.
* The decision to anticoagulant patients with DVT indefinitely should be based upon an estimate of the risk of recurrence and bleeding in the context of the clinical nature of the episode of the DVT (eg, provoked or unprovoked DVT, reversible or irreversible risk factors as well as the patient's values and preferences (eg, occupation, life expectancy, burden of therapy).

## Table 5: Provoked and Unprovoked Conditions Related to VTE

| Provoked Conditions | Unprovoked or Persistent Risk Factors |
|---|---|
| Major surgery with general anesthesia >30 minutes | Collagen vascular diseases |
| Pregnancy, particularly with cesarean delivery | Antiphospholipid syndrome |
| Lower limb plaster cast | Active cancer |
| Short-term immobilization for >3 days | Myeloproliferative disorders |
| Prolonged air travel for >12 hours | Thrombophilia |
| Hormonal contraception | |
| Hormone replacement therapy | |
| Acute infectious disease | |
| Direct trauma to the leg | |

### Table 6: Patients with contraindications to anticoagulation

| Absolute contraindications | Relative contraindications |
|---|---|
| **Active bleeding** | Recurrent bleeding from multiple gastrointestinal telangiectasias |
| **Severe bleeding diathesis** | Intracranial or spinal tumors |
| **Platelet count <50,000/micro (sometimes lower depending upon the strength of the indication)** | Platelet count <100,000/micro |
| **Recent, planned, or emergent high bleeding-risk surgery/procedure** | Large abdominal aortic aneurysm with concurrent severe hypertension |
| **Major trauma** | Stable aortic dissection |
| **History of intracranial hemorrhage (ICH) particularly recent ICH** | Recent, planned, or emergent low bleeding-risk surgery/procedure |

## SPECIAL POPULATIONS

Special populations of patients with acute PE require specific consideration including those listed in (Table 7).

### Table 7: Selection of Anticoagulants

| Factor | Preferred anticoagulant | Comments |
|---|---|---|
| Cancer | LMWH- factor $x_a$ inhibitors | If Just diagnosed, metastatic, very symptomatic, vomiting, on cancer chemotherapy |
| Patients prefer oral anticoagulant | Apixaban<br>Warfarin | |
| Once daily oral therapy preferred | Warfarin | Warfarin required bridging |
| Liver disease and coagulopathy | LMWH | Apixaban is contraindicated if INR is raised because of liver disease and warfarin is difficult to control |
| Antiphospholipid syndrome | LMWH | Patients with antiphospholipid syndrome are treated withUFH, monitoring APTT can be problematic because the effect of the autoantibodies on APTT prolongation is unpredictable. |
| Renal disease and Crcl<25ml/min | Warfarin | LMWH contraindicated with severe renal impairment<br>Apixaban requires dose adjustment |
| Coronary artery disease | Warfarin, apixaban, edoxaban | |
| GI bleeding or dyspepsia | Warfarin, apixaban | |
| Poor compliance | Warfarin | INR monitoring make, rivaroxaban, or edoxaban more compliance |
| Thrombolytic therapy uses | UFH infusion | Greater experience with its use in patients has thrombolytic therapy |
| Availability of reversal agent | Warfarin, UFH<br>Dabigatran | Apixaban antidote not readily available |
| Pregnancy or at-pregnancy risk | LMWH | Potential for other agents to cross the placenta |

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