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Bariatric venous thromboembolism prophylaxis: an update on the literature

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Abstract

Introduction: Rates of obesity have been increasing worldwide and with the current situation obesity now represents an epidemic. Bariatric surgery is one the most effective ways to help reduce weight and sustain weight loss. Venous thromboembolism is a major cause of morbidity and mortality among bariatric surgery patients with no clearly established guidelines on prophylaxis.

Areas covered: In this review the authors summarize clinical studies evaluating unfractionated heparin (UFH) and low molecular weight heparins (LMWH) in bariatric surgery patients. The authors present studies that assessed venous

thromboembolic (VTE)-related risk stratification but also various dosing regimens of heparin products in this population of patients. Moreover, the authors will also present the feasibility of using direct oral anticoagulants (DOACs) for venous thromboembolism (VTE) prevention along with providing a summary of few current guidelines for VTE prevention in bariatric surgery patients.

Expert opinion: Based on the data presented in this review, the authors conclude that LMWHs may be better options than UFH for VTE prophylaxis in bariatric surgery patients. We also conclude that risk stratifying bariatric patients may be a better approach when deciding on the best thromboprophylaxis modality, dose and duration.

Keywords: anti-Xa, bariatric surgery, direct oral anticoagulants, low molecular weight heparin, prophylaxis. venous thromboembolism

1. Introduction

In the past decade obesity was declared an epidemic with the projection that by 2030, 58% of the world's population will be obese (1). Bariatric surgery remains one of the most effective methods for sustained weight loss among morbidly obese patients (2). Bariatric surgeries encompass procedures causing gastric restriction (as in gastric banding and gastric sleeve), or combination of gastric restriction and malabsorption as in Roux-en-Y gastric bypass and duodenal switch. However, venous thromboembolism (VTE) continues to be a significant cause of morbidity and mortality among bariatric surgery patients with a 1-3% incidence of symptomatic deep vein thrombosis (DVT) and 0.3-2% incidence of symptomatic pulmonary embolism (PE) during and after bariatric surgery (3-5).

Obesity itself is an independent risk factor for DVT and PE (6). Ageno et al. estimated an OR of 2.3 VTE incidence in obese patients, which is similar to other established risk factors such as Factor V Leiden and estrogen use (7). Proposed mechanisms for the increased risk of VTE (venous thromboembolism) in obese patients are not only limited to clinical factors such as immobility and venous stasis, but also due to a chronic inflammatory state created by the

adipose tissue that dysregulates metabolic hemostasis (6). Adipose tissue secretes inflammatory cytokines causing recruitment of pro-inflammatory M1 macrophages and secretion of TNF alpha and IL-6, which activates the prothrombotic signaling pathway in vascular cells and impairs fibrinolysis by increased expression of plasminogen activator inhibitor-1 (6). Additionally, the bariatric procedure itself increases intrabdominal pressure creating oxidative stress and endothelial dysfunction (1).

Finks et al. further identified risk factors for VTE in bariatric surgery patients. Patient-related risk factors include male sex, age above 60, smoking status, and BMI. Procedure-related risk factors include open bariatric procedures, an operative time greater than 3 hours, and anastomotic leaks. (8) Despite the wide spread use of laparoscopic surgery, the incidence of VTE is still high reaching up to 2 % (9). Postoperative complications increase the risk of VTE, major complications occurred in 22.6 % prior to VTE in a study done by Helm et al. (10)

Strategies to reduce VTE risk include mechanical (compression devices, early ambulation, inferior vena cava filter) or pharmacologic (heparin, LMWH (low molecular weight heparin), and DOACs (direct oral anticoagulants)) but there is no consensus on the safest or most effective thromboprophylaxis strategy for bariatric surgery patients. Furthermore, optimal dosing of pharmacologic prophylaxis is unclear among obese patients as they are usually excluded from clinical trials.

Although most of the studies done on the topic are retrospective and observational, few, however, are randomized controlled trials; hence the level of evidence is generally weak.

The goal of this review is to provide an update on the existing literature concerning VTE prophylaxis in bariatric surgery patients, shed light on eagerly needed areas of research and suggest our approach to VTE prophylaxis in this subset of patients.

2. Risk-adjusted approach to VTE prophylaxis

Commonly used VTE risk calculators include Kucher, Rogers, Caprini, Pannucci, and Scarborough (11-16). Nonetheless, Caprini's risk score is the most widely used and validated for VTE risk in multiple disciplines of surgery but not specifically for bariatric surgery (17-20).

Aminian et al. performed a case-controlled study that examined VTE risks in patients undergoing bariatric surgery between 2007-2012, and they attempted to develop the first risk calculator to guide anticoagulation use post-discharge from the hospital. Regression-based techniques were used to create a risk assessment tool to predict risk of post-discharge VTE. The model was validated using the 2013 American College of Surgeons-National Surgical Quality Improvement Program dataset.

The outcome measured was VTE rates within 30 days post-operatively confirmed by imaging and requiring treatment. The strongest risk factors included congestive heart failur2 (CHF) (OR 6.58), paraplegia (OR 5.71), return to operating room (OR 5.11), dyspnea at rest (OR 3.95), non-gastric band surgery (OR 2.44), age > 60 years (OR 1.96), Male (OR 1.92), BMI >/ 50 kg/m2 (OR 1.67), length of stay (LOS) >/ 3 days (OR 1.58), and operation time >/ 3 hours (OR 1.57). The team was able to generate a risk model that was calibrated using Hosmer-Lemeshow. The test is available at http://www.riskcalc.org which has better predictive value than BMI alone. However, the history of previous VTE and hypercoagulable disorders were not included in the database (3). In fact, thrombophilia has been shown in some reports to be prevalent in obese patients and thus could be an important risk factor for development of VTE in these patients (21). For example, Hollander et al reported protein S deficiency to be significantly more prevalent in obese patients versus controls (2.97% versus 0.21%)(1) .

Another predictive tool was developed by Dang et al. called the BariClot using history of VTE, operative time, race and functional status. It predicted the risk of

VTE and thus stratified patients to very high, high, medium and low risk groups. Which therefore allows for an informed clinical decision for the choice of anticoagulation and VTE prophylaxis.(22)

3. Pharmacologic agent, dosing, duration

3.1 UFH (unfractionated heparin) and LMWH (low molecular weight heparin)

To our knowledge, there are no randomized controlled trials have been conducted comparing unfractionated heparin, LMWH, and oral anticoagulants for efficacy and safety in the prevention of VTE prophylaxis in bariatric surgery patients; rather, most of them involved medically ill hospitalized obese patients (23).

Birkenmeyer et al., using The Michigan Bariatric Surgery Collaborative, conducted an observational cohort study to compare different methods of VTE prophylaxis pre and postoperatively: UFH (pre)/UFH (post), UFH (pre)/LMWH (post), LMWH (pre)/LMWH (post). They found a significantly lower VTE incidence in the UFH/LMWH group (57%, OR=0.43, $p<0.03$) and LMWH/LMWH (66%, OR=0.34, $p<0.001$) compared to UFH/UFH that was used as a reference for comparison, with no significant difference in in the rates of hemorrhage among the treatment strategies.

High-risk subgroup (predicted risk of VTE ≥1% using their predictive model) comprised only 5% of the total study population; which was reflected in the finding of no statistically different outcomes among treatment groups in this population.

As a conclusion from this study, low-molecular-weight heparin is more effective than unfractionated heparin for the prevention of postoperative VTE among patients undergoing bariatric surgery with no increased rates of bleeding (24).

A limitation of this study was that neither the doses nor the duration of anticoagulation were discussed.

The EFFORT trial, a pilot randomized double-blind trial compared fondaparinux (direct anti-factor Xa inhibitor- AFXA inhibitor) given postoperatively at 5 mg subcutaneously versus enoxaparin (LMWH) given pre and postoperatively at a dose of 40 mg subcutaneously twice daily as VTE prophylaxis strategy to reduce the incidence of VTE in patients undergoing laparoscopic bariatric surgery. Both medications were given during the hospital length of stay of the patients then discontinued upon discharge from the hospital. The average length of stay was 2.5 days. It was found that although fondaparinux was more effective at maintaining recommended AFXA activity level, both regimens were equally effective with insignificant rates of DVT (2.4% versus 2.2%(p =1.00)) (25).

In another effort to determine the efficacy of LMWH in preventing VTE, Abuoglu et al. recently published another approach: LMWH (nadroparin 0.2 ml) was given 12 hours before and restarted 24 hours after surgery (nadroparin 0.4 ml for 15 days post-surgery) in 368 patients and found that the DVT incidence was 0% even after 36 months follow up. However, this study may have underrepresented the incidence of DVT as only symptomatic DVTs were assessed (26).

3.2. Dosing of heparin and LMWH

Another layer of complexity to bariatric VTE prophylaxis is the dosing of pharmacologic agents. The safety and efficacy of heparin and LMWH dosing in the obese population are unclear as obese patients are often excluded or underrepresented in randomized controlled trials.

Heparin has a narrow therapeutic window and nonlinear pharmacokinetic profile, making it challenging to dose. Prophylactic VTE dosing for heparin is fixed and typically administered at 5,000 units subcutaneously every 8 hours,

while therapeutic heparin is dosed according to weight and adjusted according to aPTT (activated partial thromboplastin time).

Heparin dosing has been shown to be variable in relation to patients' body weights.Shin et al. explored the dosing regimens of heparin in obese patients receiving heparin infusions through retrospective chart review at one institution. Patients were assigned to four different weight categories, <100kg, 100-124kg, 125-150 kg, and >150kg and compared to weight-matched controls. There was a significant difference in time to therapeutic aPTT based on TBW (total body weight) in all four groups, but most pronounced in the >150kg group where more than 30% in this group remained subtherapeutic in the first 24 hours. Mean first therapeutic heparin doses were smaller in the larger weight groups with an average dosing regimen of 11.3-13 units/kg per hour compared to controls who received 16 units/kg per hour (27).

A meta-analysis performed by Ikesaka et al. looking at the efficacy and safety of weight adjusted unfractionated heparin found that patients receiving weight-adjusted prophylaxis (defined as doses higher than 5000 IU subcutaneously every 8 hours or as the use of a subcutaneously UFH protocol adjusting the dose based on weight and level of AFXA) had lower rates of VTE (0.54 versus 2 %) with no increased risk of bleeding (28). However, physicians often deviate from this method.

Concerning low molecular weight heparin, a randomized controlled trial performed by Miranda et al., showed that the attainment of therapeutic AFXA level (0.32-0.54IU) was achieved with a higher dose enoxaparin (60mg) versus 40 mg with an average AFXA level of 0.25 ± 0.09 IU/mL in group 1 (received enoxaparin 40 mg subcutaneously daily) versus 0.35 ± 0.13 IU/mL in group 2 (received enoxaparin 60 mg subcutaneously daily) (P=0.001) (23).

Simoneau et al. assessed the effect of a fixed dose of dalteparin (7500 IU) on AFXA level in the morbidly obese patient and found that 60 % of patients had a

therapeutic range of AFXA levels. They demonstrated that patients with increased weight (>181 kg) had a higher probability of subtherapeutic AFXA level (29).

Tseng et al. attempted to evaluate weight adjusted tinzaparin with 75 IU per kg for 10 days after surgery, VTE rates were 0.5% at 30 days, with major bleeding occurring in 1.6% with in hospital VTE rates of 0l2% and 1.8%. authors concluded that the use of extended thromboprophylaxis reduces VTE rates and appears to be a safe strategy. (30)

Another study done by Scholten et al. (31) compared the use of LMWH enoxaparin 30 mg twice daily versus 40 mg twice daily . All patients received a unified protocol that included early ambulation, graduated compression stockings, and intermittent pneumatic compression. This comparison yielded results consistent with lower risk of DVT with the higher dosing (5.4% vs 0.6% with $p<0.01$) with no significant difference in bleeding (31).

3.3. Anti-Xa level monitoring

LMWH strongly inhibits Factor Xa by binding antithrombin;therefore the activity can be monitored via serum levels of AFXA and not aPTT.(32). The peak level of AFXA level is reached 3-5 hours after administration of the third dose (33, 34).

Target AFXA levels have been relatively well defined for therapeutic doses of LMWH in several studies (1, 4, 24, 25), but not well defined for prophylactic doses, especially in obese patients due to lack of pharmacokinetic profile. From the studies published to date, we concluded that a reasonable AFXA target range for LMWH VTE prophylaxis might be 0.2-0.5 IU/mL (35).

Because LMWH is administered subcutaneously, it has been theorized that absorption may be prolonged in obesity (36). However, if the volume of distribution is limited to intravascular volume, then dosing by total body weight

may lead to supratherapeutic dosing and increased risk of hemorrhage, leading some to suggest using BMI or lean body weight for dosing (37). As of 2012, CHEST guidelines recommend AFXA monitoring when total body weight exceeds 150kg, but this rationale has been challenged by various studies, some mentioned below, which question whether AFXA levels correlate with clinical events such as thrombosis or bleeding in obese populations.

In a retrospective case series , Paige et al. compared the bleeding risk and the anti-Xa levels among patients who had undergone gastric bypass and received BMI-dosed LMWH regimens (32). There was no statistical difference between the average AFXA value between groups that had been transfused for bleeding events and those who had not.

In a comprehensive literature review, Egan et al. found that monitoring AFXA levels had no impact on clinical outcomes on VTE or bleeding between obese and normal weight individuals because of the pharmacodynamics/kinetics of LMWH (36). The volume of distribution is proportional to the dose and total body weight. Clearance does not differ between obese and normal weight individuals as it follows typically first order kinetics. In any particular clinical scenario, patient-specific risk factors for thrombosis and hemorrhage should be considered. Given currently available data, determining AFXA concentration would not significantly affect the decision-making process. This review included clinical pharmacokinetic data in obesity and evaluated more LMWH entities (e.g., tinzaparin, bemiparin, nadroparin, logiparin, parnaparin) than the 2009 state-of-the-art review by Nutescu and others. Consistency in pharmacokinetics and clinical outcomes across many LMWHs thus strengthens the conclusions reached in the current study (34, 36). In another study done by schinjns et al. in 2018 suggested that the anti Xa activity is inversely correlated with total body weight TBW. Thus patients with increase in TBW had insufficient anti-Xa activity.(38)

Additionally, Gaborit et al. concluded in a prospective monocenter study using dalteparin 5000 IU twice daily that lean body weight and estimated glomerular filtration rate are the main factors influencing anti Xa level.(39)

To date, there has been no RCT comparing clinical outcomes in obese populations according to AFXA. AFXA levels may be a flawed marker for LMWH activity. For instance, Brophy et al. suggested that in patients with impaired renal function, thrombin generation time may be a better marker of activity as smaller active heparin fragments not measured by AFXA activity can accumulate and increase bleeding risk. (40)

Based on the existing data, the authors do not recommend using AFXA levels to monitor LMWH activity in obese populations. However, this recommendation cannot be extrapolated to other special populations such as those with malignancy, renal impairment, inherited coagulopathies, and pregnancy. (refer to table 1)

3.4. Oral anticoagulants

Direct oral anticoagulants (DOACS) offer a convenient option for anticoagulation as they have fixed dosing and a wide therapeutic range. However, studies to determine therapeutic range were conducted in healthy individuals with normal absorptive capacity, which may not be easily extrapolated to obese patients with surgically altered GI absorption due to gastric bypass.

There is limited data on the use of DOACs in bariatric patients. Hakeam et al. reviewed the literature on the use of DOACS in major GI tract surgeries (resection or bypass), which consisted of mainly case reports and case series.(41) DOACs have varying bioavailability based on P-glycoprotein (P-gp) efflux transporter, cytochrome P450, and the amount of GI surface area available (41). Rivaroxaban was shown to have the highest bioavailability (80%), followed by edoxaban(61%), apixaban(50%), and dabigatran(7%). DOACs are substrates of the P-gp efflux transporters, which are found on the apical membranes of the gastrointestinal (GI) tract and pump substrate into the intestinal lumen, thereby limiting their absorption. The expression of P-gp is lowest in the duodenum and highest in the distal ileum. Therefore, gastric bypass can expose the distal

segments of the bowel where P-gp is highly expressed, which could decrease DOAC bioavailability.

Rivaroxaban and edoxaban are mainly metabolized in the stomach. When rivaroxaban is released directly into the small intestine without passing through the stomach, absorption is reduced by 29-56% (41). Theoretically, this would make them poor VTE prophylaxis agents for bariatric surgery, particularly in procedures that reduce stomach size. On the other hand, Apixaban is absorbed independently of pH in the distal small bowel, making it theoretically safe in patients with small gastric pouches or remnant stomachs with no bowel resections. However, further studies are needed to confirm these claims. Dabigatran is a reversible direct inhibitor of thrombin and administered as a pro-drug which is activated by serum and hepatic esterase. It is administered with tartaric acid spherules in order to reduce its variability of absorption that is dependent on the acidic environment, which is why it is often associated with dyspepsia. Theoretically, Dabigatran also makes a poor choice for bariatric VTE prophylaxis with the added complication of increased risk of marginal ulcer formation. Based on the lack of clinical data, DOACs are still best avoided as first-line anti-coagulation in patients who have undergone bariatric surgery.

Interestingly, little literature exists to our knowledge on the use of vitamin K antagonists (VKA) for VTE prophylaxis in bariatric surgery patients. A study led by Betchel et al. showed higher rates of bleeding in patients receiving VKA (warfarin) with higher readmission rates (10%) in the first 30 days post discharge. Therefore, extrapolating from the above plus knowing that appropriate dosing requires bridging, INR monitoring, diet restrictions and knowledge of medications interaction, Warfarin is currently not an appropriate prophylactic agent in the bariatric surgery population.

3.5. Duration of anticoagulation

Bariatric surgery patients have an increased risk for venous thromboembolism postoperatively especially due to immobilization. Early ambulation is essential in this population as well as the use of mechanical prophylaxis**.** Mechanical prophylaxis use and its duration is mostly used based on discretion of the treating surgeon. To date, there are no randomized trials comparing mechanical prophylaxis to chemoprophylaxis but rather data is merely based on retrospective studies that mostly excluded high risk bariatric patients (43, 44). Patients at increased risk of bleeding would most likely benefit from mechanical prophylaxis during the duration of decreased mobility, taking into account the practical problems associated with their use in obese patients. The duration of anticoagulation in the postoperative phase is variable and not well defined in the literature. Froehling et al. demonstrated an increasing risk of postoperative VTE from 0.3 to 1.9 % up to 30 days post-discharge (4). Another study done by Moaad et al. mentioned earlier showed the presence of alteration in the coagulation profile up to two weeks post-bariatric surgery; thus suggesting to possibly anticoagulated patients for at least 2 weeks post operatively (42).

Other Studies done for extended post-discharge VTE prophylaxis showed improved VTE rates with no difference in bleeding events with the use of pharmacological thromboprophylaxis. Raftopoulos et al. included 308 patients divided into two groups 132 patients receiving enoxaparin 30 mg twice daily until discharge and enoxaparin 40 mg daily ten days post discharge. The rate of VTE was 4.5 % in the first group and none in the second group with a p=0.006, and no increased risk of bleeding with most of the thrombotic events occurring post-discharge (45).

4. Current guidelines

The American College of Chest Physicians (refer to table 2) and the Society for Bariatric surgery currently recommend that pharmaco-prophylaxis and mechanical VTE prophylaxis be administered to all bariatric surgery patients.
Aminian et al. and Martin et al. have proposed guidelines based on risk factors (3) (47).Aminian et al. recommend risk stratifying bariatric surgery patients based on the risk calculator described above into moderate, high, and very high-risk categories. In moderate-risk patients, i.e., all bariatric surgery patients with no additional risk factors, they recommend early and aggressive post-operative mobilization, pneumatic compression, and in-hospital prophylaxis. (3) In high-risk patients, i.e., VTE risk > 0.4%, a history of DVT/PE, hypercoagulable disorder, or chronic venous insufficiency, they recommend adding discharge prophylaxis for two weeks. In very high-risk populations, i.e., VTE risk >1%, they recommend post-discharge prophylaxis for four weeks, LMWH dosing based on AFXA levels, and to consider screening these patients with DVT duplex.

Flaws in these recommendations are that there have still been no RCTs to determine optimal dosage and duration of VTE prophylaxis in bariatric surgery patients.

The European society of anesthesiology VTE Guidelines Task Force published in 2018 guidelines on perioperative venous thromboembolism prophylaxis in patients undergoing bariatric surgery. They divided patients into low risk and high-risk patients. High-risk patients were defined as any of the following, or combinations: age >55 years, BMI >55 kg m^2, history of VTE, venous disease, sleep apnea, hypercoagulability or pulmonary hypertension.
They suggested the use of anticoagulant or IPC (intermittent pneumatic compression) for the low-risk patient. For high-risk patients the recommendations were to combine IPC and anticoagulation during or after a bariatric procedure.
They recommended the use of LMWH with 3000 to 4000 IU subcutaneously every 12 hours for low-risk patients and 4000 to 6000 IU every 12 hours for

patients with high-risk of VTE. Extended prophylaxis for patients with a high risk of VTE during post-discharge periods for 10 to 15 days (48).

The use of inferior vena cava filters IVCF is still controversial with no clear safety and efficacy for its use. The use of temporary IVCF is suggested when full pharmacologic or mechanical thromboprophylaxis are fully contra indicated . (49)

LMWH is approved by the FDA for VTE prophylaxis at a fixed dose, while weight-based dosing is used for the treatment of VTE. There is no consensus on the proper dosing regimen in obese patients as fixed dosing may not provide sufficient anticoagulation and weight-based dosing may make obese patients' anticoagulation supratherapeutic(34, 50). Studies on dosing of LMWH specifically enoxaparin for VTE prophylaxis have mainly been done on medically ill obese patients rather than bariatric patients and have supported weight-based dosing at 0.5mg/kg for maintaining patients in the recommended AFXA level range (51, 52).

5. Conclusion

In summary, the authors advocate a risk-adjusted approach to VTE prophylaxis using the risk calculator developed by Aminian et al. and modulating therapy based on risk. Randomized controlled studies are necessary to explore optimal postoperative duration of VTE prophylaxis and comparison of an anticoagulant agent (LMWH, UH, and DOACs). At this time, the authors do not recommend the use of DOACs in bariatric surgery patients given the lack of data and the theoretical risk of altered pharmacodynamics based on altered GI tract anatomy and absorption. According to the available data, LMWH and UFH appear equally useful for VTE prophylaxis in bariatric populations with no consensus on weight-based dosing versus fixed. There is no evidence to support the use of AFXa levels to titrate LMWH dose in bariatric populations as they do not appear to correlate clinically to thrombosis or bleeding events. New markers of LMWH activity need to be explored such as thrombin generation time.

Further studies should explore the use of antiplatelet agents in reducing VTE risk in bariatric populations.

6. Expert opinion

Bariatric surgery patients are at increased risk of thrombosis but also bleeding. Finding the balance between both risks entail proper evaluation of risk factors, whether patient related or procedure related, but also require the presence of interventions proven to be effective in this population of patients. Based on the ACCP guidelines, bariatric surgery is considered at moderate risk for VTE based on Rogers score or Caprini score. Therefore, the suggested recommendations, for those not at high risk of bleeding, include LMWH, low-dose unfractionated heparin, or mechanical prophylaxis (preferably IPC)(20) . The lack of randomized controlled trials has likely limited guideline developers from considering bariatric surgery patients a unique population of patients when assessing risks of VTE postoperatively. Moreover, to date, there are no reliable evidence-based risk assessment tools that can guide clinicians when determining the VTE prophylaxis modalities and duration of use in bariatric patients. Many risk factors have been identified in the literature and they include prior VTE, higher body mass index (BMI), age, gender, immobility, obesity hypoventilation syndrome, pulmonary hypertension, venous stasis disease, operative time, thrombophilia and type of operation. There is no one risk stratification model that incorporates all these factors together thus limiting the validity of clinical outcomes in the respective studies. (8, 53-56).

The lack of randomized high-quality data comparing various pharmacologic modalities also has generated ambiguity in terms of the proper choice of anticoagulation for prophylaxis in this population of patients. Many of the available studies compare different dosing regimens with lack of control groups and also enroll small number of patients thus limiting clinically meaningful conclusions(57).

However, upon evaluation of current data, LMWHs seem to be more effective than UFH for prevention of VTE in bariatric surgery patients with no increased risk of bleeding.

Dosing of parenteral heparins in obese patients poses another challenge in this population as they are at risk of thrombosis and bleeding at the same time. Although AFXa monitoring seems to be a plausible method of ensuring patients are in the therapeutic ranges (not well defined for prophylaxis), time to reach the therapeutic level based on higher dosing of heparins did not correlate with improved VTE-related or bleeding clinical outcomes in the current available data. We believe that an approach similar to the one adapted by the European society of anesthesiology VTE Guidelines Task Force (table 2) be used when clinicians are deciding on VTE prophylaxis strategies for their bariatric patients. Bariatric patients are heterogeneous in their risk profiles (along with the characteristics of surgery used) and thus personalizing the strategy used may lead to more effective prophylaxis.

Randomized controlled trials are eagerly needed to evaluate all aspects of thromboprophylaxis in bariatric surgery patients. These aspects include methods of prophylaxis (pharmacologic and/or nonpharmacologic), various pharmacologic agents (parenteral or oral), dosing, duration of anticoagulation and risk stratification. These trials could be difficult to appropriately conduct as they most likely require multicenter approach with involvement of high number of patients as the incidence of VTE in bariatric surgery is relatively low.

Article highlights

- Venous thromboembolism remains to be an important source of morbidity and mortality for bariatric surgery patients.
- Patient-related risk factors for VTE in bariatric surgery patients include but not limited to age, gender, smoking/hormone use, BMI, previous VTE, thrombophilia, immobility, venous stasis, pulmonary hypertension, and obesity hypoventilation syndrome.
- Procedure-related risk factors include open bariatric procedures, and long operative time.

- Though not based on randomized controlled trials, current data suggest that LMWH is more effective than UFH in preventing VTE with no increase in bleeding risk.
- There is no clear data on proper dosing of heparins in bariatric patients though many suggest higher dose LMWH in those with higher BMI.
- DOACs, though convenient, are not currently an appropriate method of prophylaxis due to lack of data and also to their pharmacodynamics/kinetics properties.

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References

1. Holländer SW, Sifft A, Hess S, Klingen HJ, Djalali P, Birk D. Identifying the bariatric patient at risk for pulmonary embolism: prospective clinical trial using duplex sonography and blood screening. Obesity surgery. 2015;25(11):2011-7.
2. Nguyen NT, Masoomi H, Magno CP, Nguyen XM, Laugenour K, Lane J. Trends in use of bariatric surgery, 2003-2008. Journal of the American College of Surgeons. 2011;213(2):261-6.
3. Aminian A, Andalib A, Khorgami Z, Cetin D, Burguera B, Bartholomew J, et al. Who Should Get Extended Thromboprophylaxis After Bariatric Surgery?: A Risk Assessment Tool to Guide Indications for Post-discharge Pharmacoprophylaxis. Annals of surgery. 2017;265(1):143-50.
4. Froehling DA, Daniels PR, Mauck KF, Collazo-Clavell ML, Ashrani AA, Sarr MG, et al. Incidence of venous thromboembolism after bariatric surgery: a population-based cohort study. Obesity surgery. 2013;23(11):1874-9.
5. Hamad GG, Choban PS. Enoxaparin for Thromboprophylaxis in Morbidly Obese Patients Undergoing Bariatric Surgery: Findings of the Prophylaxis

Against VTE Outcomes in Bariatric Surgery Patients Receiving Enoxaparin (PROBE) Study. Obesity Surgery. 2005;15(10):1368-74.
6. Lentz SR. Thrombosis in the setting of obesity or inflammatory bowel disease. Blood. 2016;128(20):2388-94.
7. Ageno W, Becattini C, Brighton T, Selby R, Kamphuisen PW. Cardiovascular risk factors and venous thromboembolism. Circulation. 2008;117(1):93-102.
8. Finks JF, English WJ, Carlin AM, Krause KR, Share DA, Banerjee M, et al. Predicting risk for venous thromboembolism with bariatric surgery: results from the Michigan Bariatric Surgery Collaborative. Annals of surgery. 2012;255(6):1100-4.
9. Jamal MH, Corcelles R, Shimizu H, Kroh M, Safdie FM, Rosenthal R, et al. Thromboembolic events in bariatric surgery: a large multi-institutional referral center experience. Surgical endoscopy. 2015;29(2):376-80.
10. Helm MC, Simon K, Higgins R, Kindel TL, Gould JC. Perioperative complications increase the risk of venous thromboembolism following bariatric surgery. The American Journal of Surgery. 2017;214(6):1135-40.
11. Merkow RP, Bilimoria KY, McCarter MD, Cohen ME, Barnett CC, Raval MV, et al. Post-discharge venous thromboembolism after cancer surgery: extending the case for extended prophylaxis. Annals of surgery. 2011;254(1):131-7.
12. Kucher N, Koo S, Quiroz R, Cooper JM, Paterno MD, Soukonnikov B, et al. Electronic alerts to prevent venous thromboembolism among hospitalized patients. N Engl J Med. 2005;352(10):969-77.
13. Rogers SO, Jr., Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. Journal of the American College of Surgeons. 2007;204(6):1211-21.
14. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. Dis Mon. 2005;51(2-3):70-8.
15. Pannucci CJ, Laird S, Dimick JB, Campbell DA, Henke PK. A validated risk model to predict 90-day VTE events in postsurgical patients. Chest. 2014;145(3):567-73.
16. Scarborough JE, Cox MW, Mureebe L, Pappas TN, Shortell CK. A novel scoring system for predicting postoperative venous thromboembolic complications in patients after open aortic surgery. Journal of the American College of Surgeons. 2012;214(4):620-6; discussion 7-8.
17. Bahl V, Hu HM, Henke PK, Wakefield TW, Campbell DA, Jr., Caprini JA. A validation study of a retrospective venous thromboembolism risk scoring method. Annals of surgery. 2010;251(2):344-50.
18. Caprini JA, Arcelus JI, Hasty JH, Tamhane AC, Fabrega F. Clinical assessment of venous thromboembolic risk in surgical patients. Seminars in thrombosis and hemostasis. 1991;17 Suppl 3:304-12.
19. Pannucci CJ, Swistun L, MacDonald JK, Henke PK, Brooke BS. Individualized Venous Thromboembolism Risk Stratification Using the 2005

Caprini Score to Identify the Benefits and Harms of Chemoprophylaxis in Surgical Patients: A Meta-analysis. Annals of surgery. 2017;265(6):1094-103.
20. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e227S-e77S.
21. Overby DW, Kohn GP, Cahan MA, Galanko JA, Colton K, Moll S, et al. Prevalence of Thrombophilias in Patients Presenting for Bariatric Surgery. Obesity Surgery. 2009;19(9):1278-85.
22. Dang JT, Switzer N, Delisle M, Laffin M, Gill R, Birch DW, et al. Predicting venous thromboembolism following laparoscopic bariatric surgery: development of the BariClot tool using the MBSAQIP database. Surgical endoscopy. 2019;33(3):821-31.
23. Miranda S, Le Cam-Duchez V, Benichou J, Donnadieu N, Barbay V, Le Besnerais M, et al. Adjusted value of thromboprophylaxis in hospitalized obese patients: A comparative study of two regimens of enoxaparin: The ITOHENOX study. Thrombosis research. 2017;155:1-5.
24. Birkmeyer NJ, Finks JF, Carlin AM, Chengelis DL, Krause KR, Hawasli AA, et al. Comparative effectiveness of unfractionated and low-molecular-weight heparin for prevention of venous thromboembolism following bariatric surgery. Archives of Surgery. 2012;147(11):994-8.
25. Steele KE, Canner J, Prokopowicz G, Verde F, Beselman A, Wyse R, et al. The EFFORT trial: preoperative enoxaparin versus postoperative fondaparinux for thromboprophylaxis in bariatric surgical patients: a randomized double-blind pilot trial. Surgery for Obesity and Related Diseases. 2015;11(3):672-83.
26. Abuoglu HH, Muftuoglu MAT, Odabasi M. A New Protocol for Venous Thromboembolism Prophylaxis in Bariatric Surgery. Obes Surg. 2019;29(2):729-34.
27. Shin S, Harthan EF. Safety and efficacy of the use of institutional unfractionated heparin protocols for therapeutic anticoagulation in obese patients: a retrospective chart review. Blood Coagulation & Fibrinolysis. 2015;26(6):655-60.
28. Ikesaka R, Delluc A, Le Gal G, Carrier M. Efficacy and safety of weight-adjusted heparin prophylaxis for the prevention of acute venous thromboembolism among obese patients undergoing bariatric surgery: a systematic review and meta-analysis. Thrombosis research. 2014;133(4):682-7.
29. Simoneau M-D, Vachon A, Picard F. Effect of prophylactic dalteparin on anti-factor Xa levels in morbidly obese patients after bariatric surgery. Obesity surgery. 2010;20(4):487-91.
30. Tseng E, Kolesar E, Handa P, Douketis J, Anvari M, Tiboni M, et al. Weight-adjusted tinzaparin for the prevention of venous thromboembolism after bariatric surgery. Journal of Thrombosis and Haemostasis. 2018;16(10):2008-15.

31. Scholten DJ, Hoedema RM, Scholten SE. A Comparison of Two Different Prophylactic Dose Regimens of Low Molecular Weight Heparin in Bariatric Surgery. Obesity Surgery. 2002;12(1):19-24.
32. Paige JT, Gouda BP, Gaitor-Stampley V, Scalia PG, Klainer TE, Raum WJ, et al. No correlation between anti-factor Xa levels, low-molecular-weight heparin, and bleeding after gastric bypass. Surgery for Obesity and Related Diseases. 2007;3(4):469-75.
33. Nutescu EA, Spinler SA, Wittkowsky A, Dager WE. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. The Annals of pharmacotherapy. 2009;43(6):1064-83.
34. Sacha GL, Greenlee KM, Ketz JM. The use of anti-factor Xa monitoring in a selection of patients receiving enoxaparin at a large academic medical center. Journal of thrombosis and thrombolysis. 2016;42(4):479-85.
35. Wei MY, Ward SM. The anti-factor Xa range for low molecular weight heparin thromboprophylaxis. Hematology reports. 2015;7(4).
36. Egan G, Ensom MH. Measuring anti–factor Xa activity to monitor low-molecular-weight heparin in obesity: a critical review. The Canadian Journal of Hospital Pharmacy. 2015;68(1):33.
37. Celik F, Huitema AD, Hooijberg JH, van de Laar AW, Brandjes DP, Gerdes VE. Fixed-dose enoxaparin after bariatric surgery: the influence of body weight on peak anti-Xa levels. Obesity surgery. 2015;25(4):628-34.
38. Schijns W, Deenen M, Aarts E, Homan J, Janssen I, Berends F, et al. The Effect of Obesity on Anti-Xa Concentrations in Bariatric Patients. Obesity surgery. 2018;28(7):1997-2005.
39. Gaborit B, Moulin P-A, Bege T, Boullu S, Vincentelli C, Emungania O, et al. Lean body weight is the best scale for venous thromboprophylaxis algorithm in severely obese patients undergoing bariatric surgery. Pharmacological research. 2018;131:211-7.
40. Brophy DF, Martin EJ, Gehr TW, Carr Jr ME. Enhanced anticoagulant activity of enoxaparin in patients with ESRD as measured by thrombin generation time. American journal of kidney diseases. 2004;44(2):270-7.
41. Hakeam HA, Al-Sanea N. Effect of major gastrointestinal tract surgery on the absorption and efficacy of direct acting oral anticoagulants (DOACs). Journal of thrombosis and thrombolysis. 2017;43(3):343-51.
42. Moaad F, Zakhar B, Anton K, Moner M, Wisam S, Safy F, et al. Is LMWH sufficient for anticoagulant prophylaxis in bariatric surgery? Prospective study. Obesity surgery. 2017;27(9):2331-7.
43. Frantzides CT, Welle SN, Ruff TM, Frantzides AT. Routine anticoagulation for venous thromboembolism prevention following laparoscopic gastric bypass. JSLS: Journal of the Society of Laparoendoscopic Surgeons. 2012;16(1):33.
44. Clements RH, Yellumahanthi K, Ballem N, Wesley M, Bland KI. Pharmacologic prophylaxis against venous thromboembolic complications is not mandatory for all laparoscopic Roux-en-Y gastric bypass procedures. Journal of the American College of Surgeons. 2009;208(5):917-21.

45. Raftopoulos I, Martindale C, Cronin A, Steinberg J. The effect of extended post-discharge chemical thromboprophylaxis on venous thromboembolism rates after bariatric surgery: a prospective comparison trial. Surgical endoscopy. 2008;22(11):2384-91.
46. Cossu ML, Pilo L, Piseddu G, Tilocca PL, Cossu F, Noya G. Prophylaxis of venous thromboembolism in bariatric surgery. Chirurgia italiana. 2007;59(3):331-5.
47. Martin K, Beyer-Westendorf J, Davidson B, Huisman M, Sandset P, Moll S. Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. Journal of Thrombosis and Haemostasis. 2016;14(6):1308-13.
48. Afshari A, Ageno W, Ahmed A, Duranteau J, Faraoni D, Kozek-Langenecker S, et al. European Guidelines on perioperative venous thromboembolism prophylaxis: Executive summary. European Journal of Anaesthesiology (EJA). 2018;35(2):77-83.
49. Comes RF, Mismetti P, Afshari A. European guidelines on perioperative venous thromboembolism prophylaxis: Inferior vena cava filters. European Journal of Anaesthesiology (EJA). 2018;35(2):108-11.
50. Lalama JT, Feeney ME, Vandiver JW, Beavers KD, Walter LN, McClintic JR. Assessing an enoxaparin dosing protocol in morbidly obese patients. Journal of thrombosis and thrombolysis. 2015;39(4):516-21.
51. Rondina MT, Wheeler M, Rodgers GM, Draper L, Pendleton RC. Weight-based dosing of enoxaparin for VTE prophylaxis in morbidly obese, medically-Ill patients. Thrombosis research. 2010;125(3):220-3.
52. Freeman A, Horner T, Pendleton RC, Rondina MT. Prospective comparison of three enoxaparin dosing regimens to achieve target anti-factor Xa levels in hospitalized, medically ill patients with extreme obesity. American journal of hematology. 2012;87(7):740-3.
53. Becattini C, Agnelli G, Manina G, Noya G, Rondelli F. Venous thromboembolism after laparoscopic bariatric surgery for morbid obesity: clinical burden and prevention. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery. 2012;8(1):108-15.
54. Winegar DA, Sherif B, Pate V, DeMaria EJ. Venous thromboembolism after bariatric surgery performed by Bariatric Surgery Center of Excellence Participants: analysis of the Bariatric Outcomes Longitudinal Database. Surgery for Obesity and Related Diseases. 2011;7(2):181-8.
55. Sapala JA, Wood MH, Schuhknecht MP, Sapala MA. Fatal pulmonary embolism after bariatric operations for morbid obesity: a 24-year retrospective analysis. Obesity surgery. 2003;13(6):819-25.
56. Sugerman HJ, Sugerman EL, Wolfe L, Kellum Jr JM, Schweitzer MA, DeMaria EJ. Risks and benefits of gastric bypass in morbidly obese patients with severe venous stasis disease. Annals of surgery. 2001;234(1):41.
57. Kalfarentzos F, Yarmenitis S, Kehagias I, Karamesini M, Dimitrakopoulos A, Maniati A, et al. Prophylaxis of venous thromboembolism using two different doses of low-molecular-weight heparin (nadroparin) in bariatric surgery: a prospective randomized trial. Obesity surgery. 2001;11(6):670-6.

58. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-e96S.
59. ASMBS updated position statement on prophylactic measures to reduce the risk of venous thromboembolism in bariatric surgery patients. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery. 2013;9(4):493-7.
60. Imberti D, Baldini E, Pierfranceschi MG, Nicolini A, Cartelli C, De Paoli M, et al. Prophylaxis of venous thromboembolism with low molecular weight heparin in bariatric surgery: a prospective, randomised pilot study evaluating two doses of parnaparin (BAFLUX Study). Obes Surg. 2014;24(2):284-91.
61. Borkgren-Okonek MJ, Hart RW, Pantano JE, Rantis PC, Jr., Guske PJ, Kane JM, Jr., et al. Enoxaparin thromboprophylaxis in gastric bypass patients: extended duration, dose stratification, and antifactor Xa activity. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery. 2008;4(5):625-31.
62. Kothari SN, Lambert PJ, Mathiason MA. Best Poster Award. A comparison of thromboembolic and bleeding events following laparoscopic gastric bypass in patients treated with prophylactic regimens of unfractionated heparin or enoxaparin. Am J Surg. 2007;194(6):709-11.
63. Singh K, Podolsky ER, Um S, Saba S, Saeed I, Aggarwal L, et al. Evaluating the safety and efficacy of BMI-based preoperative administration of low-molecular-weight heparin in morbidly obese patients undergoing Roux-en-Y gastric bypass surgery. Obes Surg. 2012;22(1):47-51.
64. Ojo P, Asiyanbola B, Valin E, Reinhold R. Post discharge prophylactic anticoagulation in gastric bypass patient-how safe? Obes Surg. 2008;18(7):791-6.
65. Heffline MS. Preventing vascular complications after gastric bypass. J Vasc Nurs. 2006;24(2):50-4; quiz 5.

Table 1: Summary of characteristics and outcomes of included studies for prevention of venous thromboembolism in bariatric surgery patients

References	Design	N=	Method of Anticoagulation	Dosing of Anticoagulation	Duration of Anticoagulation	VTE Incidence	Bleeding risk
Birkmeyer et al. (24)	Prospective cohort	4,402	Pre and post op UFH	NR	NR	0.68	0.46

		4,482	1. Pre op UFH and postop LMWH 2. Pre and postop LMWH	NR	NR	0.29	0.6
		15,891	Pre and post op LMWH	NR	NR	0.25	0.38
Imberti et al. (60)	Prospective randomized trial	131	Pre- and post-op LMWH	Parnaparin 4,250 U q24h	14.1 days	PE 0.76	6.1
		119	Pre- and post-op LMWH	Parnaparin 6400 U q24h	14.1 days	DVT 0.76	
Borkgren-Okonek et al(61)	Prospective cohort	124	Pre-op UFH Post-op and post-discharge LMWH	UFH 5000 Postop enoxaparin 40 mg q12h for BMI<50, with dose adjusted as per AFXA level Post-discharge Enoxaparin once daily	Pre-op and 10 days post-discharge	0.8	3.2
		99	Pre-op UFH Post-op and post-discharge LMWH	UFH 5,000 Post-op enoxaparin 60 mg q12h for BMI >50 Post-op dose adjusted by antifactor-Xa level Post-discharge enoxaparin once daily	Pre-op and 10 days post-discharge	0	1
Frantzides et al (43)	Prospective cohort	435	SCD and LMWH	Enoxaparin 40 mg q12h	NR	PE 1.1 DVT 1.6	4.8
Kothari et al. (62)	Prospective cohort	238	LMWH	Enoxaparin 40 mg q12h	Pre-op to discharge	0	5.9
		238	UFH	5,000 U q8h	Pre-op to discharge	0.42	1.3
Hamad and Choban(5)	Prospective cohort	180	Post-op LMWH	Enoxaparin 40 mg q12h	0.5–1.5 (range)	PE 0.6 DVT 0	1.7
		84	Post-op LMWH	Enoxaparin 40 mg q24h	0.5–5 (range)	PE 1.2 DVT 0	0
		180	Post-op LMWH	Enoxaparin 40 mg q24h	0.5–1 (range)	PE 0 DVT 0	1.7
		100	Pre-op LMWH	Enoxaparin	NA	PE 2	0

				30 mg once		DVT 0	
		124	Post-discharge LMWH	Enoxaparin 30 mg q24h	10	PE 1.6 DVT 0.8	0.8
Steele et al.(25)	Randomized controlled trial	71	Pre and post-op LMWH	Enoxaparin 40mg q12h	Pre-op and post-op to discharge	2.4	5.1
		66	Post-op fondaparinux	Fondaparinux 5 mg q24h	Post-op to discharge	2.2	3
Kalfarentzos et al. (57)	Randomized controlled trial	30	Pre and post-op LMWH	Nadroparin 5,700 q24h	Pre-op to discharge	0	0
		30	Pre and post-op LMWH	Nadroparin 9,500 q24h	Pre-op to discharge	0	6.7
Scholten et al.(31)	Prospective cohort	92	Pre and post-op LMWH	Enoxaparin 30 mg q12h	NR	5.4	1.1
		389	Pre and post-op LMWH	Enoxaparin 40 mg q12h	NR	0.6	0.26
Singh et al.(63)	Retrospective cohort	11	Pre and post-op LMWH	Enoxaparin 30 mg q12h (BMI less than 40)	NR	0	0
		145	Pre and post-op LMWH	Enoxaparin 40 mg q12h (BMI 41–49)	NR	0	3.5
		9	Pre and post-op LMWH	Enoxaparin 50 mg q12h (BMI 50–59)	NR	0	0
		5	Pre and post-op LMWH	Enoxaparin 60 mg q12h (BMI more 59)	NR	0	20
Cossu et al. (46)	Prospective cohort	86	Pre- and post-op and Post-discharge UFH-adjusted dose by aPTT	UFH 20,000–37,500 U SC daily in hospital then 5,000/7,000 U SC twice daily	Pre-op to minimum of 15 days post-discharge	1.2	2.3
		65	UFH at induction of anesthesia	UFH intravenous 2,500–5,000 U single dose	NA	3.1	0
Ojo et al.(64)	Prospective cohort	59	Post-op and post-discharge LMWH	Enoxaparin 40 mg q12h	Post-op to 14 days post-discharge	NR	0

		68	Post-op and post-discharge LMWH	Enoxaparin 60 mg q12h	Post-op to 14 days post-discharge	NR	0
Heffline et al.(65)	Prospective cohort	462	Pre-op aspirin and post-op UFH	Aspirin 650 mg UFH 5,000 U q12h	NA	PE 2.2 DVT 4.5	NR
		455	Pre-op aspirin and post-op UFH and warfarin	Aspirin 650 mg UFH 5,000 U q12h Warfarin adjusted to INR goal <1.8	Warfarin given for 30 days post-discharge	PE 0.2 DVT 1.1	0

Abbreviations: N= Number of patient; VTE= venous thromboembolism; DVT=deep venous thrombosis; UFH= unfractionated heparin; LMWH= low molecular weight heparin; PE= pulmonary embolism; U=units; Q12h= every 12 hours; INR=international Normalized Ratio; aPTT=activated partial thromboplastin time; NR=not reported; SCD= sequential compression device; SC= subcutaneously; NA=not available

Table 2. Summary of published guidelines for VTE prophylaxis in bariatric surgery

ACCP Guidelines (2012)(58)

1. For general and abdominal-pelvic surgery patients at moderate risk for VTE (3.0%; Rogers score, > 10; Caprini score, 3-4) who are not at high risk for major bleeding complications, low-molecular-weight heparin LMWH) (Grade 2B), low-dose unfractionated heparin (LDUH) (Grade 2B), or mechanical prophylaxis, preferably with IPC (Grade 2C), over no prophylaxis.
2. For general and abdominal-pelvic surgery patients at moderate risk for VTE (3.0%; Rogers score, > 10; Caprini score, 3-4) who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, mechanical prophylaxis preferred with IPC, over no prophylaxis (Grade 2C).
3. For general and abdominal-pelvic surgery patients at high risk for VTE (~6.0%; Caprini score, ≥5) who are not at high risk for major bleeding complications, pharmacologic prophylaxis with LMWH (Grade 1B) or LDUH (Grade 1B) over no prophylaxis.
4. For high-VTE-risk general and abdominal- pelvic surgery patients who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C).
5. Mechanical prophylaxis with elastic stockings or IPC should be added to pharmacologic prophylaxis (Grade 2C).

European Society of Anesthesiology Guidelines (2018)(48)

1. Recommend using only anticoagulants or IPC for obese patients with a low risk of VTE during and after bariatric procedures (Grade 2C).
2. Recommend using anticoagulants and IPC together for obese patients with high risk of VTE (age >55,
BMI >55kg/m^2, history of VTE, venous stasis disease, sleep apnea, hypercoagulability or pulmonary hypertension.
3. Recommend using LMWH over low dose UFH (GRADE 1C).

4. A dose of LMWH (3000 to 4000 IU every 12 hours subcutaneously) depending on BMI is acceptable for obese patients with a lower risk of VTE
and 4000 to 6000 IU every 12 hours depending on BMI is acceptable for obese patients with high risk for VTE (Grade 2B).
5. Recommend extended prophylaxis for patients at high-risk for VTE during the post discharge period for 10-15 days (Grade 1C).

ASMBS Guidelines (2013)(59)

1. Recommend early ambulation for all bariatric patients
2. Recommend mechanical prophylaxis for all patients when practically feasible.
3. Recommend combination of mechanical and chemoprophylaxis based on clinical judgement and risk of bleeding.
4. Though data is conflicting, based on highest-quality data, LMWHs offer better VTE prophylaxis than UFH without increasing the risk of bleeding.
5. Most discharge VTE events occur within the first 30 days after surgery and extended thromboprophylaxis should be considered. There is insufficient data to make definitive recommendations.

Abbreviations: LMWH, low molecular weight heparin; UFH, unfractionated heparin; VTE, venous thromboembolism; IPC, intermittent pneumatic compression; BMI, body mass index; ASMBS, american society for metabolic and bariatric surgery