What is the impact of Superficial Vein Thrombosis?

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Disclosure

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I have no financial relationship(s) to disclose.
Background

✓ ST is considered as minor condition with few complications and a good prognosis

✓ Evidence suggests that it is not so benign and can be associated with venous thromboembolism, hypercoagulable states and malignancy
Demographic characteristics

- Incidence in the general population: 3-11%
  May be underestimated (pts with minor symptoms, not present for medical attention)
- Female/male ratio: 6 to 4
- Mean age of presentation: 60 yrs
- Often two or more factors have to be present
- Age is important; the older the patient, the fewer factors are needed
VVs and STP

• Prevalence of STP in pts with VVs: 4-59%
• GSV system involved in 60-80%
• SSV system involved in 10-20%
• Bilateral: 5-10%
• STP more frequently confined to varicose tributaries
• Mechanisms: defect in fibrinolysis & PLT aggregation (further work is needed)
VVs and STP
Hypercoagulable states & STP

• Saphenous trunk thrombosis denotes often a more significant thrombotic process.

• In the absence of VVs, malignancy, and autoimmune diseases the risk of STP was:
  - 6-fold for factor V Leiden mutation
  - 4-fold for factor II G20210A mutation
  - 13-fold for anti-thrombin III, protein C & S deficiency
Hypercoagulable states & STP

- Pts with STP without VVs have high prevalence of hypercoagulable states (3.6-72%)

- Arguably pts with spontaneous STP without VVs, or when thrombosis is extending to the GSV main trunk should be screened for hypercoagulability
Pregnancy & STP

• Information limited: 2 studies & both may have underestimated the prevalence as only symptomatic pts were evaluated

• 14 (0.05%) cases in 30,040 pregnancies diagnosed by D/S, within 48 hrs of delivery

  James et al, Cardiovasc Surg 1996

• 49 (0.068%) in 72,200 deliveries (10 prior)

Malignancy & STP

• Malignancy in 13% among 106 limbs with STP
  *Barrellier MT, Phlebologie 1993*

• Malignancy 18% among 56 limbs with ascending STP from 398 limbs with STP in the GSV or SSV system
  *Krause et al, Vasa 1998*

• With the exception of these two retrospective studies the relationship of STP with malignancy appears to be weak in the literature and further work is needed
  *Naschitz et al, Angiology 2003*
DVT & STP

- DVT in association with STP: 6-53%
- Thrombus propagation can occur in a contiguous or in non-contiguous fashion
- Contiguous:
  a. extension from GSV into CFV
  b. extension from SSV into POPV
  c. extension through perforators
  d. extension from deep to superficial veins?
Thrombosis extension to SFJ
DVT & STP

✓ Prevalence of DVT with STP in the presence of VVs was 13% and 24.5% in two studies

Skillman et al, J Vasc Surg 1990
Jorgensen et al, J Vasc Surg 1993

✓ STP at GSVak and DVT: 17-19%
STP at GSVbk and DVT: 4-5%

Bergqvist & Jaroszewski, BMJ 1986
PE & STP

• Most studies available included small number of patients

• Prevalence ranges from 1.5% to 33%
  - Zollinger et al, Arch Surg 1962
  - Unno et al, Surg Today 2002
  - Verlato et al, J Vasc Surg 1999

• Unclear whether PE associated with STP arises from clot extended into the deep veins or from clot detachment when it is confined to superficial veins
Diagnostic approach

• Poor correlation between clinical exam and surgical findings

  *Gjores JE, Angiology 1962*

• Most of the literature recommends D/S for confirmation of diagnosis, STP extension, DVT exclusion, and F-up
Diagnostic approach

Three identifiable patterns of STP on D/S:

a. short segment associated with VVs (no further work up)
b. short segment without VVs (possibility of systemic disease)
c. extensive saphenous STP (high possibility of concurrent DVT and risk of PE)
Considerations in the management

Problems in the literature

a. Lack of consistency in the end points
b. Inadequate F-Up
c. Small number of patients
d. Limited evaluation to rule out VTE
e. Most of retrospective nature
Considerations in the management

✓ No place for antibiotics

✓ The role of aspirin and NSAIDs orally or locally and hirudoid locally is not well defined. Mostly alleviate the pain and local inflammatory signs

✓ LMWH or heparin (evidence in the DVT treatment)

✓ STENOX study: LMWH (10 days) better than ES or NSAIDs but only in regard to thrombus extension but not for development of VTE

*Ach Intern Med 2003*
Fondaparinux for the Treatment of Superficial-Vein Thrombosis in the Legs

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BACKGROUND
The efficacy and safety of anticoagulant treatment for patients with acute, symptomatic superficial-vein thrombosis in the legs, but without concomitant deep-vein thrombosis or symptomatic pulmonary embolism at presentation, have not been established.

METHODS
In a randomized, double-blind trial, we assigned 3002 patients to receive either fondaparinux, administered subcutaneously at a dose of 2.5 mg once daily, or placebo for 45 days. The primary efficacy outcome was a composite of death from any cause or symptomatic pulmonary embolism, symptomatic deep-vein thrombosis, or symptomatic extension to the saphenofemoral junction or symptomatic recurrence of superficial-vein thrombosis at day 47. The main safety outcome was major bleeding. The patients were followed until day 77.
RESULTS

The primary efficacy outcome occurred in 13 of 1502 patients (0.9%) in the fondaparinux group and 88 of 1500 patients (5.9%) in the placebo group (relative risk reduction with fondaparinux, 85%; 95% confidence interval [CI], 74 to 92; \( P < 0.001 \)). The incidence of each component of the primary efficacy outcome was significantly reduced in the fondaparinux group as compared with the placebo group, except for the outcome of death (0.1% in both groups). The rate of pulmonary embolism or deep-vein thrombosis was 85% lower in the fondaparinux group than in the placebo group (0.2% vs. 1.3%; 95% CI, 50 to 95; \( P < 0.001 \)). Similar risk reductions were observed at day 77. A total of 88 patients would need to be treated to prevent one instance of pulmonary embolism or deep-vein thrombosis. Major bleeding occurred in one patient in each group. The incidence of serious adverse events was 0.7% with fondaparinux and 1.1% with placebo.

CONCLUSIONS

Fondaparinux at a dose of 2.5 mg once a day for 45 days was effective in the treatment of patients with acute, symptomatic superficial-vein thrombosis of the legs and did not have serious side effects. (Funded by GlaxoSmithKline; ClinicalTrials.gov number, NCT00443053.)
Consideration of the generally “acceptable” failure rates in strategies to diagnose venous thromboembolism

**CALISTO**: rate of symptomatic DVT or PE in untreated pts was 1.3%

Among pts evaluated for suspected DVT but with normal venogram or DS, 1.3% & 0.6% respectively, will return with symptomatic DVT or PE

_Hull et al. Circulation 1981;64:622_
_Johnson et al. JAMA 2010;303:438_

Among pts with suspected PE but with normal conventional or CT pulmonary angiogram, 1.7% & 1.2% respectively, will return with symptomatic DVT or PE

_vanBeek et al. Clin Radiol 2001;56:838_
These historical comparisons and the extremely low mortality among untreated pts with STP support an initial “no anticoagulation treatment” approach unless conservative measures fail to resolve symptoms or DVT develops.

Treatment with Fondaparinux for 45 days may be reasonable in case of severe symptoms, thrombosis in the proximal saphenous vein, or in recurrent disease.

Cost-effectiveness issues
Therapy with Fondaparinux 2.5 mg daily for 45 days costs $2,124 to $7,380.
Considerations in the management

✓ Surgical treatment
  a. local thrombectomy
  b. SFJ ligation and stripping or vein excision

✓ Selection of patients with favourable risk/benefit profile for surgical treatment is a problem due to the lack of RCTs against anticoagulation
STP on a varicose GSV close to SFJ
Considerations in the management

- **ES** should be used in all cases as adjunctive treatment
- STP away from SFJ, SPJ, or at the bk segment without associated DVT: **ES**, NSAIDs, or aspirin
- STP associated with DVT: anticoagulation
- STP close to SPJ or SFJ: anticoagulation or thrombectomy and ligation ± stripping
Considerations in the management

- Patients with STP treated conservatively with ES, NSAIDs, or aspirin require F-Up (clinical or D/S) in about 7-10 days

- If symptoms worsen or D/S evidence of clot propagation: anticoagulation or surgery
GSV mature thrombus with recanalisation
Conclusions

- Prospective studies with consistent end points and large number of patients are needed to define the natural history (pathogenesis, progression, DVT, PE) of STP and its association with other pathologies.

- RCTs are needed to establish the best treatment in various settings of STP and to evaluate their cost-effectiveness.
May 5-8, 2011
Sani Beach Hotel, Chalkidiki, Greece
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Institute of Vascular Diseases, Greece

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