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Review

Conservative treatment of venous thromboembolism

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SUMMARY

Venous thromboembolism is a frequent and serious vascular disease that can lead to serious complications. Rational and accurate establishment of the diagnosis enables early treatment that reduces the occurrence and severity of acute and chronic complications.

Conservative treatment of this disease has reached a turning point with the introduction of novel direct oral anticoagulants. According to present guidelines, standard treatment with low molecular heparines such as Fondaparinux and vitamine K antagonists still remain a clinically effective therapeutic option not only in the acute phase, but also in the secondary and long term prophylaxis of the disease. Direct oral anticoagulants represent an important alternative to conventional anticoagulants and appeared in new ESC recommendations of pulmonary embolism.

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1. Introduction

Deep vein thrombosis (DVT) is a common disease and represents a significant cause of mortality and morbidity mainly in hospitalised patients. According to literature annual incidence in general population counts at 0.5–1 case/1000 which in Germany amounts to 80 thousand new cases a year [1,2].

Pulmonary embolism (PE) is a potentially life-threatening acute complication of DVT that, for instance in the United States kills more women than breast cancer (approximately 60 thousand cases a year) [3].

In pregnant women it is the leading cause of death. In the EU, one out of ten deaths at in-patient departments is due to venous thromboembolism. Estimated annual mortality in connection with venous thromboembolism surpasses 500 thousand cases.

Post thrombotic syndrome, a serious late complication of DVT presenting months or years after the acute DVT significantly reduces the quality of life in the long run.

According to 2007's "report of the independent expert working group on the prevention of venous thromboembolism in hospitalised patients" the estimated annual incidence of venous thromboembolism in 25 member states of the EU with 454 million inhabitants amounts to 640 thousand cases of DVT and 383 thousand cases of pulmonary embolism.

2. Diagnosis of DVT and PE

Clinical presentation and symptoms of DVT are non-specific. Raising suspicion of DVT is the crucial point in setting off diagnostic-therapeutic cascade. The commonest presenting symptom is a unilateral, sudden swelling of a limb. Commonest complaint of verified DVT patients is a feeling pain or of tension in the affected

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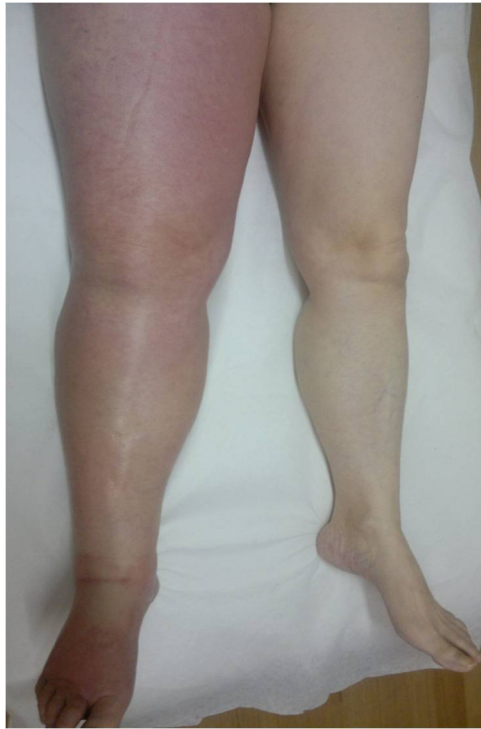


Fig. 1. Clinical presentation of extensive proximal phlebotrombosis as per Phlegmasia coerulea dolens.

limb. Cyanosis and accentuated venous filling are among other common findings. All suspicious findings should be verified given the potential for serious complications.

Clinical history and physical examination alone lead to diagnosis in only 10–20% of cases thus are not sufficient to verify the diagnosis (Fig. 1).

Wells scoring system is another strategy that relies on Clinical Probability (CP) based on clinical criteria, risk factors for DVT, preceding conditions and co-existing diseases (Table 1). This way, two, maybe three distinct groups of patients (9% representing low CP, 52% representing high CP) showing different prevalence of DVT can be demonstrated. Patients with high probability should be directed straight away to an imaging modality (most commonly compressive ultrasound), whereas low CP patients will need a D dimer level test [4]. D dimers are degradation products of fibrin in a blood clot, hence point to the presence of a blood clot and increased fibrinolysis. D-dimer level is a sensitive but highly non-specific parameter. Elevated D dimer levels can be found in an array of conditions such as pregnancy, post-surgery, trauma, tumours and infections as well as in the elderly. The value of the

Table 1
Assessment of clinical probability of DVT according to Wells scoring system.

Clinical characteristics	Score
Presence of tumour	1.0
Short term lower extremity immobilisation or paralysis	1.0
Bed ridden { > 3 days}, complex surgery { < 12 weeks}	1.0
Pain/induration along deep veins	1.0
Swollen limb	1.0
Swollen calf > 3 cm compared to the other	1.0
Compressible oedema of affected limb	1.0
Collateral veins	1.0
Documented past history of DVT	1.0
Other diagnosis as likely as DVT	-2.0
Score ≥ 2.0: high probability of DVT	
Score < 2.0: low probability of DVT	

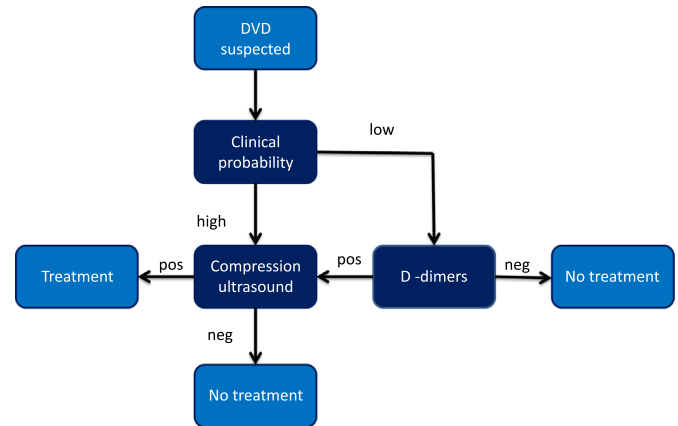


Fig. 2. Diagnostic flow-chart of DVT.

D-dimer test lies in its high negative predictive value. The high sensitivity D dimer test is able to exclude DVT 93–96% accuracy [4]. One must take into account, that the information provided by the most commonly used bed side tests, both qualitative and semi quantitative are considered to be moderately sensitive. D-dimer test alone is not suitable for the exclusion of DVT [5]. The proper and systematic use of risk stratification by CP evaluation and D-dimer testing may lead to a 40–50% reduction in ultrasound scan numbers. Low clinical probability and normal D-dimer levels reliably exclude DVT eliminating need for further investigation (Fig. 2). This approach is quite reasonable especially in the outpatient setting, since D-dimer levels in hospitalised patients often tend to be elevated due to co-morbidities.

At present diagnosis of DVT heavily relies on duplex ultrasonography. It is a modality that is readily available, highly reliable, sensitive, non-invasive with no known biological side effects. Above all in hands of an experienced sonographer this technique offers vast amount of information on organ morphology and their function. It is an invaluable tool in differential diagnostics. A non-compressible vein with the demonstration of intraluminal thrombus (Fig. 3) or absence of blood flow makes the diagnosis of DVT certain (Fig. 4). Significant dilatation of the affected vein is a common finding. Absence of or modified venous ultrasound signal with no or reduced fluctuation of flow with breathing make the diagnosis of DVT likely. Absence of flow fluctuation upon breathing in groin area point to thrombosis in iliac veins. Absence of reaction to Valsalva manoeuvre likewise is a sign of proximal DVT. Collaterals bridging clogged vein segments are a sign of older DVT.

Clinical presentation of pulmonary embolism is similarly non-specific as in DVT: sudden onset shortness of breath, cough, syncope, haemoptysis, tachypnoea, tachycardia and cyanosis [6]. Massive pulmonary embolism often leads to severe hypotension and cardiogenic shock. All suspicious cases therefore need immediate evaluation. Hemodynamic compromise in a patient with suspected PE is highly significant for it plays a major role in patient mortality in the acute phase of the disease.

After the clinical probability assessment with help of Well's or revised Geneva scoring system (low, intermediate or high clinical probability of DVT, pulmonary embolism likely or unlikely) an imaging technique should be used for definitive establishment of diagnosis.

In high risk, hemodynamically unstable patients CT angiography (Fig. 5) should be performed without delay. Increasingly though bedside echocardiography is performed to verify the diagnosis. Urgent actions like thrombolysis, endovascular techniques or surgical procedures (embolectomy) save lives.

In stable, suspected PE patients (non high risk) a CT angiography guided algorithm is preferred to establish the diagnosis.

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