Who Should Get Extended Thromboprophylaxis After Bariatric Surgery?

A Risk Assessment Tool to Guide Indications for Post-discharge Pharmacoprophylaxis

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Objective: To determine the risk factors for 30-day postdischarge venous thromboembolism (VTE) after bariatric surgery and to identify potential indications for extended pharmacoprophylaxis.

Background: VTE is among most common causes of death after bariatric surgery. Most VTEs occur after hospital stay; still a few patients receive extended pharmacoprophylaxis postdischarge.

Methods: From American College of Surgeons-National Surgical Quality Improvement Program, we identified 91,963 patients, who underwent elective primary and revisional bariatric surgery between 2007 and 2012. Regression-based techniques were used to create a risk assessment tool to predict risk of postdischarge VTE. The model was validated using the 2013 American College of Surgeons-National Surgical Quality Improvement Program dataset (N = 20,575). Significant risk factors were used to create a user-friendly online risk calculator.

Results: The overall 30-day incidence of postdischarge VTE was 0.29% (N = 269). In those experiencing a postdischarge VTE, mortality increased about 28-fold (2.60% vs 0.09%; P < 0.001). Among 45 examined variables, the final risk-assessment model contained 10 categorical variables including congestive heart failure, paraplegia, reoperation, dyspnea at rest, nongastric band surgery, age ≥60 years, male sex, BMI ≥50 kg/m², postoperative hospital stay ≥3 days, and operative time ≥3 hours. The model demonstrated good calibration (Hosmer-Lemeshow goodness-of-fit test, P = 0.71) and discrimination (c-statistic = 0.74). Nearly 2.5% of patients had a predicted postdischarge VTE risk ≥1%.

Conclusions: More than 80% of post-bariatric surgery VTE events occurred post-discharge. Congestive heart failure, paraplegia, dyspnea at rest, and reoperation are associated with the highest risk of post-discharge VTE. Routine post-discharge pharmacoprophylaxis can be considered for high-risk patients (ie, VTE risk >0.4%).

Keywords: bariatric surgery, complication, deep vein thrombosis, gastric bypass, morbidity, mortality, pharmacoprophylaxis, pulmonary embolism, sleeve gastrectomy, thrombosis, venous thromboembolism

After Bariatric Surgery?

The obesity epidemic worldwide and the exponential rise in morbid obesity have led to a significant increase in bariatric surgery over the past two decades driven by the advancements in surgical techniques and use of laparoscopy.1–3 Despite a substantial decrease in the postoperative adverse events because of key improvements in multidisciplinary perioperative surgical care of morbidly obese patients, bariatric surgery is associated with certain postoperative complications.4

Venous thromboembolism (VTE) remains a major cause of morbidity and mortality after bariatric surgery.5–9 Reported rates of deep vein thrombosis (DVT) are 1–3% and 0.3–2% for pulmonary embolism (PE).7–10 Given the significant VTE risk in these patients, both the American College of Chest Physicians and the American Society for Metabolic and Bariatric Surgery have recommended that in addition to mechanical prophylaxis some form of pharmacoprophylaxis be administered to all bariatric surgery patients in the absence of contraindications.1,11–12

Greater majority of VTE events after bariatric surgery occur after the discharge from the hospital but within the 30-day postoperative period.13 Furthermore, certain VTE risk factors such as body mass index (BMI), age, sex, personal history of VTE, obesity hypoventilation syndrome, immobility, pulmonary hypertension, operative time, and procedure type have been identified.14–15 However, such risk profiles are not well established and there is little evidence to guide a risk-adjusted approach to VTE prevention postbariatric surgery.

Despite the customary inhospital use of mechanical and pharmacoprophylaxis, it is unclear who should receive a more aggressive chemoprevention perhaps with a higher dose or a more extended prophylaxis period after their hospital discharge. Hence, we aimed to determine the risk factors for 30-day postdischarge VTE after bariatric surgery and to identify potential indications for extended pharmacoprophylaxis.

METHODS

The study is based on analysis of data from the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database. The ACS-NSQIP prospectively collects detailed data on over 300 variables, including standardized and audited demographic variables, preoperative comorbidities, laboratory values, and 30-day postoperative mortality and morbidity outcomes for patients undergoing major surgical procedures in academic and community hospitals in North America (435 participating sites in 2013 and 374 sites in 2012). The program has utilized several mechanisms to ensure that the data collected are of the highest consistency and reliability.16
We identified adult obese patients (BMI ≥30 kg/m²), who underwent bariatric surgical procedures including adjustable gastric banding (AGB), sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), biliopancreatic diversion-duodenal switch (BPD-DS), and revisional surgery using their respective Current Procedural Terminology codes (AGB: 43770; SG: 43843, 43775; RYGB: 43644, 43645; BPD-DS: 43845; and revision 43848, 43860, 43865). Patients who underwent emergency surgery or unrelated concurrent procedures, such as hysterectomy, had a surgery in the 30 days before the index bariatric surgery, preoperative sepsis, disseminated cancer, and American Society of Anesthesiology (ASA) class 5 (Moribund) were excluded. Based on the inclusion/exclusion criteria, 91,963 patients from 2007 to 2012 were included. As we aimed to evaluate postdischarge VTE occurrence, patients who developed VTE in the index hospital stay were further excluded (N = 54) making the study cohort for statistical analysis at 91,909 patients. In addition, 20,575 patients with the same criteria were identified in the ACS-NSQIP 2013 database to examine the validity of risk model.

The primary outcome was the occurrence of postdischarge VTE (including DVT or PE) within 30-days of the index bariatric surgery. The ACS-NSQIP defines DVT as a new thrombus within the venous system confirmed with imaging studies and requiring therapy. The PE should be documented with ventilation-perfusion lung scan (V-Q scan), CT scan, pulmonary arteriogram, or any other definitive modality (including direct pathology examination such as autopsy). A postdischarge VTE variable implies events, which occurred after hospital discharge after index bariatric surgery.

Independent demographic variables were sex, age, race/ethnicity, weight, and BMI. Lifestyle factors included smoking status and alcohol use. Examined comorbidities included diabetes (and insulin usage), hypertension, history of pulmonary diseases [pneumonia, dyspnea, and chronic obstructive pulmonary diseases (COPD)], congestive heart failure (CHF), history of coronary artery disease (CAD) (binary variable representing angina, myocardial infarction, cardiac interventions, and cardiac surgeries), history of atherosclerotic peripheral vascular diseases (PVD), history of kidney diseases (renal failure and being on dialysis), history of cerebrovascular diseases (transient ischemic attack and stroke), paraplegia, and steroid/immunosuppressant use for chronic conditions. The functional status (dependent/independent) and the ASA score were also collected. Preoperative laboratory variables included serum creatinine, albumin, hematocrit, and platelet count. The effect of type of surgery, operative time, return to the operating room, and length of stay (LOS) were also assessed. All variables were clearly defined in the ACS-NSQIP database user guide.¹⁶

Statistical analyses were carried out using the STATA software (Stata Corp, TX) version 12. The estimates on the study variables are expressed as mean ± standard deviation (SD) and frequencies (%). Patients were categorized into postdischarge VTE and no VTE subgroups. Univariate analyses using student’s t test or Wilcoxon rank-sum test for continuous variables, and Pearson χ² test or Fisher exact test for categorical variables were used to assess potential risk factors for postdischarge VTE. Multiple logistic regression with stepwise variable selection was used to construct a model for prediction of the primary outcome. Independent risk factors with a significant association with postdischarge VTE (P < 0.1) in univariate analyses were entered into a model. With backward elimination procedure, only significant risk factors (P < 0.05) were kept in the model. Afterward, a forward stepwise selection was also utilized which achieved the same model. Once a stable model was developed, all eliminated variables were rechecked and none had a significant effect on the model. Odds ratio (OR) and 95% confidence intervals (CI) were used as measures of magnitude of association.

The receiver-operating characteristic (ROC) curve showed the sensitivity and specificity of various cut-points for calculated risk to predict postdischarge VTE and the best cut-points were specified with Youden’s J index (sensitivity + specificity − 1). The calibration of the model was tested using the Hosmer-Lemeshow goodness-of-fit test. The discriminatory capability of the model was assessed using the c-statistic.¹⁷–¹⁹ The risk model based on the 2007–2012 ACS-NSQIP dataset was then validated using the 2013 dataset. The regression equation used to generate the risk assessment model was utilized to construct a free online version of the calculator using the Cleveland Clinic Risk Calculator Constructor (http://www.r-calc.com).

RESULTS

We identified 91,963 patients who underwent bariatric surgeries between 2007 and 2012. Thirty-day total and postdischarge frequencies of DVT were 0.22% (N = 207) and 0.19% (N = 178), respectively. Furthermore, 30-day total and postdischarge frequencies of PE were 0.17% (N = 154) and 0.13% (N = 124), respectively. Overall, 83% (269/323) of postbariatric surgery VTE events occurred after hospital discharge (Figure 1).

Baseline characteristics of patients who underwent primary and revisional bariatric surgery between 2007 and 2012 have been summarized in Table 1. Patients had a mean age of 45.01 ± 11.62 years and BMI of 45.91 ± 7.90 kg/m². Seventy-nine percent of cohort were female, and 74% were white. After excluding the 54 patients,

![FIGURE 1. Postoperative occurrence of deep vein thrombosis and pulmonary embolism in 30 days after bariatric surgery.](image-url)
who developed VTE during their original hospital stay, we identified 269 (0.29%) patients who suffered from postdischarge VTE. Compared with those with no VTE, the mean age of the postdischarge VTE patients was higher (48.03 vs 44.99 years old; \( P < 0.001 \)). The percentage of males among postdischarge VTE patients (34.20%) was higher compared with non-VTE patients (20.87%; \( P < 0.001 \)). Mean BMI was 49.16 kg/m\(^2\) in postdischarge VTE patients and 45.90 kg/m\(^2\) in non-VTE patients (\( P < 0.001 \)).

Selected perioperative characteristics of the study cohort are presented in Table 2. Overall postoperative mortality was 0.10% (\( N = 95 \)). Among those with postdischarge VTE, the mortality rate was 2.60% (\( N = 7 \)) compared with 0.09% (\( N = 86 \)) among those with no 30-day postoperative VTE (\( P < 0.001 \)). Patients with postdischarge VTE had a significantly higher proportion of ASA classes III and IV (75.47%, \( N = 203 \)) compared with those patients with no VTE (65.52%, \( N = 60,016 \); \( P = 0.006 \)). The frequencies of RYGB were similar between patients with postdischarge VTE (59.11%) and those with no VTE (57.16%; \( P = 0.520 \)). The frequency of SG was higher in the VTE group (23.05%) compared with non-VTE patients (13.48%; \( P < 0.001 \)) and the frequency of AGB placement was higher in the non-VTE (26.87%) compared with postdischarge VTE patients (9.29%; \( P < 0.001 \)).

Higher frequencies of BPD-DS and revisional surgeries were found in postdischarge VTE patients (5.20% and 3.35%) compared with non-VTE patients (1.42% and 1.07%; \( P < 0.001 \)), respectively. Compared with RYGB, AGB was associated with lower risk of postdischarge VTE (OR = 0.33; 95% CI 0.22–0.51), but SG (OR = 1.65; 95% CI 1.23–2.22), BPD-DS (OR = 3.54; 95% CI 2.04–6.13), and revisional surgery (OR = 3.03 95% CI 1.54–5.94) were associated with a higher risk of postdischarge VTE. Finally, mean LOS was also higher among patients with postdischarge VTE (2.69 days) compared with those with no VTE (1.88 days; \( P < 0.001 \)).

Of the 45 examined variables, the final risk assessment model for prediction of postdischarge VTE contained 10 categorical variables including history of CHF (OR = 6.58; 95% CI 1.95–22.20), paraplegia (OR = 5.71; 95% CI 1.36–24.02), return to operating room (OR = 5.11; 95% CI 3.25–8.04), dyspnea at rest (OR = 3.95; 95% CI 1.57–9.95), nongastric band surgery (OR = 2.44; 95% CI 1.55–3.85), age ≥60 years (OR = 1.96; 95% CI 1.39–2.75), male sex (OR = 1.92; 95% CI 1.44–2.57), BMI ≥50 kg/m\(^2\) (OR = 1.67; 95% CI 1.26–2.23), LOS ≥3 days (OR = 1.58; 95% CI 1.16–2.14), and operative time ≥3 hours (OR = 1.57; 95% CI 1.13–2.18) (Table 3). The calculated multiple logistic regression equation was the following:

\[
L = -7.337 + (\text{congestive heart failure} \times 1.883) + (\text{paraplegia} \times 1.743) + (\text{return to operating room} \times 1.631) + (\text{dyspnea at rest} \times 1.375) + (\text{non-gastric band surgery} \times 0.893) + (\text{age} \geq 60\text{years} \times 0.67) + (\text{male sex} \times 0.655) + (\text{BMI} \geq 50\text{kg/m}^2 \times 0.516) + (\text{postoperative hospital stay} \geq 3\text{days} \times 0.455) + (\text{operative time} \geq 3\text{hrs} \times 0.451).
\]
TABLE 2. Perioperative characteristics of the study cohort stratified on the occurrence of post-discharge VTE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study Cohort N = 91,963</th>
<th>Post-discharge VTE N = 269</th>
<th>No VTE N = 91,640</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Class † – N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)– No Disturbance</td>
<td>444 (0.48)</td>
<td>1 (0.37)</td>
<td>443 (0.48)</td>
<td>0.006</td>
</tr>
<tr>
<td>(2)– Mild Disturbance</td>
<td>31,168 (33.89)</td>
<td>64 (23.79)</td>
<td>30,911 (33.89)</td>
<td>0.67</td>
</tr>
<tr>
<td>(3)– Severe Disturbance</td>
<td>58,281 (63.37)</td>
<td>193 (71.75)</td>
<td>58,080 (63.37)</td>
<td>0.17</td>
</tr>
<tr>
<td>Operation type – N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AGB</td>
<td>24,650 (26.80)</td>
<td>25 (9.29)</td>
<td>24,624 (26.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SG</td>
<td>12,422 (13.51)</td>
<td>62 (23.05)</td>
<td>12,351 (13.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RYGB</td>
<td>52,578 (57.17)</td>
<td>159 (59.11)</td>
<td>52,383 (57.16)</td>
<td>0.52</td>
</tr>
<tr>
<td>BPD-DS</td>
<td>1319 (1.43)</td>
<td>14 (5.20)</td>
<td>1303 (1.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Revisinal</td>
<td>994 (1.08)</td>
<td>9 (3.35)</td>
<td>979 (1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Operation time (minute) – mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AGB</td>
<td>69.11 ± 32.21</td>
<td>86.56 ± 47.00</td>
<td>69.10 ± 32.19</td>
<td>0.007</td>
</tr>
<tr>
<td>SG</td>
<td>100.55 ± 48.16</td>
<td>117.66 ± 55.54</td>
<td>100.48 ± 48.10</td>
<td>0.005</td>
</tr>
<tr>
<td>RYGB</td>
<td>135.08 ± 55.68</td>
<td>147.00 ± 62.90</td>
<td>135.03 ± 55.66</td>
<td>0.007</td>
</tr>
<tr>
<td>BPD-DS</td>
<td>176.24 ± 94.18</td>
<td>164.21 ± 83.48</td>
<td>176.36 ± 94.33</td>
<td>0.631</td>
</tr>
<tr>
<td>Revisinal</td>
<td>200.13 ± 101.74</td>
<td>189.67 ± 76.87</td>
<td>199.63 ± 101.45</td>
<td>0.769</td>
</tr>
<tr>
<td>LOS (day) – mean ± SD</td>
<td>7.08 ± 1.22</td>
<td>2.69 ± 0.64</td>
<td>1.88 ± 1.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Return to operating room</td>
<td>1625 (1.77)</td>
<td>28 (10.41)</td>
<td>1593 (1.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality – N (%)</td>
<td>95 (0.10)</td>
<td>7 (2.60)</td>
<td>86 (0.09)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AGB indicates adjustable gastric banding; ASA, American Society of Anaesthesiology; BPD-DS, biliopancreatic diversion-duodenal switch; LOS, length of stay; RYGB, Roux-en-Y gastric bypass; SD, standard deviation; SG, sleeve gastrectomy; VTE, venous thromboembolism.

† As the focus is only on postdischarge VTE, we have excluded the 54 patients who developed VTE during the original hospital stay from the subgroup analysis.

| Patients categorized as ASA class 5 (Moribund) at the time of the index surgery have been excluded from the study cohort.

The estimated probability of 30-day postdischarge VTE for a given patient is calculated using the following formula:

Estimated probability of composite adverse event (100%) = EXP [L] / (1 + EXP [L]).

The notation EXP is equivalent to e^x, where “e” is the base of natural logarithm (2.718). The model demonstrated a good calibration (Hosmer-Lemeshow goodness-of-fit test, x^2 = 4.58; P = 0.711) and discrimination (c-statistic = 0.741).

The generated risk model based on 2007–2012 ACS-NSQIP was subsequently validated on the validation dataset (2013, N = 20,575), which showed a relatively similar performance (c-statistic = 0.66; 95% CI 0.59–0.73). Of note, data of “paraplegia” was not available in the validation dataset, which could negatively affect the model performance.

On the basis of the regression equation and the parameter estimates listed in Table 3, a risk calculator for postdischarge VTE was developed. A user-friendly version of the risk calculator is accessible at http://www.r-calc.com under the bariatric surgery formula tab. When the required values are entered into the calculator, the percent estimate of postdischarge VTE after bariatric surgery is calculated. A few examples on the estimated probability of postdischarge VTE:

- Estimated risk in a healthy young woman with BMI of 40 kg/m^2 undergoing uncomplicated RYGB would be 0.16%.
- Estimated risk in 63 years old man with BMI of 60 kg/m^2 undergoing SG with a postoperative LOS of 5 days would be 1.56%.
- Estimated risk in 48 years old woman with BMI of 38 kg/m^2 and preoperative dyspnea undergoing RYGB which needed reoperation and a prolonged LOS for a surgical complication would be 4.82%.

Performance of the risk assessment tool at different cut-points has been shown in Table 4. For example, cut-point >0.2% includes 50% of patients with a sensitivity of 82% and specificity of 50% for prediction of postdischarge VTE. With increasing cut-point to >0.5%, the percentage of included patients decreases to 12% along with a reduction in sensitivity to 43% and an increase in specificity to 88%. Nearly 2.5% of patients had a predicted postdischarge VTE risk >1%.

BMI >50 kg/m^2 alone was a poor predictor of postdischarge VTE (c-statistic = 0.60) with a sensitivity of 40% and a specificity of

TABLE 3. Predictive Factors of Postdischarge VTE Based on Multivariate Analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Crude OR</th>
<th>Adjusted OR (95% CI)</th>
<th>Estimate</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>13.68</td>
<td>6.58 (1.95–22.20)</td>
<td>1.88</td>
<td>0.62</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>9.20</td>
<td>5.71 (1.36–24.02)</td>
<td>1.74</td>
<td>0.73</td>
</tr>
<tr>
<td>Return to operating room</td>
<td>7.04</td>
<td>5.11 (2.59–10.15)</td>
<td>1.63</td>
<td>0.23</td>
</tr>
<tr>
<td>Dyspnea at rest</td>
<td>6.06</td>
<td>3.95 (1.57–9.95)</td>
<td>1.37</td>
<td>0.47</td>
</tr>
<tr>
<td>Nongastric band surgery</td>
<td>3.43</td>
<td>2.44 (1.55–3.85)</td>
<td>0.89</td>
<td>0.23</td>
</tr>
<tr>
<td>Age ≥60 (yrs)</td>
<td>2.03</td>
<td>1.96 (1.39–2.75)</td>
<td>0.67</td>
<td>0.17</td>
</tr>
<tr>
<td>Male</td>
<td>2.10</td>
<td>1.92 (1.44–2.57)</td>
<td>0.65</td>
<td>0.15</td>
</tr>
<tr>
<td>BMI ≥50 (kg/m^2)</td>
<td>2.00</td>
<td>1.67 (1.26–2.23)</td>
<td>0.52</td>
<td>0.15</td>
</tr>
<tr>
<td>LOS ≥3 (day)</td>
<td>2.72</td>
<td>1.58 (1.16–2.14)</td>
<td>0.46</td>
<td>0.16</td>
</tr>
<tr>
<td>Operation Time ≥3 (hrs)</td>
<td>2.45</td>
<td>1.57 (1.13–2.18)</td>
<td>0.45</td>
<td>0.17</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; CHF, congestive heart failure; CI, confidence interval; LOS, length of stay; OR, odds ratio; SEE, standard error of estimate; VTE, venous thromboembolism.
Rogers, those who suffered from a postdischarge VTE had a mortality rate of 2.60%.

We also found that patients who developed postdischarge VTE as compared with those with no VTE were older black males with a higher BMI, who had a higher prevalence of dyspnea at rest, CHF, PVD, paraplegia, and COPD at baseline. In addition, they had significantly higher ASA scores, underwent lengthier operations and had more BPD-DS and revisional procedures, stayed in the hospital longer, and needed more reoperations. Moreover, after the multivariate analysis, we found 10 major risk factors for postdischarge VTE all of which increased the risk of VTE by at least 1.5-fold and subsequently were used to generate a risk calculator. CHF was found to be the strongest independent predictor increasing the likelihood of postdischarge VTE by near seven-fold, followed by the presence of paraplegia (near 6-fold), 30-day return to the operating room (more than five-fold), and dyspnea at rest that independently accounted for a near four-fold increase in the likelihood of postdischarge VTE. Age greater than 60 years, male sex, super-obesity (BMI ≥ 50 kg/m²), procedures other than AGB placement, longer operation (≥3 hrs), and lengthier index hospital stay (≥3 days) were also found to be independent risk factors for postdischarge VTE.

Historically, there have been a few VTE risk assessment models, such as Kucher, Rogers, Caprini, Pannucci, and Scarborough models, that are either considered accurate assessment tools for higher-risk patients only, complex to use with too many predictors, or created using only vascular surgery patients which would limit their use for other surgical procedures such as bariatric surgery.

Merkow et al identified predictors of post-discharge VTE in patients undergoing cancer surgery using ACS-NSQIP data and after demonstrating that over 33% of all VTE events occurred post discharge, advocated for extended prophylaxis in higher-risk patients. Winegar et al also evaluated the 90-day VTE events after bariatric surgery using the Bariatric Outcomes Longitudinal Database and found that greater than 70% of VTE events ensued after the patient was discharged; furthermore, the majority of the occurrences fell within the 30-day period. In our current study, >80% of post-bariatric surgery VTE events occurred postdischarge. Thus, it is important to identify risk factors for VTE after discharge so patients with a higher risk profile could theoretically benefit from a more aggressive prophylaxis.

To our knowledge, our study is the first to evaluate these predictors and generate a risk calculator for postdischarge VTE events in patients undergoing primary and revisional bariatric surgery using a large multicenter database. Our results are consistent and have expanded on the findings from the study by Finks et al which using the Michigan Bariatric Surgery Collaborative database created a risk calculator for all postoperative VTE events post bariatric surgery. Like our study they identified higher age and BMI, male sex, longer surgery (≥3 hours), and non-AGB placement procedures along with a prior history of VTE as independent risk factors for postoperative VTE. However, our study identified additional strong cardiopulmonary risk factors in CHF, dyspnea at rest, and paraplegia as a marker of immobility all of which have been recognized in other postsurgical VTE risk assessment models.

In addition, unlike the study by Finks et al the accuracy and performance of our risk calculator was internally validated using the 2013 ACS-NSQIP database. Using the ACS-NSQIP data, which is a robust clinical, validated, and audited database, enabled us to consider multiple perioperative variables from a large sample size of patients from both the academic and community centers. The user-friendly online version of this calculator can assist in risk assessment and decision making.

Choosing a particular cut-point on estimated risk of postdischarge VTE to guide extended pharmacoprophylaxis can be arbitrary. By choosing a lower cut-point, which is associated with a higher sensitivity but lower specificity (Table 4), a higher percentage of patients will receive extended prophylaxis that may in turn translate into higher costs and adverse events such as bleeding. In our opinion, a risk >0.4% can be a reasonable indication for extended pharmacoprophylaxis: 20% of patients would need postdischarge prophylaxis with sensitivity, specificity, and Youden’s J index of 53%, 80%, and 33. Compared with BMI ≥ 50 kg/m² alone, which some bariatric centers use as a criterion for extended pharmacoprophylaxis, the former provides higher sensitivity (53% vs 40%) and specificity (80% vs 75%), whereas impacting fewer patients (20% vs 24%). Overall, cut-point of risk >0.3 has the best performance (Youden’s J index = 36), but include almost one third of bariatric patients and 40% of nonobese band patients.

| TABLE 4. Performance of Risk Calculator in Various Cut-points to Detect Postdischarge VTE |
|---------------------------------|--------|--------|--------|--------|
| Cut-point | Patients Included (%) | Sensitivity (%) | Specificity (%) | Youden’s J |
| >0.2% | 50 | 82 | 50 | 32 |
| >0.3% | 29.5 | 65 | 71 | 36 |
| >0.4% | 20 | 53 | 80 | 33 |
| >0.5% | 12 | 43 | 88 | 31 |
| >0.75% | 6.5 | 32 | 94 | 26 |
| >1% | 2.5 | 20 | 97 | 17 |
| >3% | 0.5 | 3 | 99.5 | 2.5 |
| For Comparison: BMI >50 kg/m² | 24 | 40 | 75 | 15 |

Youden’s J index is a statistic that captures the accuracy performance of a diagnostic test in conjunction with Receiver Operating Characteristic (ROC) analysis which is used to identify the best cut-point and is obtained using the following formula: sensitivity + specificity – 1.

BMI, Body Mass Index; VTE, Venous Thromboembolism.

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A predicted risk >1% can represent 2.5% of patient population who are very high risk to develop postdischarge VTE (specificity = 97%). Therefore, the threshold depends on how aggressive versus how conservative the physicians want to offer prophylactic anticoagulation. In considering extended pharmacoprophylaxis, predicted risk of VTE, potential benefits, and possible complications (including the risk of bleeding) of available medications, and cost should be taken into account.

Once the higher-risk patients for postdischarge VTE are identified, the question remains as to how to adequately carry out VTE prophylaxis beyond their hospital stay. No clear consensus exists on the choice, timing, and duration of thromboprophylaxis after bariatric surgery.29,30 A large literature review by Huo et al1 showed that low-molecular-weight heparin (LMWH) was efficacious, associated with low rates of clinically relevant bleeding complications, and was cost-effective in patients at high risk for VTE. Results of a cohort study from Michigan Bariatric Surgery Collaborative indicated that LMWH was more effective (>50%) than unfractionated heparin for the prevention of postoperative VTE among patients undergoing bariatric surgery. This difference was more pronounced in patients at high risk of postbariatric surgery VTE. In addition, the rate of postoperative hemorrhage was similar in patients who were taking either prophylactic doses of LMWH or unfractionated heparin (1.6%).32 Although unfractionated heparin is much less expensive than LMWH, there is a trend toward the use of LMWH over unfractionated heparin for prophylaxis.33 Low-molecular-weight heparins bind specifically to antithrombin III and have a better bioavailability through easier subcutaneous absorption (which may be important in severely obese patients). The half-life of LMWHs is longer than that for unfractionated heparin, which translates to less frequent injections. In addition, heparin-induced thrombocytopenia and osteoporosis are less common in LMWH-treated patients.33

Ample literature have demonstrated that cancer patients undergoing surgery have twice the risk of postoperative VTE and three times the risk of fatal PE compared with patients undergoing surgery for benign disease and the risk period seems to extend beyond the index hospital stay.34,35 Furthermore, a large French national multicenter study showed that thromboprophylaxis less than 4 weeks may be a predictive of the occurrence of VTE after major cancer operations.36 Hence most centers worldwide, administer a 4-week course of LMWH as extended thromboprophylaxis postdischarge after major cancer operations.11,37,38 In a study comparing inhospital-only versus extended 10-day pharmacoprophylaxis using enoxaparin (30 mg administered subcutaneously every 12 hrs) in 308 consecutive patients undergoing bariatric surgery at a single center. Rafaopoulos et al39 showed that the 30-day VTE rate was significantly higher in the group that only received in-hospital prophylaxis (4.5% vs 0%; P = 0.006).

However, bariatric patients add a complexity to customary plans such as the one used in cancer patients, chiefly because of inability to adjust the prophylactic dosage of the anticoagulant of choice based on patient’s weight. Multiple studies have shown that using a higher dose of enoxaparin (60 mg vs 40 mg) administered subcutaneously every 12 hours in the perioperative period especially for patients with BMI ≥60 kg/m² was safe and did not lead to any increased risk of clinically significant bleeding.40,41 Moreover, safety of pharmacoprophylaxis using the extended (10-day to 14-day course) high-dose LMWH has also been shown in multiple studies.42,43

In a study comparing extended VTE prophylaxis using BMI-driven 40 mg versus 60 mg enoxaparin (administered subcutaneously every 12 hrs up to 10 days postdischarge) involving 223 patients undergoing RYGB, Borkgren-Okonk et al44 used serial serum anti-factor Xa levels during the hospital stay to adjust the dosage of enoxaparin for results outside the target VTE prophylactic range after the third dose and patients were subsequently discharged with the adjusted dose for a total of 10 days: 21% of patients in the 40 mg group and 31% in the 60 mg group did not reach the target VTE prophylactic range by the third enoxaparin dose and needed adjustments. Therefore, concerns have been expressed that fixed prophylactic doses of anticoagulants may be inadequate in severely obese patients.44 Nevertheless, because of paucity of high-quality literature to guide exact dosing and duration of extended VTE pharmacoprophylaxis, perhaps anti-Xa levels could be utilized to monitor and adjust dosing of the LMWH after discharge for those higher-risk patients that would benefit from an extended thromboprophylaxis. Anti-Xa activities measured at the time of peak plasma concentration (4 hrs after subcutaneous injection) yield the best correlation with clinical effect. Target anti-Xa levels for LMWHs are not well defined, but some studies have suggested peak concentrations of 0.2—0.4 IU/mL for VTE prophylaxis.44

Certain limitations need to be taken into consideration when interpreting our results. There are inherent limitations when the ACS-NSQIP database is used that can introduce both selection and misclassification bias. ACS-NSQIP captures only a sample of all surgical patients from participating centers and does not collect data unique to bariatric surgery patients. Some cases of VTE might not be diagnosed and/or captured in the database. There are significant risk factors such as oral contraceptives, previous history of VTE, major venous stasis, and acquired and congenital hypercoagulable disorders such as the antiphospholipid syndrome, factor V Leiden, prothrombin gene mutation, and protein C, S, and antithrombin deficiencies that significantly increase the risk of VTE, which are not captured in ACS-NSQIP database. Particularly, patients with a previous episode of VTE are at an even higher risk for recurrence when exposed to a higher-risk condition—that is, after a major general surgical procedure such as bariatric surgery.45 Extended thromboprophylaxis after bariatric surgery has been suggested in these conditions.46 We were also unable to identify cases of catheter-related DVT in the study cohort. In addition, data regarding the mode and duration of thromboprophylaxis is not available in ACS-NSQIP database and could not be assessed in the current study. Nonetheless, more than 95% of ACS-NSQIP institutions prescribe perioperative thromboprophylaxis in compliance with quality improvement guidelines.47 Finally, we did not include all early postoperative adverse events in the multivariate analysis. Although certain serious complications, such as anastomotic leak, are likely to be significant risk factors for VTE,47 they will likely also increase LOS beyond 3 days or lead to a reoperation both of which are included in the final regression model and the risk calculator. Including all postoperative complications in the regression model along with factors such as LOS and return to operating room, which are considered collective proxies for postoperative morbidity, will introduce collinearity leading to a decrease in the robustness of the model.

Based on the findings of current study and other available literature, a VTE risk stratification and prophylaxis for bariatric surgical patients can be suggested (Table 5). Specifically, extended VTE prophylaxis may be directed depending on the careful assessment of the individual patient’s risk utilizing the suggested risk calculator. Obviously, the suggested indications, along with the type, dose, and duration of pharmacoprophylaxis should be examined by high quality trials.

In conclusion, as most of postbariatric surgery VTE events occurred after hospital discharge, routine postdischarge pharmacoprophylaxis can be considered for high-risk patients. Congestive heart failure, dyspnea at rest, paraplegia, and reoperation are associated with the highest risk for occurrence of 30-day postdischarge.
TABLE 5. Suggested VTE Prevention Strategies in Bariatric Surgical Patients

<table>
<thead>
<tr>
<th>Level of Risk</th>
<th>Patients’ Characteristics</th>
<th>Suggested Prevention Strategies</th>
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<tbody>
<tr>
<td>Moderate Risk</td>
<td>All bariatric surgical patients without additional risk factors</td>
<td>Early and aggressive postoperative mobilization in hospital pharmacoprophylaxis.&lt;sup&gt;1&lt;/sup&gt; In hospital pharmacoprophylaxis.&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>High Risk</td>
<td>A calculated post-discharge VTE risk &gt;0.4%&lt;sup&gt;†&lt;/sup&gt; Past history of DVT or PE Congenital or acquired hypercoagulable conditions (eg, positive factor V Leiden, prothrombin 20210A) Significant chronic venous insufficiency</td>
<td>Early and aggressive postoperative mobilization in hospital pharmacoprophylaxis.&lt;sup&gt;1&lt;/sup&gt; In hospital pharmacoprophylaxis.&lt;sup&gt;1&lt;/sup&gt; Extended postdischarge prophylaxis for 2 weeks&lt;sup&gt;†&lt;/sup&gt;</td>
</tr>
<tr>
<td>Very High Risk</td>
<td>A calculated postdischarge VTE risk &gt;1%&lt;sup&gt;§&lt;/sup&gt;</td>
<td>Early and aggressive postoperative mobilization in hospital pharmacoprophylaxis&lt;sup&gt;1&lt;/sup&gt; Extended post-discharge prophylaxis for 4 weeks&lt;sup&gt;†&lt;/sup&gt; Consider LMWH dose adjustment based on anti-Xa level&lt;sup&gt;†&lt;/sup&gt; Consider DVT screening with Duplex</td>
</tr>
</tbody>
</table>

VTE. We believe a calculated VTE risk >0.4% based on our risk calculator and/or presence of congenital or acquired hypercoagulable conditions, history of VTE, or significant venous stasis can be important indications for extended postdischarge pharmacoprophylaxis after bariatric surgery. A small subset (2.5% of patient population) of very high-risk patients with a calculated VTE risk >1% may benefit from even more aggressive preventive measures (Table 5). These patients may also be candidates for tighter postoperative screening compared with general bariatric surgical cases. Further studies ideally randomized control trials are needed to decide which agent, at what dosage and duration should be considered for extended VTE pharmacoprophylaxis. These recommendations are subject to change as more data become available.

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REFERENCES


