Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P38
March 20th, 2025

Antenatal Venous Thromboembolism and the performance of risk assessment tools

S. Milne[1], J. Lennon[1], C. Manning[1], K. Ryan[2], S. Lindow[1], B. Byrne[1]

1. Department of Obstetrics and Gynaecology, Coombe Women and Infants University Hospital, Cork Street, Dublin 8, Ireland.
2. Department of Haematology, St. James's Hospital, Dublin 8, Ireland.

Abstract

Aim

The aim of this study was to identify the prevalence of risk factors in women who developed an antenatal VTE and determine whether they met criteria using various risk assessment tools for antenatal thromboprophylaxis.

Methods

A retrospective study was conducted of 63 cases of antenatal VTE's. A chart review was conducted to risk assess each patient using the RCOG, HSE and Coombe VTE prophylaxis tools to determine if they met criteria for antenatal thromboprophylaxis.

Results

No risk factors were identified in 21/63 (33%) of the VTE group compared to 63/126 (50%) of the control group ($p<0.05$). Of the VTE group, 12/63 (19%) met RCOG criteria for prophylaxis compared to 2/126 (1.6%) of the control group (chi-sq 19.1, $p<0.001$). Using the Coombe criteria 7/63 (11%) of the VTE group versus 1/126 (0.8%) of the control group met criteria (chi-sq 8.7, $p<0.05$). There was a statistically significant difference (chi-sq, 9.2, p+0.01) between the groups when assessed using the HSE VTE prophylaxis tool with 6/63 (9.5%) of the VTE group and 1/126 (0.8%) of the control group meeting criteria.

Discussion

Risk assessment tools are helpful in predicting women at risk of developing VTE compared to controls, but do not identify the majority of cases.

Introduction

The term venous thromboembolism (VTE) encompasses two conditions, namely deep vein thrombosis (DVT) and pulmonary embolism (PE). The incidence of VTE is increased four to six-fold in pregnancy due to changes in physiology leading to increased venous stasis in the lower

limbs and changes in the coagulation system, including an increase in the procoagulant factors X, VIII and fibrinogen and a decrease in protein S activity along with suppression of fibrinolysis and a decrease in endogenous anticoagulant activity. It is estimated that VTE complicates 1-2 in every 1000 pregnancies[1] and although uncommon, remains the leading cause of direct maternal mortality in the developed world with an incidence of 0.92 per 100,000 pregnancies from 2017-2019 in the UK and Ireland[2]. While VTE is more common in the postpartum period, VTE related deaths can occur in all three trimesters of pregnancy[3].

Factors that are known to increase the risk of VTE in the general population can increase the risk in pregnancy, but the absolute risk is unclear. Not alone are there pre-existing risk factors for VTE, there are also pregnancy-associated and transient risk factors[4], making risk assessment in pregnancy complex. This has led to the development of risk assessment tools (RATs). One example of a RAT for VTE in pregnancy is the Royal College of Obstetrician and Gynaecologists (RCOG) risk assessment tool popularised following the publication of the Green-top Guideline No.37a in 2009[5]. This tool is based on the premise that risk factors increase the risk of VTE in a cumulative fashion. Different RATs have been developed subsequently, with some variation in the risk factors identified and in the threshold for VTE prophylaxis commencement[6]. It is recommended that every pregnant woman should be risk assessed for VTE in early pregnancy to identify those at high risk, with the aim of prescribing low molecular weight heparin (LMWH) to prevent VTE. This risk assessment should be repeated on admission to hospital, or if the woman develops any additional risk factors during her pregnancy[5].

VTE can be prevented by non-pharmacological methods such as mobilization, hydration, graduated compression stockings, pneumatic devices and pharmacological methods such as aspirin and Low molecular weight heparin (LMWH). LMWH has been proven to reduce the risk of VTE in both medical and surgical patients[7]. In women with a previous VTE and no thromboprophylaxis, the recurrence rate in pregnancy ranges from 2.4 %[8] to 6.2%[9] antenatally and up to 8.3% postnatally[10]. These rates are reduced to 1.2%[11] and 5.5%[12] in retrospective cohort studies where LMWH is prescribed. A meta-analysis conducted (that included four clinical trials with 476 women) to examine the efficacy of LMWH used antenatally +/- postnatally compared to no treatment showed a reduction in the relative risk of VTE of 0.39 but with wide confidence intervals (95% CI: 0.08 – 1.98)[13]. Thus the efficacy of LMWH in preventing VTE in pregnancy is largely derived from small studies.

Against this backdrop, the identification of those at greatest risk of thrombosis is paramount but RATs have not been validated in pregnancy[5]. There is a paucity of randomised control trials including pregnant women demonstrating the efficacy of RATs in identifying those at greatest risk of VTE and clarifying the threshold risk above which thromboprophylaxis improves clinical outcome. The optimum dose of LMWH is unclear[14]. Most of the current guidance is based on expert group opinion based on limited observational data.

In this study, we looked at the incidence of antenatal VTE in our population and the prevalence of risk factors for VTE in this cohort compared to a control group. We applied various RATs to see if these women could have been identified and whether or not, the different tools would have triggered thromboprophylaxis and potentially prevention of their thrombosis.

Methods

A retrospective study was carried out in a tertiary level university maternity hospital in Dublin, Ireland. The Coombe Hospital is one of the largest provider of women's healthcare in Europe delivering more than 8000 babies annually. Prior to January 2020 women with previous VTE, or those who were on lifelong anticoagulation, or who had significant thrombophilia were identified at booking, were referred to the obstetric haematology clinic and commenced on LMWH if appropriate. No other formal antenatal risk assessment for VTE was applied to the remaining women. Cases of antenatal VTE were identified from a database of women who attended the specialized obstetric haematology clinic for management between January 1st 2012 and December 31st 2019. Controls were identified as the women who gave birth immediately before and after each index case and these were identified from the hospital In Patient Management System (IPMS). Chart review was conducted to record risk factors for VTE at booking, and if the risk profile changed in index cases and controls before the gestation at which the diagnosis of the VTE was made. Each patient was risk assessed using the RCOG VTE prophylaxis tool, the Health Service Executive (HSE) VTE prophylaxis guideline and our Coombe VTE prophylaxis guideline (introduced in Jan 2020). These tools are shown in figure 1-3. Anonymised patient information was recorded electronically. Statistical analysis was carried out using IBM SPSS Version 24.0 (IBM, Armonk, NY, USA) with further calculations performed using socialsciencestatistics.com. The study was approved by the hospital Quality Audit Committee.

Results

67 women with antenatal VTE were identified from the database. Four were excluded from the study following chart review for the following reasons: diagnosis of thrombophlebitis (1); VTE was diagnosed postnatally (2); and there was no pregnancy outcome details for one woman (1). 63 women were identified with an antenatal VTE; 25 with PE and 35 with DVT and 3 women with both a DVT and PE. 25 women (39.6%) presented in the first (4-12 completed weeks), 18 (28.5%) in the second (13-27 completed weeks) and 20 (31.7%) in the third trimester (28-42 weeks). 33.3% (21/63) developed their VTE prior to booking at the hospital for antenatal care**.** Two women developed a VTE despite antenatal thromboprophylaxis. 126

controls were identified as the women who gave birth immediately before or after the delivery of each of the 63 cases of antenatal VTE.

Risk factors for VTE are recorded in table 2 for both the VTE group and the control group. There were no risk factors for VTE identified in 21/63 (33%) of the VTE group compared to 63/126 (50%) of the control group ($p< 0.05$). Individual risk factors which were statistically significant when the VTE group is compared with the control group were previous VTE, family history of VTE and varicose veins. Of the VTE group, 19% met RCOG criteria for VTE prophylaxis compared to only 1.6% of the control group (chi-sq 19.1, $p<0.001$). Using the Coombe criteria for VTE prophylaxis 11% of the VTE group versus 0.8% of the control group met the criteria (chi-sq 8.7, $p<0.05$). There was also a statistically significant difference (chi-sq 9.2, $p=0.01$) between the VTE and control groups when assessed using the HSE VTE prophylaxis tool with 9.5% of the VTE group meeting criteria for prophylaxis and only 0.8% of the control group meeting criteria for prophylaxis.

Table 1 compares demographic data of the 63 women who were diagnosed with antenatal VTE and the 126 controls matched by time of birth who did not have a VTE. There was no statistically significant difference in mean gestational age at booking, maternal age, and parity between the index and control groups using T-test analysis. However, there was a statistically significant difference ($t=2.20$, $p<0.05$) in maternal weight at booking between the VTE group and the control group with the mean (SD) weight at booking of 73.7 (17.3) kgs in the VTE group and 68.3 (15.0) kgs in the control group.

Discussion

Pregnancy is a physiological state that increases a woman's risk of VTE. Although a rare event, an antenatal VTE is a serious complication in pregnancy. The risk of thrombosis should be balanced with the risk of bleeding when LMWH is prescribed. There is little randomised controlled data capturing risks and benefits of screening for risk factors and using LMWH. In the Cochrane review that attempted to capture the efficacy of using LMWH to prevent recurrent thrombosis, the rate of symptomatic VTE was 1/240 in the heparin group compared to 4/236 in the no heparin group (OR 0.39: CI 0.08 – 1.98)[13]. The antenatal and postnatal occurrence of VTE despite thromboprophylaxis is of the order of 1.2% in observational studies[14]. Heparin was associated with a twofold increase in minor bleeding, fivefold increase in local skin reactions and 22 fold increase in raised liver enzymes compared to controls[14]. Caution is needed when heparin is administered antenatally. It is reassuring that heparin does not cross the placenta and therefore poses no risk to the fetus but there is data to suggest

that prolonged use of LMWH is associated with osteopenia and osteoporosis. Women may be ineligible for neuraxial anaesthesia in the event of labour occurring following LMWH administration within the preceding 12 to 24 hours. This can limit the options for analgesia in labour and expose the woman to the increased risk of general anaesthesia should caesarean delivery be required. Other potential consequences of antenatal LMWH, that haven't been captured in the medical literature such as the psychological impact of 'medicalisation' of the pregnancy needs to be researched.

Thus it is critical to correctly identify women most at risk of VTE to avoid unnecessarily anticoagulating women with minimal risk. It is also important that once risks are identified, counselling occurs about both non-pharmacological and pharmacological methods of VTE prophylaxis.

In this study while risk factors for VTE were identified in two thirds of those with VTE, they were also prevalent in the control group (50%). The risk factors that were more prevalent in the VTE group were a personal history of VTE, a family history of VTE or the presence of varicose veins. Our study shows that RATs are helpful in predicting women at risk of developing VTE antenatally when compared to controls, but do not identify the majority of cases. The more cumbersome RCOG identified one in 5 cases while the simpler Coombe and HSE tools identified one in ten cases. One out of every three women who developed an antenatal VTE had no risk factors, a finding that is consistent with other studies[15]. Of note, two thirds of women who died of antenatal VTE in the 2018 MBRACE report had no identifiable risk factors[16].

In this study, 19 of the 61 cases of antenatal VTE occurred prior to booking with the hospital for antenatal care. This presents the challenge of how to risk assess these patients and emphasises the importance of preconceptual risk assessment in either primary care or preconceptual clinics. It also emphasises the need to educate women about the potential signs and symptoms of VTE should they become symptomatic prior to engaging with medical services in their pregnancy.

The limitations of this study is that it is a retrospective cohort and the focus is on VTE that presents in the antenatal period only. Risks for VTE identified at the booking visit over the study period included history of VTE, significant thrombophilia and indication for lifelong anticoagulation. These women were referred to our clinic and commenced on prophylactic heparin. There was no formal antenatal VTE assessment other than this. The strength of the study is that all cases were captured over the time frame because of the specialised clinic database where data is accrued prospectively. Detailed chart review was performed. The numbers are small but antenatal VTE is a rare event.

This study highlights the limitations of current RATs for antenatal VTE and the need for adequately powered prospective studies to determine the factors that have a clinically significant absolute risk for VTE and differentiate index cases from controls.

Table 1:

Demographics of antenatal VTE cohort (63) compared to controls (126).

Number Mean (SD)	VTE (63)	Controls (126)	T test (p-value)
Mean gestation at booking (weeks)	12.7 (3.5)	12.5 (3.8)	0.37 (p=NS)
Mean age (years)	32.6 (6.3)	31.1 (5.4)	1.66 (p=NS)
Mean parity	1.2 (1.2)	1.1 (1.4)	0.84 (p=NS)
Mean maternal weight at booking (kgs)	73.7 (17.3)	68.3 (15.0)	2.20 (p<0.05)
Mean BMI (kg/m^2)	27.2 (6.2)	25.3 (5.5)	2.1 (p<0.05)

Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P38
March 20th, 2025

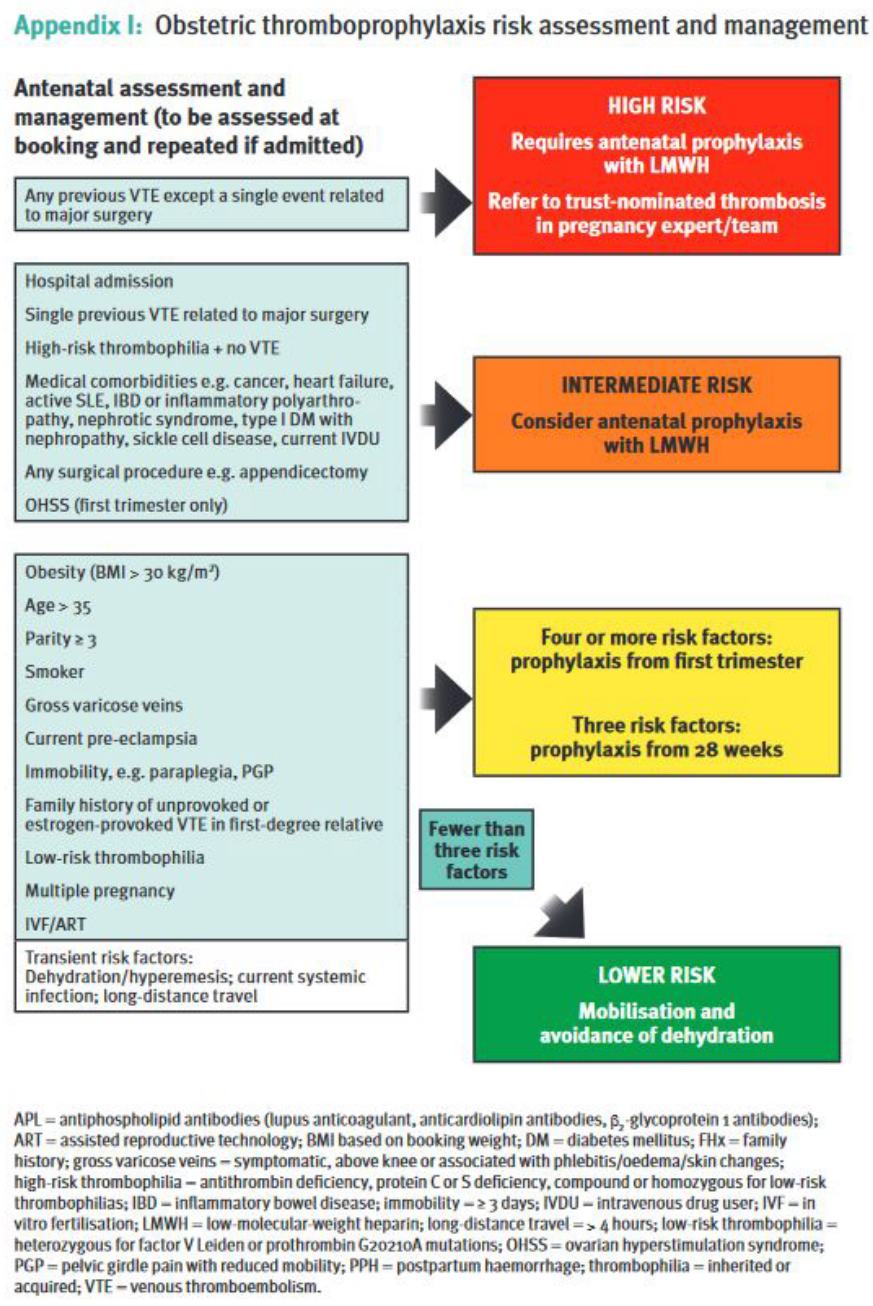
Table 2:

Risk factors for venous thromboembolism in antenatal VTE cohort compared to controls.

	Venous Thromboembolism	Controls	Chi-sq test (significance)
Number (%)	63	126	
RCOG score at booking	12 (19%)	2 (1.6%)	19.1 (p<0.001)
Coombe score at booking	7 (11%)	1 (0.8%)	8.7 (p<0.05)
HSE criteria at booking	6 (9.5%)	1 (0.8%)	9.2 (p=0.01)
No risk factors	21 (33%)	63 (50%)	4.7 (p<0.05)
Age >35	25 (39.7%)	34 (27%)	3.2 (p=NS)
BMI>35	7 (11%)	10 (7.9%)	0.52 (p=NS)
Parity >3	11 (7.5%)	13 (10%)	1.9 (p=NS)
Previous VTE	2 (3.2%)	0	4.0 (p<0.05)
Family history VTE	12 (19%)	2 (3%)	16 (p<0.001)
Varicose veins	4 (6.3%)	0	8.6 (p<0.05)
Family history thrombophilia	1 (1.6%)	1 (0.8%)	0.25 (p=NS)
Cigarette /E cigarette smoking	10 (15.9%)	10 (7.9%)	2.8 (p=NS)
IVF treatment	5 (7.9%)	5 (4%)	1.3 (p=NS)

Other	4 (6.3%)	2 (1.6%)	3.1 (p=NS)

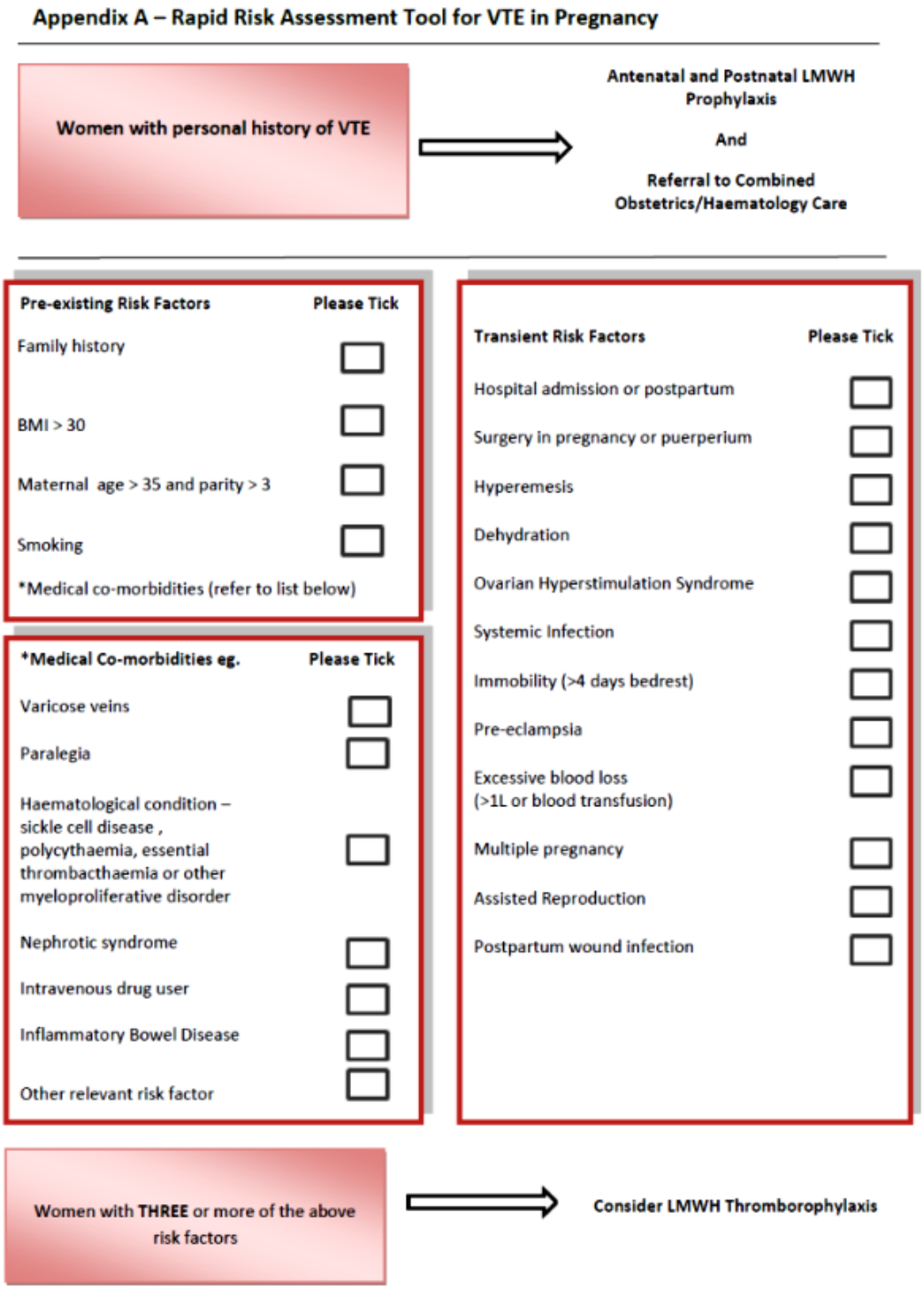
Figure 1: RCOG antenatal VTE risk assessment tool RCOG = Royal College of Obstetricians and Gynaecologists Guideline 37a



Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P38
March 20th, 2025

Figure 2: HSE antenatal VTE risk assessment tool



IMJ
Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P38
March 20th, 2025

Figure 3: Coombe antenatal VTE risk assessment tool.

ANTENATAL
RAPID RISK ASSESSMENT TOOL FOR VTE THROMBOPROPHYLAXIS

All antenatal women require assessment

- **At first booking visit**
- **At every antenatal admission**

Please tick all risk factors that apply

It is recommended that women should be considered for antenatal **THERAPEUTIC ANTICOAGULATION** with any **one** of the following:

- Receiving long term anticoagulation ☐
- Anti-thrombin deficiency ☐
- Metallic mitral valve ☐
- VTE or PE in current pregnancy ☐

Weight adjusted LMWH **treatment** dose
Refer to Medical Clinic

It is recommended that women should be considered for **ANTENATAL THROMBOPROPHYLAXIS** with any **one** of the following:

- BMI > 40 (during hospital admission) ☐
- Severe hyperemesis (during hospital admission) ☐
- Cancer (Current) ☐
- Nephrotic syndrome ☐
- Surgery in pregnancy ☐
- History of unprovoked VTE ☐
- History of oestrogen related VTE ☐
- Protein C or Protein S deficiency ☐
- Suspected/confirmed COVID-19 (If confirmed, continue for 4 weeks) ☐

Weight adjusted LMWH dose
See Dosing Table

It is recommended that women should be considered for **ANTENATAL THROMBOPROPHYLAXIS** with **three or more** of the following:

- 1st degree family relative with unprovoked or oestrogen provoked VTE ☐
- BMI > 30 ☐
- Maternal age > 35 ☐
- Parity > 3 ☐
- Smoker ☐
- Gross varicose veins ☐
- Immobility (Bed rest > 4 days) ☐
- Medical co morbidities i.e. SLE, Sickle cell, IBD, Polycythaemia ☐

Weight adjusted LMWH dose
See Dosing Table

** **REGIONAL ANAESTHESIA CAN BE PERFORMED 12 HOURS AFTER A PROPHYLACTIC DOSE OF TINZAPARIN OR ENOXAPARIN AND 24 HOURS AFTER A TREATMENT DOSE OF TINZAPARIN OR ENOXAPARIN ASSUMING NORMAL RENAL FUNCTION** **

Contraindications to low-molecular weight heparin (LMWH) - please tick any that apply

☐ Active bleeding or considered at high risk of major haemorrhage
☐ Imminent delivery
☐ Where it is anticipated the woman will be delivered in the next 24hrs
☐ Allergies to LMWH
☐ History of Heparin-induced thrombocytopenia (HIT)
☐ Severe thrombocytopenia (< 50)

Is Thromboprophylaxis indicated? YES ☐ NO ☐ **Date:** _____

Signature: _____ **Print name:** _____

Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P38
March 20th, 2025

Declarations of Conflicts of Interest:

None declared.

Corresponding Author:
Sarah Milne,
Department of Obstetrics and Gynaecology,
The Coombe Hospital,
Cork Street,
Dublin 8,
Ireland.
E-Mail: sarahmilne91@gmail.com

References:

1. Collins S, Arulkumaran S, Hayes K, Jackson S, Impey L. Oxford Handbook of Obstetrics and Gynaecology.
2. Knight M, Bunch K, Tuffnell D, et al, on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons Learned to Inform Maternity Care From the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2017-19. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2021.
3. Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ 3rd. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. Ann Intern Med. 2005;143:697-706.
4. Hart C, Bauersachs R, Scholz U, et al. Prevention of venous thromboembolism during pregnancy and the puerperium with a special focus on women with hereditary thrombophilia or prior VTE- Position paper of the Working Group in Women's Health of the Society of Thrombosis and Haemostasis (GTH). Hamostaseologie. 2020;40(5):572-90.
5. Nelson-Piercy C, MacCallum P, Mackillop L. Reducing the risk of thrombosis and embolism during pregnancy and the puerperium. RCOG Green-top Guideline No.37a. [Internet]. 2009. Available from: http://www.rcog.org.uk/womens-health/clinicalguidance/reducing-risk-of-thrombosis-greentop37a.
6. Pandor A, Daru J, Hunt BJ, et al. Risk assessment models for venous thromboembolism in pregnancy and in the puerperium: a systematic review. BMJ Open. 2022;12:e065892.
7. National Institute for Health and Clinical Excellence. Venous thromboembolism: reducing the risk. Reducing the risk of venous thromboembolism in patients admitted to hospital. NICE clinical guideline 92. London: NICE; 2010.
8. Brill-Edwards P, Ginsberg JS, Gent M, et al; Recurrence of Clot in This Pregnancy Study Group. Safety of withholding heparin in pregnant women with a history of venous thromboembolism. N Engl J Med. 2000;343(20):1439-44.

9. Pabinger I, Grafenhofer H, Kaider A, et al. Risk of pregnancy-associated recurrent venous thromboembolism in women with a history of venous thrombosis. J Thromb Haemost. 2005;3(5):949-54.
10. DeStefano V, Martinelli I, Rossi E, et al. The risk of recurrent venous thromboembolism in pregnancy and the puerperium without antithrombotic prophylaxis. Br J Haematol. 2006;135(5):386-391.
11. Cox S, Eslick R, McLintock C. Effectiveness and safety of thromboprophylaxis with enoxaparin for prevention of pregnancy-associated venous thromboembolism. J Thromb Haemost. 2019;17(7):1160-70.
12. Roeters van Lennep JE, Meijer E, Klumper FJ, Middeldorp JM, Bloemenkamp KW, Middeldorp S. Prophylaxis with low-dose low-molecular-weight heparin during pregnancy and postpartum: is it effective? J Thromb Haemost. 2011;9(3):473-80.
13. Middleton P, Shepherd E, Gomersall JC. Venous thromboembolism prophylaxis for women at risk during pregnancy and the early postnatal period. CDSR. 2021.
14. Middledorp S, Naue C, Kohler C. Thrombophilia, thrombosis and thromboprophylaxis in pregnancy: for what and in whom? Hamostaseologie. 2022;42:54-64.
15. Jaya-Bodestyne SL, et al. Risk factors for pregnancy-associated venous thromboembolism in Singapore. J Perinat Med. 2021;49(2):153-8.
16. Knight M, Bunch K, Tuffnell D, et al, on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons Learned to Inform Maternity Care From the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2018.