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Timing of Low Molecular Weight Heparin Administration in Breast Surgery and Post-Operative Haematoma Formation

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Abstract

Aims
The aims of this study were to: identify current practice regarding low molecular weight heparin (LMWH) prophylaxis in elective breast surgery, to determine if timing of administration of LMWH prophylaxis or specific patient demographic factors impacts the rate of post-operative haematoma formation.

Methods
Retrospective cohort study involving 100 patients who underwent elective breast surgery in a tertiary centre in Ireland in 2017. Medical charts were reviewed to collect data on; timing of LMWH administration, incidence of post-operative haematoma and patient's age, BMI, smoking status and anti-coagulant use. Statistical analysis was then performed.

Results
Forty-two patients (42%) received enoxaparin pre-operatively and thirty-one patients (31%) post-operatively. Incidence of post-operative haematoma was 4% (n=4). Of the haematoma group, three patients (75%) received post-operative enoxaparin (p=0.166). Independent patient factors did not significantly impact rate of haematoma formation.

Conclusions
Post-operative haematoma rate is 4%. Timing of LMWH prophylaxis administration did not significantly affect this rate.

Keywords: low molecular weight heparin, haematoma, breast surgery

Introduction

Venous thromboembolism (VTE) disease, including deep vein thrombosis (DVT) and pulmonary embolism (PE) is the second leading cause of death in cancer patients and 4th in surgical patients. Breast cancer is the second most common cancer in Ireland and breast cancer patients have 3-4 times the risk of developing VTE than demographically similar patients without cancer [1, 2]. Development of VTE in these patients doubles their risk of mortality [3]. 2016 NICE guidelines recommend all patients undergoing elective surgery greater than one hour should receive low molecular weight heparin (LMWH) combined with mechanical anti-VTE devices [4]. American Society of Breast Surgeons (ASBrS) generated guidelines for venous thromboembolism (VTE) prophylaxis for patients undergoing breast surgery in 2016 [5.] These recommendations state patients undergoing surgery duration >3 hours, patients at high risk for VTE or those undergoing mastectomy with immediate reconstruction should receive chemoprophylaxis. Day case procedures that last less than 1 hour or those patients at low VTE risk do not have to

receive VTE chemoprophylaxis. Currently the ASBrS outline that the acceptable risk of VTE after breast operations ranges from less than 1-4% with a comparable risk of re-operation rate for post-operative haematoma of 2-6% depending on operation type [5.]

Haematoma is a subcutaneous collection of blood arising from leakage of uncauterised blood vessels. Smaller haematomas may present as ecchymosis and suggillation of the chest wall, whilst larger cause wound distortion and severe pain. Therefore complications from post-operative haematoma are proportionate to their size. In general haematoma increases the risk of wound infection [6] and thus pose a threat to reconstructions. Larger volume haematomas may require repeat surgery for evacuation, potentially delaying adjuvant medical oncology treatment. Additionally the delay in wound healing resulting from a complication such as haematoma has been shown to increase risk of systemic breast cancer recurrence by up to threefold in patients with primary breast cancer compared to those without wound complication [7, 8]. However advancements have been made to decrease bleeding risk through the implementation of electrocautery instruments in breast surgery.

In breast surgery, conflicting evidence regarding optimum timing of administration of VTE prophylaxis exists, with some studies reporting an association between pre-operative administration and wound haematoma formation. O'Donnell & Weitz[11] delineated that higher doses (>3400 U/d) of LMWH are linked to increased bleeding risk but administration of lower dose LMWH 2 hours pre-operatively is as effective as DVT prophylaxis without increased risk of bleeding. Despite this there are no consensus guidelines currently in existence regarding timing of thromboprophylaxis. Thus further research is warranted to determine if pre or post-operative administration of VTE prophylaxis effects post operative haematoma rates without increasing risk of VTE.

Methods

A cohort sample of 100 patients who underwent elective breast surgery at the Symptomatic Breast Unit in University Hospital Limerick, the main Mid Western tertiary breast referral centre in 2017 was identified retrospectively. All patients who underwent any type of breast surgery in 2017 were eligible to be included. Patients less than 18 years of age were excluded. A sample size of 100 patients was decided to be an appropriate size to reflect ongoing practice. Medical charts were reviewed and data on: operation type, timing of administration of LMWH, incidence of post-operative haematoma, type of breast surgery, patient demographics, BMI, smoking status and anti-coagulation use was collected. Dosages of LMWH were recorded as prescribed, either 20mg or 40mg once daily subcutaneously. Administration of LMWH was between 2-6 hours before operation for the pre-operative group and between 4 and 8 hours after operation for the post-operative group. No formal guideline exists to indicate individual patient dosages. Statistical analysis was performed using chi-square test for categorical variables and Kruskal-Wallis test for continuous variables. The Ethics Committee of University Hospital Limerick granted ethical approval for the study.

Results

A cohort sample of 100 patients who underwent breast surgery in 2017 was identified retrospectively. The average age of the group was 54 years. All patients were female. Operations performed included; wire guided wide local excision (n=15), mastectomy and axillary node clearance (n=8), mastectomy and immediate reconstruction (n=6), mastectomy and sentinel lymph node biopsy (n=9), mastectomy (n=3), excision of benign breast disease: fibroadenoma and papilloma (n=9), microductectomy (n=1), wide local excision and sentinel lymph node biopsy (n=19), wide local excision and axillary node clearance (n=3), breast implant removal/periimplant drainage (n=5), unilateral breast implant insertion (n=1), sentinel lymph node biopsy alone (n=4), bilateral breast reduction (n=4), further breast cavity excision (n=5), axillary clearance alone (n=3), completion mastectomy (n=1) and open biopsy (n=3).

Timing of LMWH administration

LMWH was in the form of enoxaparin administered subcutaneously once daily, dosage ranged from 20-40mg. Of the 100 patients Seventy-three patients (73%) received prophylactic LMWH and twenty-seven patients (27%) did not. Further breakdown of the timing of LMWH administration revealed forty-two (42%) patients received enoxaparin pre-operatively and thirty-one (31%) post-operatively (Figure 1). Predominant dose was 20mg with 72 patients receiving and only one patient receiving 40mg. No other form of LMWH was administered.

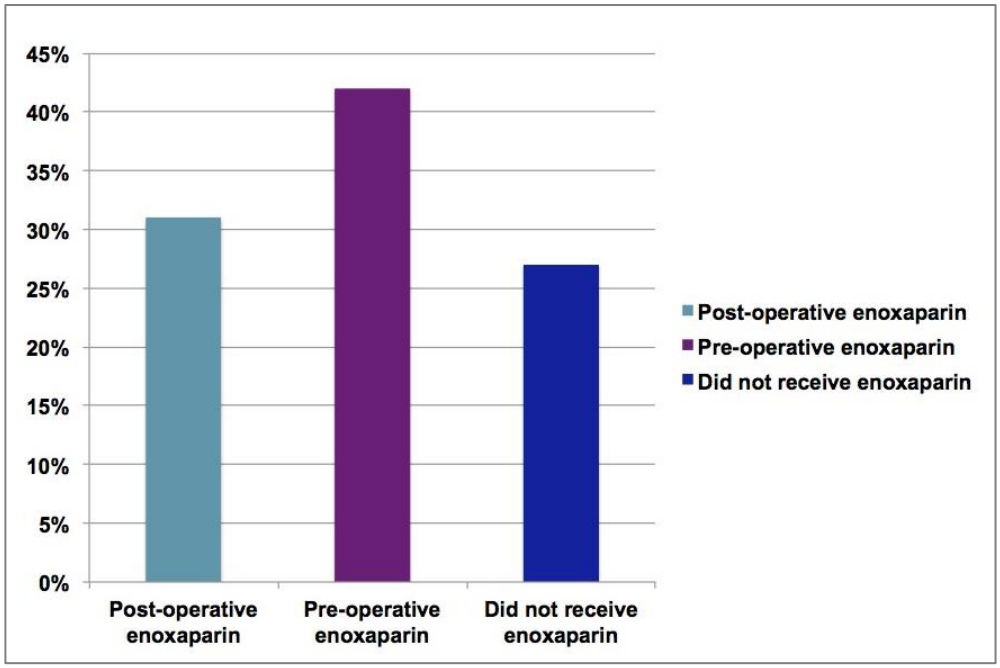

Figure 1: Distribution and timing of enoxaparin administration in breast surgery patients

Haematoma formation rates

Four patients (4%) developed post-operative haematomas with only 1 requiring re-operation. Of haematomas cases 75% patients received post-operative enoxaparin (n=3) and 25% received pre-operative (n=1). No statistical significance with timing was identified (p=0.166). Timing of haematoma development was varied. Immediate haematoma (n=1) formed within 24 hours and required re-operation. Delayed haematoma formation was between post-operative days 2 and 14.

Patient related factors and haematoma formation

Average age of the patient group was 54 years. All patients were female. The average body mass index (BMI) was 26.2. Kruskal-Wallis test showed there was no correlation between BMI and haematoma formation (p=0.842). Thirteen patients (13%) were active smokers. Of the 4 patients that developed haematomas only 1 was an active smoker, and therefore using Chi-square test there was no significant correlation (p=0.338). Eighty-seven patients (87%) were not taking any form of anticoagulant or anti-platelet agent. 13 patients (13%) were taking anti-coagulant/platelet agents for other medical conditions in the form of aspirin (n=11) and rivoraxaban (n=2). Of these thirteen patients, only one patient (1%) developed post-operative haematoma and was taking aspirin. Further analysis of this group using Chi-square test revealed no statistical significance between pre-operative anticoagulation use and post-operative haematoma formation (p=0.437).

Variable		Haematoma (n=)	p Value
Age			
Mean age	**54**		**0.55**
BMI			0.84
Mean BMI	26.2	4	
Smoking Status			0.34
Ex-smoker	n=36	0	
Non-Smoker	n=51	3	
Smoker	n=13	1	
Anti-Coagulant Use			0.43
None	n=87	3	
Aspirin	n=11	1	
Rivaroxaban	n=2	0	

Table 1: Patient related factors and haematoma formation

Discussion

Timing of clexane administration in patients undergoing breast surgery at our institution is varied and no standard protocol exists. Forty-two patients (42%) received enoxaparin pre-operatively and thirty-one (31%) post-operatively. Incidence of post-operative haematoma was 4% (n=4). Of the haematoma group, three patients (75%) received post-operative enoxaparin (p=0.166). Independent patient factors did not significantly impact rate of haematoma formation. The guidelines generated by ASBrS recommend that patients undergoing surgery duration >3 hours, patients at high risk for VTE or those undergoing mastectomy with immediate reconstruction should receive thromboprophylaxis[5]. Collectively seventy-three patients (73%) patients received enoxaparin during their admission and meet these criteria. Day case procedure guidelines recommend that last less than 1 hour or those patients at low VTE risk do not have to receive VTE thromboprophylaxis. This represents those 27% of patients that received none. These patients underwent sentinel lymph node biopsy (n=3), wire guided wide local excision (n=8), excision of fibroadenoma (n=6), excision of papilloma (n=1), further excision of skin/margins (n=4), open breast biopsy (n=5), drainage of peri-implant fluid (n=1). However one patient underwent a left mastectomy and axillary node clearance, which would meet the criteria for prophylaxis but did not receive any form of thromboprophylaxis. As such practice regarding VTE prophylaxis is predominantly in keeping with NICE and ASBrS but timing of administration is still a question.

Haematoma is a documented complication of any breast surgery. Haematoma can be detrimental to the outcome of reconstructive surgery as it can cause infection of prosthetic implants leading to explantation and secondary reinsertion [9]. Therefore it is imperative to investigate methods which could lead to guidelines to decrease their risk of haematoma formation and which is a balance between VTE prevention and post-operative bleeding risk. Previous investigations have yielded varied results. In our study 4% of patients developed post-operative haematomas, which is in keeping with acceptable risk of up to 4% depending on surgery type in the literature. Reoperation was only necessary for one of the haematomas; the other 3 were managed conservatively. In this study, operation types that resulted in post-operative haematomas were right wire guided wide local excision with sentinel lymph node biopsy, left wide local excision alone, right mastectomy with immediate reconstruction and left mastectomy and sentinel lymph node biopsy, indicating that haematoma formation is not confined to one particular procedure.

In this study, 31% patients received post-operative enoxaparin. Multiple previous studies document the safety of post-operative enoxaparin use, however they also highlight the uncertainty the surrounds the topic. The finding of increased haematoma formation rate in patients receiving post-operative LMWH is at odds with some of the reports in their literature. In 2012 a large study by Pannuci et al found no increase in haematoma formation when 1567 breast cancer patients received post operative enoxaparin compared to 2114 controls[10]. Additionally Liao et al found no increase in haematoma formation with post-operative administration of enoxaparin after TRAM flap breast reconstructions indicating post-operative LMWH to be safe, with bleeding complications of up to 5% whilst retaining its thromboprophylaxis efficacy[11]. Furthermore Lemaine et al carried out a prospective cohort study of 100 patients undergoing autologous free-flap breast reconstruction and found that administration of LMWH post-operatively yielded a low incidence of VTE and only 1% occurrence of haematoma[12].

The most comparable study to ours was carried out by Pannucci, Wachtman (10), who carried out a major retrospective study of adult plastic surgery patients. Their thromboprophylaxis regimen was 40mg subcutaneous enoxaparin once daily or 30mg twice daily if BMI was great than 40 kg/m^2. All doses were administered between 6 and 8 hours post-operatively and then continued for the entirety of the inpatient stay. Breast surgery patients represented the largest proportion of the patients that developed reoperative haematoma on this regimen with 4.78% breast reconstruction, 7.97% breast reduction and 13.64% cosmetic breast surgery patients developing reoperative haematoma. Breast surgery vs. non-breast surgery patients were proven to have significantly increased risk of reoperative haematoma ($p<0.001$). Additionally breast reduction patients were most at risk. Overall post-operative enoxaparin did not influence rate of re-operative haematoma when compared to controls that received no enoxaparin ($p=0.169$). In contrast Keith et. al [13] highlighted preoperative administration of enoxaparin generates an acceptable level of haematoma formation. This is comparable to our finding of the lowest haematoma formation group were in the preoperative enoxaparin group (n=1).

Identification of further risk factors for haematoma formation is imperative. Kaoutzanis, Winocour (14) conducted a major review of risk factors for major haematomas in aesthetic surgery which identified that again breast surgery is linked to great frequency of haematoma but both older age (42+/-13 years) and higher BMI (24.5 +/-5) statistically

increased risk of haematoma formation but smoking status did not significantly impact rates. Additionally Gupta, Yeslev (15) in a large study showed the only significant predictor is increasing age.

Although this study's findings did not match the previous studies our results were limited by our small sample size. The average age of the patients who developed haematomas in this study is 56 years. Of note the patient that developed a re-operative haematoma had a BMI in the obese range; 26.48. Only 25% (n=1) of patients that developed haematomas were smokers (p=0.34). This in keeping with the literature. The adverse effect of smoking on wound healing in breast surgery significantly increasing risk of wound infection and flap necrosis [16] is well documented, there no-specific risk documented to haematoma. Bonde, Khorasani (17) found that post-operative use of non-steroidal anti-inflammatories increase post-operative haematoma. Of the haematoma group only 25% (n=1) were using pre-operative anti-coagulation, in the form of aspirin. However this was also insignificant (p=0.43). Additionally type of breast surgery could impact haematoma formation. It is likely that the risk would rise proportionately with operation complexity. However this was not assessed in this study due to the small sample size.

In conclusion, these data indicate that LMWH administration in patients undergoing breast surgery in UHL is varied. This is likely due to a lack of standard protocol. Post-operative haematoma rate is 4% and is potentially associated with post-operative enoxaparin administration. Age, BMI, smoking status and anticoagulation use are not correlated with haematoma formation. There is a need for more definitive guidelines on the administration of LMWH in this patient cohort.

Declaration of Conflicts of Interest:
No conflict of interest to disclose.

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