SVT TREATMENT CHOICES IN PREGNANCY

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DISCLOSURES

- Society/educational board member: AVF (Secretary), EVS (Immediate past President), VLU (Board member), ISWVS (Secretary)
- ADVISORY BOARD/SPEAKER
  - MEDTRONIC
  - BOSTON SCIENTIFIC
  - CONVATEC
  - TERUMO
- BOARD PARTICIPATION
  - CDPHP
  - IAC

CLASSIFICATION OF SVT

- 1. primary SVT in varicose veins followed by sterile inflammation of the vein wall
- 2. non varicose vein SVT
  - Chest wall
  - Penile
  - Axillary web syndrome post axillary surgery
- Kalodiki E, Stvrtinova V, Allegra C, et al. Superficial vein thrombosis: a consensus statement. *Int Angiol.* 2012;31(3):203–216.

SVT

- SVT was considered benign and self limiting
- Today, SVT is perceived as a manifestation of blood hypercoagulability and inflammation of the vessel wall
- Prevalence of lower extremity SVT is 2x higher than both DVT and PE in the general population
- 10% of patients with SVT will present with DVT or PE within 90 days of onset of symptoms
- Asymptomatic DVT was found concurrently in 18.1%, and PE in 6.9% of patients with SVT.

RISK FACTORS

- Age over 35
- Overweight
- Varicose veins
- Smoking
- History of DVT/PE
- Muliparity
- Immobilisation
- HTN
- Pre eclampsia
- C section
- Inherited thrombophilia
- Acquired thrombophilia
- Convincing evidence is available that deficiency of antithrombin III (AT), protein C (PC), and protein S (PS) is a risk factor for VTE and late Fetal Loss.
- Factor V (Leiden) is associated with an increased risk for VTE, unexplained recurrent FL, late FL, and perhaps Pre-eclampsia; prothrombin G20210A is a weak risk factor for V

Inherited thrombophilia, pregnancy, and oral contraceptive use: clinical implications
Valerio De Stefano, et al sem vasc med 2003

POSITION PAPER ON THE MANAGEMENT OF PREGNANCY-ASSOCIATED SUPERFICIAL VENOUS THROMBOSIS. BALKAN WORKING GROUP FOR PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM

DARKO ANTIC, ET AL

- GSV is affected in 60-80%, SSV affected in 10-20%*

1. SVT can be indicative for coexisting DVT or PE,
2. isolated SVT can be complicated by extension to DVT and/or PE,
3. SVT is confirmed as risk factor for recurrence of DVT or PE

Di Minno MND, et alPrevalence of deep vein thrombosis and pulmonary embolism in patients with superficial vein thrombosis: a systematic review and meta-analysis. *J Thromb Haemost.* 2016;14(5):964–972

INCIDENCE AND PROGNOSIS OF SUPERFICIAL VEIN THROMBOSIS DURING PREGNANCY AND THE POST-PARTUM PERIOD: A DANISH NATIONWIDE COHORT STUDY

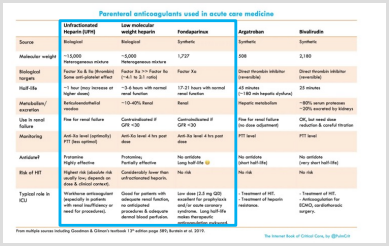
HANKE M G WIEGERS, ET AL
LANCET HAEMATOL 2023

- 1.2 million pregnancies, 710 SVT diagnoses from conception to 12 weeks post partum.
- Incidence was highest in the third trimester
- Of the 211 women with antepartum SVT, 22 were diagnosed with VTE
- Conclusion:
  - SVT incidence is low
  - Once SVT was diagnosed the risk of developing venous thromboembolism during the same pregnancy was high

ANTICOAGULANTS NOT USED IN PREGNANCY

- Warfarin
- DOACs

ANTICOAGULANTS



Parenteral anticoagulants used in acute care medicine

	Unfractionated heparin (UFH)	Low molecular weight heparin	Fondaparinux	Argatroban	Bivalirudin
Source	Biological	Biological	Synthetic	Synthetic	Synthetic
Molecular weight	~5,000 Heterogeneous mixture	~5,000 Heterogeneous mixture	1,727	508	2,180
Biological targets	Factor Xa & IIa (thrombin) Some anti-platelet effect	Factor Xa >> Factor IIa (~4:1 to 3:1 ratio)	Factor Xa	Direct thrombin inhibitor (reversible)	Direct thrombin inhibitor (irreversible)
Half-life	~1 hour (may increase at higher doses)	~3-4 hours with normal renal function	17-21 hours with normal renal function	45 minutes (~180 min hepatic dysfunc)	25 minutes
Metabolism/ excretion	Reticuloendothelial reuptake	~10-40% Renal	Renal	Hepatic metabolism	~80% serum proteases ~20% excreted by kidneys
Use in renal failure	Fine for renal failure	Contraindicated if GFR <30	Contraindicated if GFR <30	Fine for renal failure (no dose adjustment)	OK, but need dose reduction & careful titration
Monitoring	Anti-Xa level (optimally) PTT (less optimal)	Anti-Xa level 4 hrs post dose	Anti-Xa level 4 hrs post dose	PTT level	PTT level
Antidote?	Protamine Highly effective	Protamine, Partially effective	No antidote Long half-life	No antidote (short half-life)	No antidote (very short half-life)
Risk of HIT	Highest risk (absolute risk usually low, depends on dose & clinical context)	Considerably lower than unfractionated heparin.	No risk	No risk	No risk
Typical role in ICU	Workhorse anticoagulant (especially in patients with renal insufficiency or need for procedures).	Good for patients with adequate renal function, no anticipated procedures, & adequate dermal blood perfusion.	Low dose (2.5 mg QD); excellent for prophylaxis and/or acute coronary syndrome. Long half-life makes therapeutic anticoagulation awkward.	- Treatment of HIT. - Treatment of heparin resistance.	- Treatment of HIT. - Anticoagulation for ECMO, cardiothoracic surgery.

From multiple sources including Goodman & Gilman's textbook 13th edition page 585; Burstein et al. 2019.

The Internet Book of Critical Care, by @IntCrit

FONDAPARINUX AND ENOXAPARIN

- Fondaparinux is a factor Xa inhibitor and does not inhibit thrombin (IIa). Will NOT cause HIT
- Enoxaparin on the other hand, binds to antithrombin to form a complex molecule that can irreversibly inactivate clotting factor Xa and it has less activity against thrombin
- **monitoring Xa level for prophylactic enoxaparin**
- **Indications:**
  - **Pregnancy.**
  - **Borderline renal function (note that GFR <30 ml/min is a contraindication to enoxaparin).**
  - **Morbid obesity.**

TREATMENT BENEFITS OF FONDAPARINUX AND LMWH IN NON PREGNANT PATIENTS

- Fondaparinux 2.5 mg subcutaneously once per day for 45 days in **nonpregnant** patients with acute, symptomatic lower-limb superficial vein thrombosis at least 5 cm in length **reduced the risk of developing VTE to 0.2% from 1.3% and of recurrent superficial vein thrombosis to 0.3% from 1.6%** **may cross the placenta*
- LMWH at various doses and for various durations (maximum of 30 days) **seemed to reduce the risk of VTE to 2.9% from 4.4%** in the **nonpregnant** population, but this was pooled across various comparators, including placebo, aspirin, nonsteroidal anti-inflammatory agents, and compression stockings

Decousus H, et al.; CALISTO Study Group. Fondaparinux for the treatment of superficial-vein thrombosis in the legs. *N Engl J Med*. 2010;363(13):1222-1232.

Di Nisio M, et al Treatment of lower extremity superficial thrombophlebitis. *JAMA*. 2014;311(7):729-730

SUMMARY OF EVIDENCE

American Society of Hematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy

Shannon M. Bates,[1] Anita Rajasekhar,[2] Saskia Middeldorp,[3] Claire McLintock,[4] Marc A. Rodger,[5,6] Andra H. James,[7] Sara R. Vazquez,[8] Ian A. Greer,[9] John J. Riva,[10,11] Meha Bhatt,[12] Nicole Schwab,[13] Daniella Barrett,[14] Andrea LaHaye,[15] and Brian Rochwerg[16,17]

- There were no direct data from either randomized trials or observational studies that examined the effect of treatment of acute superficial vein thrombosis specifically in pregnant patients.
- No studies reported the risk of neonatal bleeding or congenital malformation specifically in the population of pregnant women with superficial vein thrombosis.

RECOMMENDATION:

- For pregnant women with proven acute superficial vein thrombosis, the ASH guideline panel *suggests* that **LMWH be used** over not using any anticoagulant (conditional recommendation, low certainty in evidence about effects)
- Treatment should continue for 6 weeks post partum

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- Conclusions and research needs for this recommendation
- The guideline panel determined that there is a **low certainty** in evidence for a net health benefit from using anticoagulant interventions for acute superficial vein thrombosis. For more distal or less symptomatic superficial vein thrombosis and for patients who are needle averse, the benefits of intervening may be less. On the basis of the body of available evidence, it is likely that anticoagulant interventions reduce the risk of developing VTE. There is low certainty that there is an effect of these interventions on other outcomes. **However, because of very low certainty in evidence or no published information about other outcomes, lack of better evidence is not proof that such an effect does not exist and does not allow firm conclusions.**

MY THOUGHTS

- High index of suspicion
  - Physical exams
  - Ultrasounds are simple to perform
- Should be a multidisciplinary approach
  - OB
  - Hematology/vascular medicine
  - Vascular specialist
- Close observation with patient education