

Appendix

Investigators and Institutions Participating in the KAF Cohort Study

The KAF Cohort Study investigators include Dr. Rita Selby, Dr. William H. Geerts, Dr. Hans J. Kreder, and Dr. Richard Jay, Sunnybrook Health Sciences Centre, Toronto; Dr. Mark A. Crowther, St. Joseph's Hospital, Hamilton; Dr. Emil Schemitsch, St. Michael's Hospital, Toronto; Dr. Maurice Bent, North York General Hospital, Toronto; and Dr. Peter Weiler, Toronto East General Hospital, Toronto, Ontario, Canada.

Investigation and Treatment of Clinically Suspected Deep Vein Thrombosis

The appropriate and objective investigation and management of patients with suspected deep vein thrombosis is critical to the success of the KAF Cohort Study. Fig. E-1 shows a standardized algorithm based on widely accepted, validated criteria. Clinical probability and D-dimer are not included in this algorithm because they have not been validated in trauma patients.

- Study patients with clinically suspected deep vein thrombosis should undergo ipsilateral proximal Doppler ultrasound as soon as possible after the onset of clinical suspicion. Clinically suspected deep vein thrombosis is recorded in the appropriate section of the Case Report Form. If patients develop symptoms after hours, they may receive anticoagulation overnight, with imaging arranged for the next day.
- If the Doppler ultrasound is positive for proximal deep vein thrombosis (based on a non-compressible segment of a deep vein), the patient has reached a study end-point and the administration of the study medication must be stopped. The patient should be treated as per local practice but usually with therapeutic-dose intravenous heparin or therapeutic-dose subcutaneous low-molecular-weight heparin initially, followed by long-term therapeutic-dose oral anticoagulation with warfarin (international normalized ratio [INR], 2 to 3) for approximately three months. The patient should still return for all of the subsequent scheduled follow-up visits and assessments.
- If there is no evidence of proximal deep vein thrombosis on a proximal Doppler ultrasound, a repeat Doppler ultrasound should be performed in five to seven days. If the repeat Doppler ultrasound is definitely positive for proximal deep vein thrombosis, the patient has reached a study end-point, administration of the study medication should be stopped, and the patient is managed as described above. If the repeat Doppler ultrasound is negative, the patient should continue taking the study medication (if still in the prophylaxis phase of the study) and return for all of the scheduled follow-up visits and assessments.
- If a Doppler ultrasound is nondiagnostic, a contrast venogram should be obtained, with the interpretation based on accepted venographic criteria for normal and positive studies as defined in the study protocol.

Investigation and Treatment of Clinically Suspected Pulmonary Embolism

The appropriate and objective investigation and management of patients with suspected pulmonary embolism is critical to the success of the KAF Cohort Study. Fig. E-2 is a standardized algorithm based on widely accepted, validated criteria. Clinical probability and D-dimer are not included in this algorithm because they have not been validated in trauma patients.

- Study patients with clinically suspected pulmonary embolism should be assessed as soon as possible after the onset of clinical suspicion. Clinically suspected pulmonary embolism should be recorded in the appropriate section of the Case Report Form. If patients develop symptoms after hours, they may be treated with anticoagulation overnight, with imaging arranged for the next day.
- If a patient has symptoms suggestive of pulmonary embolism and also has a swollen lower limb compatible with deep vein thrombosis, it is acceptable to start the investigation with a proximal lower-limb ultrasound. If the ultrasound is positive, further investigation for pulmonary embolism may be undertaken but is not necessary. If the ultrasound is negative or nondiagnostic, proceed with lung imaging as in Fig. E-2.
- In patients with symptoms of pulmonary embolism and no suggestive lower-limb symptoms, CT pulmonary angiography or nuclear medicine lung scanning (V/Q scan) should be selected as the first test depending on availability at the various sites.
- CT pulmonary angiography should generally be considered the diagnostic test for pulmonary embolism, especially if the patient has coexisting respiratory disease or abnormal findings on a chest radiograph or if an alternative diagnosis for the symptoms is likely. CT pulmonary angiography is considered positive only if it is a technically adequate study and shows a filling defect that is in a segmental or more proximal pulmonary artery. Subsegmental filling defects should be regarded as nondiagnostic even on a technically adequate study. This is primarily because the accuracy of CT pulmonary angiography below the segmental level is poor. When the results of CT pulmonary angiography are normal or nondiagnostic, proximal Doppler ultrasound should be done (Fig. E-2). If the Doppler ultrasound is positive for deep vein thrombosis, the patient should be treated for deep vein thrombosis. If the Doppler ultrasound is negative, clinically relevant venous thromboembolism is considered to be excluded.

- V/Q scans may be considered if the patient has no coexisting respiratory disease and has a normal-appearing chest radiograph (see Fig. E-2). If the V/Q scan shows a “high probability” of pulmonary embolism, then it is considered positive for pulmonary embolism. If the V/Q scan shows normal findings, it is considered negative for pulmonary embolism. If the V/Q scan is nondiagnostic, then a proximal Doppler ultrasound should be performed. If the Doppler ultrasound is positive for deep vein thrombosis, the patient should be treated for deep vein thrombosis. If the Doppler ultrasound is negative, then another ultrasound study should be performed in five to seven days. If the repeat Doppler ultrasound is positive, the patient should be treated for deep vein thrombosis. If the repeat Doppler ultrasound is negative, then clinically relevant venous thrombosis is considered to be excluded.
- If pulmonary embolism or deep vein thrombosis is proven on the basis of this algorithm, the patient has reached a study end-point and administration of the study medication must be stopped. The patient should be treated as per local practice, but usually with therapeutic-dose intravenous heparin or therapeutic-dose subcutaneous low-molecular-weight heparin initially followed by therapeutic-dose oral anticoagulation with warfarin (INR, 2 to 3) for approximately three months. The patient should still return for all of the subsequent scheduled follow-up visits and assessments. ■

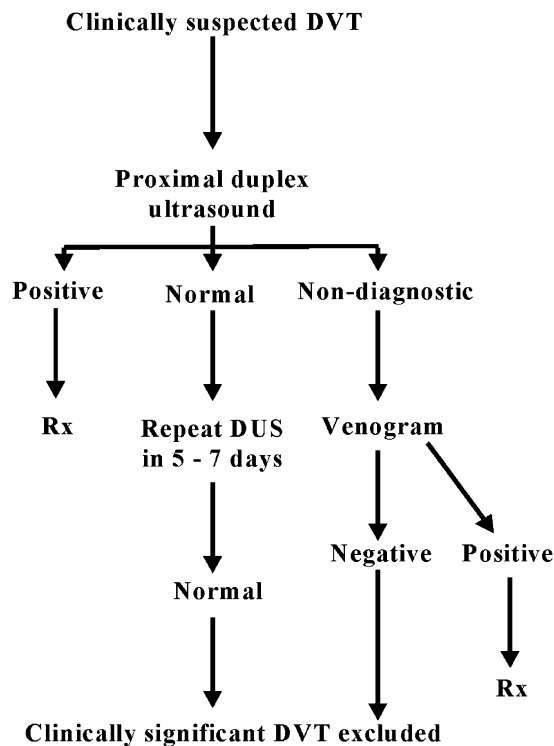


Fig. E-1

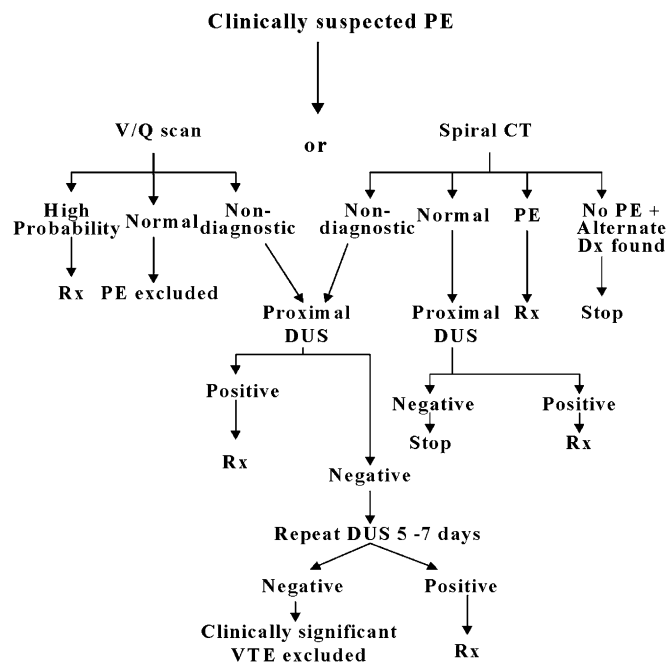


Fig. E-2

Fig. E-1 Standardized algorithm based on widely accepted, validated criteria for the appropriate and objective investigation and management of patients with suspected deep vein thrombosis (DVT). Rx = treatment and DUS = Doppler ultrasound. **Fig. E-2** Standardized algorithm based on widely accepted, validated criteria for the appropriate and objective investigation and management of patients with suspected pulmonary embolism (PE). CT = computed tomography, Rx = treatment, DUS = Doppler ultrasound, Dx = diagnoses, and VTE = venous thromboembolism.

TABLE E-1 Definition of Major Trauma

Body Region	Major Injury	Not a Major Injury
Head injury	Frank intracranial bleeding on CT scan Requiring craniotomy Requiring intracranial pressure device	Closed injury Normal imaging Considered too minor to justify imaging
Facial fracture	Requiring surgery	Not requiring surgery
Chest injury	Requiring thoracotomy, mechanical ventilation, or chest tube	Not requiring thoracotomy, mechanical ventilation, or chest tube Rib fracture Clavicle fracture
Abdominal injury	Requiring laparotomy With CT-proven hematoma or organ laceration	
Orthopaedic injury	Pelvic fracture Femoral/hip fracture Major soft-tissue injury Requiring surgery	Patellar fracture Fibular fracture Foot fracture Ligament/cartilage injury Upper-extremity fracture
Spine injury	With any neurologic deficit Requiring surgery Requiring halo vest or brace	Simple subluxation

TABLE E-2 Details of Confirmed Venous Thromboembolic Events

Age (yr)	Sex	Fracture Type	Fracture Treatment	Event
27	Male	Metatarsal	Surgery	Popliteal deep vein thrombosis
36	Female	Calcaneal	Conservative	Popliteal deep vein thrombosis
32	Female	Talar	Conservative	Calf deep vein thrombosis*
39	Male	Metatarsal	Surgery	Calf deep vein thrombosis*
48	Female	Lateral malleolar	Conservative	Calf deep vein thrombosis*
69	Male	Distal fibular	Conservative	Pulmonary embolism
58	Female	Bilateral tibial/fibular	Conservative	Pulmonary embolism

*These events were detected as protocol violations, as below-the-knee ultrasounds were not permitted in this study (see descriptions of the investigations for symptomatic deep vein thrombosis and pulmonary embolism in this Appendix).