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Treatment Strategy

Risk stratification:

 Rapid and accurate risk stratification before starting treatment is of paramount importance. The 3 key components for risk stratification are:
 (1) clinical evaluation, which can be undertaken systematically based on bedside history& physical examination.





(2) Biomarkers such as Troponin, pro-BNP, and BNP. (3)Assessment of Rt ventricular function with Echo.







Treatment:

A- General supportive measures:

- 1- Hemodynamic& respiratory support:
 - Dobutamine& dopamine or amrinone may be used in patients with PE, low cardiac index and normal BP.
 - Vassopressor drugs may be used in hypotensive patients with PE.

- The usefulness of fluid challenge is controversial& should exceed 500 ml, while monitoring CVP.

-Oxygen to correct hypoxia.

2- Analgesics for pain e.g pethidine or NSAD.





B- Anticoagulation:

- 1- Heparin:
- With strong clinical suspicion of PE, IV heparin should be started immediately without laboratory confirmation of the diagnosis unless there is contraindications (e.g recent or active bleeding).
- Initial large IV bolus of 5000 to 10.000 u should be given to inhibit platelet aggregation and release reaction, followed 24 hs later by continuous IV heparin infusion at about 1000 u/h. Partial PTT should be maintained as 1.5-2 times the control value.





- Heparin infusion should be continued for 7-10 days to allow for dissolution and/or organization of the pulmonary embolus (and deep vein thrombi).
- Heparin prevents extension and recurrence of thrombo-emboli, enhance fibrinolytic dissolution and inhibit platelet aggregation and consequently serotonin& thromboxane.





- 2- Low-molecular weight heparin (LMWH): has been shown to be as effective as UFH in the treatment of VTE.
- It has the advantages of predicatable rapid antucoagulation, a simple s.c dosing regimen, and no need for lab monitoring.
- LMWH only used in patients with symptomatic non massive stable PE.
- Enoxaparin is given in a dose of 1.0 mg/kg twice daily.





3-Oral anticoagulant:

- If the risk factors that precipitate the PE (or DVT) are still existing, warfarin is initiated on day 2 or 3 of heparin therapy.
- prothrombin time should be maintained at 1.5-1.8 times the control value, and an INR between 2-3.
- Treatment is started with a daily maintenance dose 5 mg. No need to start with a bolus dose.
- The optimal duration of treatment should be based on the recurrence risk of the specific patient.





• Low-risk of recurrence is seen in:

- Isolated distal DVT, or if the DVT or the PE is caused by a temporary or reversible risk factor.
- In patients with heterozygous factor v leiden or with heterozygous prothrombin mutation. Treatment duration in these low risk situations may be 3-6 months.
- High_risk of recurrence is seen in:
 - Proximal DVT and PE, especially in case of continuity risk factors like immobilization, cancer.
 - Groups of patients with severe diseases that Cannot be cured.



n idiopathic cases.

- these high-risk situations treatment duration should be at least 6 months(6-12).
- e very high-risk is seen in:
- Patients with homozygous factor v leiden and prothrombin mutation, anti-thrombin deficiency or if cardiolipin antibodies or upus inhibition is present in the circulation.



Also in case of combined thrombophilia with protein C deficiency and factor V leiden or prothrombin mutation and in patients with a second VTE.

n this very high-risk situations, long term oral AC- therapy.

The actual duration of oral AC- therapy in hese cases should not only be based on risk evaluation but also on an evaluation each year of quality of treatment.



So long as the risk stratification is based on dentification of thrombophilia, therefore hrombophilia screening should be performed before the start of AC-therapy in some clinical situations:

- Patients under 50 years with recurrent idiopathic PE.
- Patients with a strong family history.
- Recurrent fetal loss & still birth with severe thrombotic events.

Cimelagatran: is a new oral direct thrombin nhibitor that does not need anticoagulation nonitoring. It has a wide therapeutic range but needs monitoring of liver functions tests



Thrombolytic therapy:

- Streptokinase, urokinase or t-pa are given for highisk group (i.e patients with massive PE with shock and/or persistent systemic hypotension o those with extensive thrombosis (e,g ilio-femoral).
- An I.V injection of 100 mg of alteplase given over 90 ninutes.
- The use of thrombolysis in submassive PE with Rt ventricular hypokinesia detected by Echo is controversial.
- t is not recommended in patients without Rt ventricular over-load.



Pulmonary embolectomy:

- t is indicated for patients with massive life hreatening PE with cardiogenic shoch who emain critically ill despite medical treatment.
- Open pulmonary embolectomy carries a nortality rate of 30%.
- Fransvenous catheter suction or ragmentation of the pulmonary embolus are proaches.



Venous filters:

VC interruption (by placing filters: greenfield filters in the IVC) are indicated o prevent PE in patients with either absolute contraindication to AC-therapy or n patients who suffer from recurrent VTE despite adequate AC-therapy.

VC filters are probably indicated after surgical embolectomy.



Retrievable IVC filters require further study o validate their use. It can be left in place or 10-14 days or can remain permanent. n pelvic septic thrombophlebitis IVC

nterruption is carried out by ligation.



eatment of PE in special situations

<u>PE in pregnancy:</u>

- oral AC cross the placenta $\& \rightarrow$ abortion and embryopathies in the 1st trimester, therefore it is contrandicated.
- eparin is given during the 1st trimester & during the last six weeks before delivery due to bleeding risks.
- MWH are the long term treatment of choice during pregnancy and safe.
- All diagnostic modalities including spiral CT and angio nay be used without a significant risk to the fetus.



VTE in abnormal sites such as upper limbs:

- No thrombolytic therapy.
- Thrompophilia screening should be done first.
- If negative, AC therapy should be given for 3-6 months.

Management of unsuccessful thrombolysis in acute PE:

- Rescue surgical embolectomy.
- f there is contraindication to CT or IV contrast, V/Q can can be done.

PE in elderly :

The diagnosis of PE is missed in geriatric population because respiratory symptoms are chronic in elderly isually dismissed.



ophylactic Treatment:

Low-dose heparin for patients undergoing horacic or abdominal surgery or subjected o prolonged bed rest. It is given as 5000 u 2hs prior to surgery and then 5000u /8-12 hs bost-operatively.

MWH e.g enoxaparin 30 mg s.c given 2 hs prior to surgery and then every 12hs postoperatively. It is useful in general& orthopedic surgery.



Warfarin in a dose that yields a PT equivalent to an INR of 2-3 is effective in oone fractures& orthopedic surgery. It is started the night before surgery and continued throughout convalescence. External pneumatic compression devices applied to the legs are used when anticoagulants might cause serious pleeding, during neurosurgery or transirothral resection of the prostate



n hospitalized patients the following nonpharmacological methods are helpful:

- Elevation of the foot of the bed to 15-20 degrees.
- Early ambulation& regular leg exercises.
- Elastic Anti-phlebitic stocking (graduated compression stocking) particularly for patients with varicose veins or a history of phlebitis.



Flight prophylaxis:

 Current British guidelines suggest aspirin or LMWH or oral AC for people at high risk of PE (previous VTE or malignancy), especially in economy class syndrome associated with long distance sedentary travel >8 hs.





