

## GUIDELINES

# European guidelines on perioperative venous thromboembolism prophylaxis

## *Surgery in the obese patient*

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A systematic literature search was performed and patients were selected as obese patients undergoing bariatric surgery or obese patients undergoing nonbariatric surgical procedures. In addition, patients were stratified according to low risk of venous thromboembolism and high risk of venous thromboembolism (age >55 years, BMI >55 kg m<sup>-2</sup>, history of venous thromboembolism, venous disease, sleep apnoea, hypercoagulability or pulmonary hypertension). Prophylaxis of venous thromboembolism was analysed depending on the type of modality: compression devices of the lower extremities (including intermittent pneumatic compression and graduated compression stockings), pharmacological prophylaxis or inferior vena cava filters. Two prospective studies compared mechanical devices and pharmacological prophylaxis vs. a mechanical device alone without significant differences. A few randomised controlled studies and most of the prospective nonrandomised studies showed that low-dose low molecular weight heparin (3000

to 4000 anti-Xa IU 12 h<sup>-1</sup> subcutaneously) was acceptable for obese patients with a lower risk of venous thromboembolism, but a higher dose of low molecular weight heparin (4000 to 6000 anti-Xa IU 12 h<sup>-1</sup> subcutaneously) should be proposed for obese patients with a higher risk of venous thromboembolism. Extended prophylaxis for 10 to 15 days was well tolerated for obese patients with a high risk of venous thromboembolism in the postdischarge period. The safety and efficacy of inferior vena cava filters in bariatric surgical patients is highly heterogeneous. There were no randomised trials that analysed prophylaxis of venous thromboembolism in obese patients undergoing nonbariatric surgery. Higher doses of anticoagulants could be proposed for obese patients with a BMI more than 40 kg m<sup>-2</sup>. The lack of good quality randomised trials with a low risk of bias did not allow us to propose strong recommendations.

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Samama CM, Afshari A, for the ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. *Eur J Anaesthesiol* 2018; 35:73–76.

A synopsis of all recommendations can be found in the following accompanying article:

Afshari A, Ageno W, Ahmed A, *et al.*, for the ESA VTE Guidelines Task Force. European Guidelines on perioperative venous thromboembolism prophylaxis. Executive summary. *Eur J Anaesthesiol* 2018; 35:77–83.

### Introduction

Obesity is associated with increased risks of coronary artery disease, diabetes mellitus, hypertension, stroke and venous thromboembolism (VTE). A meta-analysis by Ageno *et al.*<sup>1</sup> included 8125 patients with VTE and 23 272 control patients. Authors identified that the incidence of a first spontaneous VTE among obese patients was more than twice that of patients with normal BMI [odds ratio (OR) 2.33; 95% confidence intervals (95% CIs) 1.68 to 3.24].<sup>1</sup> The retrospective cohort study by Fontaine *et al.*<sup>2</sup> evaluated more than 11 000 patients and assessed the risk of 90-day VTE in obese critically ill medical patients receiving chemoprophylaxis. The incidence of VTE was significantly higher in obese (OR 1.41, 95% CI 1.03 to 1.93) than in nonobese patients of similar

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illness severity ( $P=0.03$ ).<sup>2</sup> The average recurrence rate of VTE in patients is 16.7% (95% CI 11.0 to 22.3%) with BMI 25 to 30 kg m<sup>-2</sup> and 17.5% (95% CI 13.0 to 22.0%) with BMI more than 30 kg m<sup>-2</sup>, compared with 9.3% (95% CI 6.0 to 12.7%) in patients of normal weight.<sup>3,4</sup> The higher risk of VTE in obese patients is explained by changes of thrombotic mechanisms: enhanced platelet activity (adipokinins, insulin resistance, low-grade inflammation and stasis), procoagulant state (increased tissue factor, increased fibrinogen, factor VII and factor VIII, increased thrombin generation), impaired fibrinolysis related to overproduction of plasminogen activator inhibitor (PAI-1) and thrombin-activatable fibrinolysis inhibitor (TAFI), and activation of endothelial cells (tissue hypoxia).<sup>5</sup>

### Venous thromboembolism prophylaxis of obese patients undergoing bariatric surgery

The incidence of VTE after bariatric surgery varies from 0.3 to 3.3%.<sup>6,7</sup> Froehling *et al.*<sup>6</sup> estimated that the cumulative incidence of symptomatic VTE after bariatric surgery was 0.3% (95% CI 0 to 0.8) at 7 days, 1.9% (95% CI 0.5 to 3.2) at 30 days, 2.1% (95% CI 0.7 to 3.5) at 3 months and 2.1% (95% CI 0.7 to 3.6) at 6 months. In addition, Steele *et al.*<sup>7</sup> showed that the incidence of VTE after minor bariatric procedures such as laparoscopic adjustable gastric banding was significantly lower than laparoscopic or open gastric bypass ( $P < 0.01$ ). The incidence of VTE after laparoscopic adjustable gastric banding was 0.8% compared with 2.7% after laparoscopic gastric bypass and 3.3% after open gastric bypass. Open bariatric procedures had a higher risk of VTE than laparoscopic, but without a significant difference in that study.<sup>7</sup> Both studies identified that patients aged more than 55 years had a higher risk of VTE after bariatric surgery (OR 1.89; 95% CI 1.01 to 3.55) than younger patients.<sup>6,7</sup> The prospective study by Jamal *et al.*,<sup>8</sup> including 4293 obese patients, identified that the risk of postoperative VTE among morbidly obese patients undergoing bariatric surgery was increased by higher age, BMI more than 50 kg m<sup>-2</sup> and open bariatric procedures.

The exhaustive review by Bartlett *et al.*<sup>9</sup> published in 2015 analysed VTE prevention in obese patients undergoing bariatric surgery. The main limitation of most studies regarding VTE prevention in bariatric surgery is that most of them are observational and retrospective and very few are prospective and randomised controlled trials (RCTs). Therefore, recommendation levels of VTE prophylaxis in obese patients undergoing bariatric surgery will be weak because of lack of moderate or high quality of studies and with a low risk of bias.

According to this review,<sup>9</sup> VTE prophylaxis can be divided into three types:

- (1) Mechanical prophylaxis: including intermittent pneumatic compression (IPC) and graduated compression stockings (GCS);

- (2) Anticoagulants [low molecular weight heparins (LMWHs) and low-dose unfractionated heparin (LDUH)];
- (3) Inferior vena cava filters (IVCFs).

### Mechanical prophylaxis

Two studies were found in the literature that analysed prevention of VTE for obese patients in bariatric surgery using IPC. The prospective study of Gagner *et al.*<sup>10</sup> compared two groups of patients: IPC and pharmacological prophylaxis (LDUH or LMWH) vs. IPC alone. There were fewer cases of VTE (0.47 vs. 0.25%;  $P=0.53$ ) and lower mortality rate (0.35 vs. 0.25%;  $P=0.76$ ) in the IPC alone group than the combined prophylaxis group, but without significant differences. However, there were no homogeneous groups and patients were unselected in this study. The mean BMI of patients was not recorded. LDUH and LMWH were used in the first group, but the doses of these medications were unclear. The type of mechanical method was a sequential compression device (SCD), one of the most common types of IPC used in the USA.

The next prospective study by Frantzides *et al.*<sup>11</sup> compared the same two groups of patients [IPC and pharmacological prophylaxis (LMWH) vs. IPC alone], but LMWH was added in the second group if obese patients had a higher risk of VTE (history of VTE and hypercoagulability). There were fewer cases of VTE (2.7 vs. 0.48%), postoperative bleeding (4.8 vs. 0.4%) and mortality (0.12 vs. 0%) in the second group. However, groups were not homogeneous and patients were not randomised.

### Pharmacological prophylaxis

This section should be divided into three parts: modality of prophylaxis [LDUH, low molecular weight heparin (LMWH) and fondaparinux], optimal dose of anticoagulants and use of anticoagulants after discharge.

### Modality of prophylaxis

Two prospective studies by Birkmeyer *et al.*<sup>12</sup> and Kothari *et al.*<sup>13</sup> compared the efficacy of different anticoagulants. The first of these studies showed that VTE rates were significantly lower in patients receiving LMWH (preoperative)/LMWH (postoperative) (0.25%;  $P < 0.001$ ) and LDUH (preoperative)/LMWH (postoperative) (0.29%;  $P=0.03$ ) groups, than the LDUH (preoperative)/LDUH (postoperative) group (0.68%). LDUH/LMWH (0.22%;  $P=0.006$ ) and LMWH/LMWH (0.21%;  $P < 0.001$ ) were similarly effective in patients at a low risk of VTE, while LMWH/LMWH (1.46%;  $P=0.10$ ) seemed more effective than LDUH/LMWH (2.36%;  $P=0.90$ ) for high-risk patients. There were no significant differences in rates of haemorrhage among the groups. Although this study was prospective, it was unclear about the doses of the different medications.

The results of Kothari *et al.*,<sup>13</sup> also comparing LMWH and LDUH, were different. Enoxaparin 40 mg was injected subcutaneously preoperatively and on the day of the operation, and twice daily until discharge. In the LDUH group, patients received 5000 IU subcutaneously preoperatively, nothing on the day of the operation, and 5000 IU three times per day until discharge. There were no cases of deep venous thrombosis in either group. There was one pulmonary embolism in the heparin cohort ( $P=0.9$ ). Fourteen patients (5.9%) in the enoxaparin group required postoperative transfusion compared with three patients (1.3%) in the heparin group ( $P=0.011$ ). In conclusion, LDUH was potentially superior due to the excessive bleeding complications encountered with enoxaparin. However, this was not a randomised prospective cohort study and the level of quality is moderate.

A recent prospective, double-blind RCT from Steele<sup>14</sup> compared preoperative and postoperative enoxaparin 40 mg 12 h<sup>-1</sup> with postoperative fondaparinux 5 mg 24 h<sup>-1</sup> in 177 patients undergoing bariatric surgery. Magnetic resonance venography was performed 2 weeks after surgery and anti-Xa levels were measured 3 h after the first injection of both agents and before the second dose. Anti-Xa levels were within the target range (0.2 to 0.6 IU ml<sup>-1</sup> for enoxaparin and 0.39 to 0.5 IU ml<sup>-1</sup> for fondaparinux) in 32 and 74% of patients who received enoxaparin and fondaparinux, respectively. DVT was detected in two patients in each group, all asymptomatic. The incidence of bleeding complications was 5.1% with enoxaparin and 3% with fondaparinux. In conclusion, this methodologically sound RCT showed that fondaparinux may represent a suitable alternative to enoxaparin in bariatric surgery.<sup>14</sup>

### Dosing of low molecular weight heparin

A prospective randomised pilot trial by Imberti *et al.*<sup>15</sup> and another randomised control trial by Kalfarentzos *et al.*<sup>16</sup> compared two different doses of LMWH. Imberti *et al.*<sup>15</sup> found no significant differences related to LMWH doses between parnaparin 4250 and 6400 IU 24 h<sup>-1</sup>. The rates of VTE (PE 0.76 vs. 0%; DVT 0.76 vs. 0.84%) were similar in low-dose and high-dose LMWH groups. The incidence of postoperative bleeding was also similar (6.1 vs. 5%). The conclusion of this study was that low-dose LMWH is acceptable to prevent VTE.<sup>15</sup> There were clear inclusion criteria, postoperative analysis and durations of prophylaxis (days) of patients in this study. However, the groups were not completely homogeneous, as some patients in both groups used elastic stockings or IPC. Similar results were published by Kalfarentzos *et al.*<sup>16</sup> in a RCT comparing two different nadroparin doses. There was no case of VTE in any group, but postoperative bleeding was increased in the high-dose LMWH group (0 vs. 6.7%). The conclusion of this study was that the lower dose of LMWH was well tolerated in

bariatric surgery.<sup>16</sup> None of these studies analysed the efficacy of different doses of LMWH for obese patients with a higher risk of VTE.

The prospective observational cohort study by Scholten *et al.*<sup>17</sup> compared two different dose of LMWH (enoxaparin 30 vs 40 mg 12 h<sup>-1</sup>) in patients with a high risk of VTE. Lower extremity compression was used in both groups. The results were better with the higher dose of LMWH without any increase in the bleeding risk (VTE 0.6 vs. 5.4%,  $P=0.01$ ; bleeding 0.26 vs. 1.1%, non-significant).<sup>17</sup> However, these different doses were given in different periods, and the quality of the study was moderate.

Four different centres participated in another prospective cohort study published by Hamad and Coban.<sup>18</sup> Patients with a high risk of VTE were included. Different doses of LMWH and different times of administration of a LMWH (preoperative enoxaparin 30 mg 24 h<sup>-1</sup>, postoperative enoxaparin 40 or 40 mg 24 h<sup>-1</sup>, and postdischarge 30 mg 24 h<sup>-1</sup>) were compared. The incidence of VTE was lower in the patients who received 40 or 40 mg 24 h<sup>-1</sup> of enoxaparin.<sup>18</sup>

The prospective cohort study by Borkgren-Okonek *et al.*<sup>19</sup> compared two different groups: obese patients with a low risk of VTE and obese patients with a high risk of VTE. Two different enoxaparin (LMWH) doses were evaluated: enoxaparin 40 mg 12 h<sup>-1</sup> for obese patients with a low risk of VTE and enoxaparin 60 mg 12 h<sup>-1</sup> for obese patients with a high risk of VTE. The rate of VTE was similar in both groups (0.8 vs. 0%), but postoperative bleeding was higher in the low-dose group (3.2 vs. 1%). The statistical analysis was unclear. The conclusion of this study was that a high-dose of LMWH was effective for obese patients with a high risk of VTE without increasing postoperative bleeding.<sup>19</sup> Similar results were published in other studies by Singh *et al.*<sup>20</sup> and Woo and Kim.<sup>21</sup> LMWH at low doses was well tolerated for obese patients with a low risk of VTE and a high dose of LMWH should be considered for obese patients with a high risk of VTE.<sup>20,21</sup> The last review by Shelkrot *et al.*<sup>22</sup> analysed different doses of enoxaparin for obese patients undergoing bariatric procedures. Eight prospective and retrospective studies were included. None of them was a RCT. All patients included had a high risk of VTE. Three studies evaluated the incidence of VTE and other studies analysed anti-Xa levels. The studies that analysed appropriate doses of enoxaparin concluded that a dose of enoxaparin 40 mg every 12 h was superior compared with 30 mg 12 h<sup>-1</sup>. The other included studies that analysed anti-Xa levels identified that a high dose of enoxaparin 60 mg 12 h<sup>-1</sup> showed higher mean anti-Xa levels in the blood than a dose of enoxaparin of 40 mg 12 h<sup>-1</sup>. The authors concluded that standard doses of enoxaparin for VTE prophylaxis may not provide optimal protection to patients with a high risk of VTE. The use of higher than standard doses of enoxaparin is still not clear.<sup>22</sup> However,

as this review only included retrospective and prospective studies, the quality is low and the recommendation for an acceptable dose of LMWH is weak.

The prospective study by Simone *et al.*<sup>23</sup> and the prospective randomised trial by Freeman *et al.*<sup>24</sup> measured the factor Xa (anti-Xa) concentrations using different doses of enoxaparin: 40 vs. 60 mg. Obese patients with a high risk of VTE [age >70 years, heart failure, acute respiratory failure, previous VTE, cancer, stroke, sepsis or immobility (defined as  $\geq 3$  days)] were included in these studies. The results were superior in patients receiving 60 mg of enoxaparin. Anti-Xa concentrations were significantly higher in the enoxaparin 60 mg group than in the 40 mg group after the third injection.<sup>23,24</sup>

### Duration of prophylaxis

Three prospective studies by Raftopoulos *et al.*,<sup>25</sup> Cossu *et al.*<sup>26</sup> and Heffline,<sup>27</sup> and one retrospective study of Ojo *et al.*,<sup>28</sup> were included in the Bartlett review<sup>9</sup> and analysed administration of anticoagulants during the postdischarge period (from 10 to 15 days). Obese patients at a high risk of VTE were included in these studies. Extended administration of anticoagulants during the postdischarge period was well tolerated for VTE prophylaxis. The rate of VTE varied from 0 to 1.2%. Postoperative bleeding did not increase and varied from 0 to 2.3% for these patients.<sup>25–28</sup> The prospective study by Raftopoulos *et al.*<sup>25</sup> included 308 obese patients undergoing bariatric surgery with more than 1-month follow-up. The patients were divided into two groups: obese patients with only pre- and postoperative LMWH prophylaxis and obese patients with pre- and postoperative LMWH and LMWH administered during the postdischarge period (up to 10 days). All patients had at least two existing VTE risk factors (obesity and abdominal surgery) and the presence of any additional preoperative risk factors for VTE (>40 years, BMI >60 kg m<sup>-2</sup>, smoking, previous history of VTE or venous insufficiency). The rate of VTE was significantly higher in the group without extended prophylaxis (4.5 vs. 0%;  $P=0.006$ ). Morbidity was also higher in this group (12.1 vs. 1.1%;  $P<0.0001$ ). Postoperative bleeding was significantly lower in the extended prophylaxis group (0.56 vs. 5.3%;  $P=0.02$ ). The authors concluded that prophylactic anticoagulants are well tolerated for obese patients in the postdischarge period with a decreased incidence of VTE and without increasing the incidence of bleeding.<sup>25</sup>

### Inferior vena cava filters

Three studies from the Bartlett review did not find any superiority of IVCF for VTE prophylaxis in obese patients with a higher risk of VTE. The retrospective study by Li *et al.*<sup>29</sup> established that the incidences of pulmonary embolism (0.31 vs. 0.12%), DVT (0.93% vs. 0.12%) and mortality (0.31% vs. 0.03%) were higher in the IVCF group than in the no-IVCF group. The rates of

DVT and mortality were significantly higher ( $P<0.001$  and  $P=0.003$ ). Preoperative and postoperative anticoagulants (LMWH or LDUH) were used in both groups.<sup>29</sup> However, the groups were not comparable in relation to BMI or comorbidity.

The results of the retrospective study by Obeid *et al.*<sup>30</sup> were similar. IVCFs were inserted in patients with a higher risk of VTE (history of VTE, venous diseases, BMI >60 kg m<sup>-2</sup>, hypercoagulability, etc.) in the IVCF group. There were no patients with a higher risk of VTE in the second group (no IVCF) in this study. IPC, preoperative and postoperative LMWH were used in both groups. The incidences of pulmonary embolism (0.8 vs. 0.59%), DVT (1.2 vs. 0.65%) and mortality (0.81 vs. 0.22%) were lower in the no-IVCF group, but with no significant difference.<sup>30</sup>

In a prospective study, Birkmeyer *et al.*<sup>31</sup> identified that patients with IVCF had higher rates of pulmonary embolism (0.84% vs. 0.46%; OR 2.0; 95% CIs 0.6 to 6.5;  $P=0.232$ ), DVT (1.2 vs. 0.37%; OR 3.3; 95% CI 1.1 to 10.1;  $P=0.039$ ), VTE (1.9 vs. 0.74%; OR 2.7; 95% CI 1.1 to 6.3,  $P=0.027$ ), serious complications (5.8 vs. 3.8%; OR 1.6; 95% CI 1.0 to 2.4;  $P=0.031$ ) and death (0.7 vs. 0.09%; OR 7.0; 95% CI 0.9 to 57.3;  $P=0.068$ ) than the no-IVCF group.<sup>31</sup>

Three other studies showed different results. Halmi and Kolesnikov<sup>32</sup> compared the results of two different groups (IVCF and no IVCF) in a prospective study. Twenty-seven patients with a higher risk of VTE (BMI >60 kg m<sup>-2</sup>, history of VTE) were included in the IVCF group and 625 patients (some of them with higher risk of VTE) were included in the no-IVCF group. Early ambulation, IPC, preoperative LDUH 5000 IU, then 5000 IU 8 h<sup>-1</sup> or preoperative LMWH (enoxaparin) 40 mg, then 40 mg 12 h<sup>-1</sup> were allowed in both groups. If patients had a higher risk of VTE, enoxaparin 40 mg daily for 3 weeks was proposed in both groups. The incidences of PE (0 vs. 0.32%) and DVT (0 vs. 1.12%) were higher in the no-IVCF group. No deaths were recorded in either group.<sup>32</sup>

Similar results were published by Overby *et al.*<sup>33</sup> in a prospective study that used the same groups and the same indications for IVCF insertion (BMI >60 kg m<sup>-2</sup>, history of VTE, hypercoagulability, etc.). Preoperative and postoperative IPC and LDUH 5000 to 7500 U 8-hourly until discharge were used in both groups. The incidence of PE (0.63 vs. 2.94%;  $P=0.216$ ) was higher in the no-IVCF group, but the incidence of DVT (3.13 vs. 2.34%;  $P=0.744$ ) was higher in the IVCF group.<sup>33</sup>

In a study published by Gargiulo *et al.*,<sup>34</sup> obese patients who had open Roux-en-Y gastric bypass (RYGB) were included. The study consisted of three parts. During the first part (retrospective study), 31 patients (16.1%) of 193 included patients had a high risk of VTE (BMI

$>55 \text{ kg m}^{-2}$ ). IVCF was inserted only in eight patients of 31. The incidence of pulmonary embolism was 13% and mortality of patients 10%. The risk of pulmonary embolism after open RYGB reached 10.2% (95% CI 5.8 to 18). In the second part (prospective study), the protocol of insertion of IVCF was changed. Thirty-three patients (18.2%) of 181 included patients had a high risk of VTE ( $\text{BMI} >55 \text{ kg m}^{-2}$ ). IVCF was inserted for all 33 patients. No cases of pulmonary embolism or mortality were recorded in the IVCF group. The risk of PE after open RYGB reduced from 13% (95% CI 1.1 to 24.7) to 0% (95% CI 0 to 8.7). The third part of the study (prospective study) included 35 patients with a high risk of VTE ( $\text{BMI} >55 \text{ kg m}^{-2}$ ). Seventeen patients had IVCF and 18 had no IVCF before surgery. The rate of pulmonary embolism was 28% and mortality was 11% for patients without IVCF with no cases of PE or death in the IVCF group.<sup>34</sup> However, there was unclear randomisation, homogeneity of groups and statistical analysis in this part of study.

Two retrospective studies from Keeling *et al.*<sup>35</sup> and Vaziri *et al.*,<sup>36</sup> which were not included in the Bartlett review, published acceptable results of IVCF for VTE prevention. The indications for IVCF were the same as in previous studies: history of VTE, hypercoagulability, BMI more than  $55 \text{ kg m}^{-2}$ , venous diseases. There were no incidents of pulmonary embolism, postoperative complications such as bleeding or postoperative death in these studies. The rate of DVT was between 0 and 4.8%.<sup>35,36</sup>

The systematic review and meta-analysis of Brotman *et al.*<sup>37</sup> found that IVCF did not reduce the risk of VTE. The authors included five studies (four retrospective and one retrospective-prospective) in this meta-analysis. There was insufficient evidence supporting the contention that filters reduce the risk of pulmonary embolism; the data suggested that there were increased risks associated with filters [relative risk (RR) 1.21, 95% CI 0.57 to 2.56]. There was low-grade evidence that filters were associated with higher mortality (RR 4.30, 95% CI 1.60 to 11.54) and higher deep vein thrombosis rates (RR 2.94, 95% CI 1.35 to 6.38).<sup>37</sup>

A recent systematic review about prophylactic IVCF in patients undergoing bariatric surgery was published by Rowland *et al.*<sup>38</sup> in 2015. Eighteen studies were included. There were no RCTs. IVCFs were inserted preoperatively in obese patients with a higher risk of VTE. DVT rates of 0 to 20.8% and pulmonary embolism rates ranging from 0 to 6.4% were found for patients with the IVCF. This systematic review showed that IVCF did not decrease the incidence of VTE. Only a few prospective studies were included in this systematic review.<sup>38</sup>

According to published data, the safety and efficacy of IVCF use in bariatric surgical patients is highly heterogeneous. The lack of good quality of RCTs with a low risk of bias will not allow us to propose any recommendation.

### Venous thromboembolism prophylaxis in obese patients undergoing nonbariatric surgery

In a retrospective study, Wang *et al.*<sup>39</sup> compared two different doses of anticoagulants: standard dose [LDUH 7500 IU daily or LMWH (enoxaparin) 40 mg daily] vs. higher-dose [LDUH 7500 IU three times daily or LMWH (enoxaparin) 40 mg  $12 \text{ h}^{-1}$ ]. Obese patients (weight  $>100 \text{ kg}$ ) were included in this study. All types of surgical procedures were analysed. In all, 6780 patients were on standard thromboprophylaxis, of whom 103 (1.52%) developed VTE; 2461 patients received high-dose thromboprophylaxis, of whom 29 (1.18%) developed VTE ( $P=0.22$ ). Obese patients were divided into two groups: BMI less than  $40 \text{ kg m}^{-2}$  and BMI more than  $40 \text{ kg m}^{-2}$ . The incidence of VTE in patients with BMI less than  $40 \text{ kg m}^{-2}$  was similar (1.54 vs. 1.88%) in those who received standard and high doses of anticoagulants, with no significant differences (OR 1.23, 95% CI 0.72 to 2.10,  $P=0.46$ ). The incidence of VTE in patients with BMI more than  $40 \text{ kg m}^{-2}$  was significantly reduced (0.77 vs. 1.48%, OR 0.52, 95% CI 0.27 to 1.00,  $P=0.05$ ) in those receiving high-dose thromboprophylaxis. Postoperative bleeding did not increase for high-dose patients and the rate was similar to that in the standard dose group (standard dose 8.44% vs. high-dose 7.18%;  $P=0.15$ ).<sup>39</sup>

In a literature review, Vandiver *et al.*<sup>40</sup> analysed the acceptable doses of LDUH and LMWH in morbidly obese patients. Thirty-seven studies were included. Bariatric procedures and other operations were analysed together. There was no statistical analysis or groups in this review. High-dose LDUH ( $7500 \text{ IU } 8 \text{ h}^{-1}$ ) or LMWH (enoxaparin 40 mg  $12 \text{ h}^{-1}$ ) was acceptable for obese patients with BMI more than  $40 \text{ kg m}^{-2}$  with a low incidence of VTE and without increased postoperative bleeding.<sup>40</sup>

Another literature review of Ihaddadene and Carrier<sup>41</sup> analysed different doses of LDUH, LMWH and requirement for direct oral anticoagulants for obese patients in the postdischarge period. Eighty-nine studies were included. It was unclear how many of these were RCTs, prospective or retrospective studies. Bariatric procedures and other operations were analysed together. There was no statistical analysis or groups in this review. High-dose LDUH or LMWH should be recommended after surgery, but doses of direct oral anticoagulants are still unclear due to lack of RCTs.<sup>41</sup>

The retrospective cohort study of Wang *et al.*<sup>42</sup> analysed the correlation between VTE and different BMIs. A total of 33 325 patients who underwent abdominal operations and abdominal wall reconstruction were included in the study. According to BMI, patients were divided into five groups: BMI 18 to  $24.99 \text{ kg m}^{-2}$ ; BMI 25 to  $29.99 \text{ kg m}^{-2}$ ; BMI 30 to  $34.99 \text{ kg m}^{-2}$ ; BMI 34 to  $39.99 \text{ kg m}^{-2}$  and BMI more than  $40 \text{ kg m}^{-2}$ . There were no significant relationship between VTE and BMI. The incidences of

pulmonary embolism and DVT were similar in all groups of patients except for patients after abdominal wall reconstruction where patients with BMI more than  $40 \text{ kg m}^{-2}$  had a significantly higher rate of pulmonary embolism ( $P = 0.04$ ). We cannot propose any recommendation for VTE prophylaxis from this study.

In patients with a weight more than 90 kg undergoing major orthopaedic surgery, Vavken *et al.*<sup>43</sup> compared 3500 and 5000 IU of a LMWH (bemiparin). Although efficacy and safety were similar with both protocols, there was a trend in favour of higher doses in patients with higher weights.

## Recommendations

### Bariatric surgery

- Laparoscopic bariatric procedures for obese patients have a lower risk of VTE than open procedures.
- We suggest using only anticoagulants or IPC for obese patients with a low risk of VTE during and after bariatric procedures (Grade 2C).
- We recommend using anticoagulants and IPC together for obese patients with a high risk of VTE (age >55 years, BMI >55  $\text{kg m}^{-2}$ , history of VTE, venous disease, sleep apnoea, hypercoagulability or pulmonary hypertension) during and after bariatric procedures (Grade 1C).
- We recommend the use of LMWH over LDUH (Grade 1C).
- We suggest a dose of LMWH (3000 to 4000 anti-Xa IU  $12 \text{ h}^{-1}$  subcutaneously) depending on BMI as acceptable for obese patients with a lower risk of VTE (Grade 2B).
- We suggest the use of a higher dose of LMWH (4000 to 6000 anti-Xa IU  $12 \text{ h}^{-1}$  subcutaneously) as acceptable for obese patients with a higher risk of VTE (Grade 2B).
- We recommend extended prophylaxis for patients with a high risk of VTE during the postdischarge period for 10 to 15 days (Grade 1C).

### Nonbariatric surgery

- We suggest that in surgery with an indication for VTE prophylaxis, a higher prophylactic dose of LMWH (3000 to 4000 anti-Xa IU  $12 \text{ h}^{-1}$  subcutaneously) should be considered for obese patients with a BMI more than  $40 \text{ kg m}^{-2}$  undergoing nonbariatric surgery (Grade 2C).
- For additional and general recommendations, we refer to the section on 'VTE prophylaxis for obese patients in bariatric surgery'.

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