Venous thrombosis and pulmonary embolism (VTE)

hans.johnsson@karolinska.se

Thrombi may arise in all (?) venous vascular areas including the pulmonary arteries and veins.
Risk factors, pathogeneses, treatment and consequences differ dependent of its localization.
Most frequently thrombosis arise in different vein segments of the extremities (DVT).In the lower limbs (95%) and more infrequent in the upper limbs.
Only about 10 % of all thrombi are symptomatic, diagnosed and properly treated. Most thrombi are not symptomatic. Some are small and most probable naturally occurring, making no harm. But a mayor part that are not diagnosed, overlooked or found at autopsy would have benefitted treatment to inhibit progression, clinical symptoms and PE.
In spite of more and more generally used prophylactic therapies in different situations and information to the citizens' incidence of DVT and pulmonary embolism (PE) does not decline in the modern society.
Incidence varies in different parts of the world and increase with increasing age. It is more frequently occurring during winter periods, in the end of the week and in black people. Women are especially affected; because of pregnancy, contraceptive pills and hormonal replacement therapy.

Symtomatic VTE in some situations without prophylactic treatment

- General population: 1/5 000 < age 30, 1/500 > age 70
- Long air flight: Absolute risk 1/ 4 500 flights
- In hospital medical ward: 0,5-4 % depended of individual risk factors
- Plastic surgery: < 0,5%-> 3 % deepened of surgery and individual risk factors
- Orthopedic surgery: 5-> 20 % depended of surgery and if it is acute or elective

Risk factors for VTE and observational risk (OR)

- ***Some cannot be modified***
- Previous thrombosis (15-35)
- Non provoked VTE (increased recurrence rate)
- Thrombophilia (1-2 in the majority, 10-40 in some, very infrequent, extreme forms)
- Gender (2x more recurrences in males)
- Age, blood group
- **Others are acquired or transient, environmental**
- Cancer (> 6)
- Proximal thrombosis and massive PE (increased recurrence rate)
- Surgery, trauma, central venous catheters, lines and devices (5-20)
- Cardiovascular risk factors, CVD, hypertension, diabetes, obesity (4-5)
- Contraception (5-10)
- Pregnancy (6-10)
- Long sitting in air planes, busses, in front of computers or in the canoe (2-3)
- Persistent elevation of D-dimer (2x increased risk of recurrence)

Consequences of VTE

- Post thrombotic symptoms; (5-10%) Significant venous claudication and lower abdominal discomfort due to proximal vein obstruction, edema and leg ulcer because of venous valve insufficiencies
- High rate of recurrences; (2-10% annually). About 40 % within the next eight years after unprovoked VTE, VTE associated with cancer or after repeated DVT, irrespective anticoagulant treatment for 3, 6, 12, or 24 months. Compared to less than 5 % after VTE provoked by a temporary risk factor in young otherwise healthy persons. Symptomatic PE reoccurs mostly as PE and massive PE reoccurs more

often than small PE. Symptomatic DVT reoccurs mostly as DVT and proximal DVT reoccurs and send emboli to the lungs more often than isolated distal DVT.

- Pulmonary thrombotic hypertension (0,5-3 %) due to chronic pulmonary embolism or thrombosis
- High mortality rate (in general 10-20%) within next 6-12 months due to malignancy, cardiovascular disease, right heart failure or other co morbid conditions
- Decreased quality of life and risk of bleeding complications because of anticoagulant treatment

Treatment, recommendations and options

First acute phase (1-5 days)

- ***Massive PE***
- Intensive care in supine position with oxygen support**!** Parenteral anticoagulant treatment alone or in combination with thrombolytic, endovascular or surgical treatment.
- ***Submassiv PE or DVT***
- Oral or parenteral anticoagulant treatment, ambulatory or in hospital ward
- ***Massiv proximal DVT***
- Intensive care. Parenteral anticoagulant treatment alone or in combination with thrombolytic, endovascular (or surgical) treatment
- ***Isolated distal DVT in the lower limbs; options***
- Treatment with oral or parenteral anticoagulants (1-3 months)
- No anticoagulant treatment in case of low clinical suspicion, without special risk factors for VTE and negative D-dimer test
- Delay treatment with anticoagulants 4-6 days, in the absence of special risk factors, if the thrombosis at that time has extended into proximal veins.

After the first acute phase (2-6 months); against progression of the active DVT and PE

- Oral or parenteral anticoagulant treatment

Secondary prophylaxis and treatment after the active phase against recurrent DVT and PE (unlimited time); options

- Continuous oral or parenteral anticoagulant treatment
- Oral or parenteral anticoagulant treatment on demand
- Acetylsalicylic acid (?)
- Statins (??)
- Cardiovascular risk factors
- Compression stocking
- Endovascular or surgical treatment of chronic vein obstruction and chronic PE.

Old and new anticoagulant drugs

- Parenteral; heparin, low molecular weight heparin, fondaparinux (Arixtra®)
- Oral ; warfarin, thrombin inhibitor (dabigatran Pradaxa®), factor X inhibitor (rivaroxaban Xarelto®, apixaban, betrixaban, edoxaban and other in trials)

Old and new thrombolytic agents

- Streptokinase, urokinase. Indirect action, bleeding risk
- Alteplas (Actilyse®), reteplas (Rapilysin®) Indirect action, bleeding risk
- Plasmin (experimental) Direct action, low or no bleeding risk (?).