Value of pharmacologic thromboprophylaxis for prevention of thromboembolic complications in bariatric surgery

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Objective
The objective of this study was to assess safety and efficacy of pharmacologic thromboprophylaxis in morbidly obese patients undergoing bariatric surgery for prevention of silent deep vein thrombosis (DVT).
Patients and methods
This prospective study included 50 morbidly obese patients scheduled for primary one-stage laparoscopic bariatric surgery randomly allocated into one of two treatment groups according to the method of thromboprophylaxis. Group M (n=25) was subjected to mechanical prophylaxis with bilateral graduated compression stockings. Group MC (n=25) was subjected to mechanical plus pharmacologic prophylaxis using 40 mg of the low-molecular-weight heparin enoxaparin subcutaneously, 12 h before surgery, and postoperatively daily for 2 weeks. Bilateral lower limb venous duplex was done to detect silent DVT (the primary outcome measure), before discharge and after 2 weeks.
Results
Three patients developed silent DVT (6%); all of them were among group M (P=0.235, relative risk: 0.47, 95% confidence interval: 0.35–0.64). There was no significant difference between patients with DVT and those without DVT regarding age, BMI, operative time, comorbidities, or type of surgery. No bleeding complications were recorded in the two studied groups.
Conclusion
Perioperative low-molecular-weight heparin extending for 2 weeks postoperatively combined with graduated compression stockings is safe and effective for the prevention of silent DVT following laparoscopic bariatric surgery.

Keywords:
bariatric surgery, deep vein thrombosis, pulmonary embolism thromboembolic, thromboprophylaxis

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Introduction

The prevalence of obesity has been markedly accelerated during the past three decades, with marked geographical disparities. Egypt was classified among countries with high prevalence of obesity, especially in women, despite being one of the developing countries. It has been estimated that the prevalence of obesity is 26.4% in men and 48.4% in women [1].

Currently, bariatric surgery is widely adopted as the most effective therapeutic option for morbid obesity. It was estimated that 5875 procedures were performed in Egypt in 2014 including 4570 laparoscopic procedures [2]. However, it is a major surgical procedure with a risk of significant early and late morbidity and of perioperative mortality [3].

Patients undergoing bariatric surgery are at an increased risk for venous thromboembolism (VTE) [4,5]. Obesity *per se* is a moderate risk factor for VTE [6], but it interacts with other risk factors increasing the risk of VTE development and recurrence [7]. Moreover, venous hemodynamics are affected by obesity; dilatation and reduced venous flow were reported in lower limbs using color-coded duplex ultrasound [8]. Surgery adds more risk of VTE, which is higher with open procedures compared with laparoscopic procedures [9].

The optimal prophylactic method for VTE following bariatric surgery has yet to be elucidated. The main recognized options include mechanical compression devices, chemoprophylaxis, and use of inferior vena cava filters. Many studies investigated the safety and efficacy of pharmacologic prophylaxis of VTE in bariatric surgery, but no consensus on a recommendation of the ideal drug, regimen, dosing, or duration of use has been reached [10].

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This study was conducted to examine the safety and efficacy of pharmacologic thromboprophylaxis in morbidly obese patients undergoing bariatric surgery for the prevention of silent deep vein thrombosis (DVT).

Patients and methods

This prospective study included 50 morbidly obese patients scheduled for primary one-stage laparoscopic bariatric surgery in the Department of Surgery, Kasr El-Aini Hospital, Cairo University, between March 2015 and September 2015. Patients were enrolled in the study if their age was 18 years or more with a preoperative BMI greater than or equal to 40 kg/m^2 or BMI greater than or equal to 35 kg/m^2 with associated comorbidities (hypertension, dyslipidemia, type 2 diabetes mellitus, sleep apnea, and so on). All patients have a history of failure of conservative treatment of weight loss. The study was approved by the Institutional Review Board of the Faculty of Medicine, Cairo University. All of the participants provided an informed consent to participate in the study.

Exclusion criteria included documented congenital or acquired coagulation disorders, concomitant anti-coagulant or antiplatelet aggregation therapy for other risk factors, hypersensitivity to heparins, previous heparin-induced thrombocytopenia, history of recent or old thromboembolism, postoperative complications, and symptomatic postoperative thromboembolism.

Routine preoperative laboratory investigations were performed for all patients in addition to abdominal and pelvic ultrasound scan and pulmonary function test. Mini-gastric bypass or laparoscopic sleeve gastrectomy was performed according to the patient's selection after consultation with the staff of the bariatric surgery team. Participants were randomly allocated into one of two treatment groups according to the method of thromboprophylaxis. Group M included 25 patients who were subjected to mechanical prophylaxis only in the form of below-knee graduated compression stockings on both lower limbs. Group MC had – in addition to mechanical prophylaxis – pharmacologic prophylaxis using 40 mg of subcutaneous enoxaparin injections (Clexane 40 mg; Sanofi-Aventis, Karachi, Pakistan) 12 h before surgery, and postoperatively every 24 h for 2 weeks. Early postoperative ambulation was initiated in all patients as soon as they recover the effects of anesthesia to reduce venous stasis.

Bilateral lower limb venous duplex was performed before patient discharge for detection of silent DVT. The test was repeated during the follow-up visit after 2 weeks if no evidence of DVT was found on discharge. Examination was performed with a 3–7.5 MHz transducer using a Voluson E8 Machine (General Electric, Boston, MA, USA) by an experienced operator. The iliac, femoral, great saphenous, popliteal, peroneal, post-tibial, and soleal veins were evaluated on transverse and long-axis views. Examination was done in the supine position for iliac and femoral veins, and then the other veins were assessed in an upright position.

The primary outcome measure of the study was detection of silent DVT using duplex ultra-sonography. The secondary outcome measures were adverse effects of pharmacologic therapy – that is bleeding complications.

Statistical analysis

Statistical analysis was done using IBM SPSS statistics (version 22; IBM Corp., Armonk, New York, USA). Numerical data were expressed as mean, SD, and range. Qualitative data were expressed as frequency and percentage. χ^2-Test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data, comparison between the two groups was done using independent sample *t*-test or Mann–Whitney test as appropriate. All tests were two-tailed. A *P*-value less than 0.05 was considered significant.

Results

There were 45 female and five male participants with a mean age of 40.5 years and a mean BMI of 45.7 kg/m^2. Laparoscopic sleeve gastrectomy was done in 39 (78%) patients and mini-gastric bypass was done in 11 (22%) patients. All procedures were completed laparoscopically with no conversion to open surgery (Table 1).

Three (6%) patients developed silent DVT; all of them were among the 25 patients who received mechanical thromboprophylaxis only (*P*=0.235). Relative risk (RR) of combined methods was 0.47 [95% confidence interval (CI): 0.35–0.64]. There was no significant difference between patients with DVT and those without DVT regarding age, BMI, operative time, comorbidities, or type of surgery (Table 2).

The three patients who developed silent DVT were treated initially with a low-molecular-weight heparin (LMWH) (Clexane) and warfarin until international normalized ratio reaches 2–3, and then warfarin was

Table 1 Demographic and clinical characteristics of the two studied groups

	Group M (*n*=25)	Group MC (*n*=25)	*P*-value
Age (years)			
Mean±SD	38.3±9.3	41.5±10.6	0.262
Range	20–55	18–57	
Sex			
Male/female	1/24	4/21	0.349
BMI (kg/m^2)			
Mean±SD	44.6±5.3	46.9±7.8	0.229
Range	37.5–50.5	38–69.5	
Comorbidity			
Diabetes mellitus	3 (12)	4 (16)	1.000
Hypertension	7 (28)	5 (20)	0.508
Type of surgery			
Laparoscopic sleeve gastrectomy	21 (84)	18 (72)	0.306
Mini-gastric bypass	4 (16)	7 (28)	
Operative time (min)	154±36	166±45	0.303

Data are presented as mean±SD or *n* (%).

Table 2 Comparison between patients who developed silent deep vein thrombosis and those who did not

	Silent DVT		*P*-value
	Positive (*n*=3)	Negative (*n*=47)	
Age (years)	42.3±6.0	35.8±10.1	0.244
BMI (kg/m^2)	45.3±3.8	44.2±5.4	0.465
Operative time (min)	162±48	158±36	0.636
Hypertension	1 (33.3)	11 (23.4)	1.000
Diabetes mellitus	0 (0.0)	7 (14.9)	1.000
Type of surgery			
LSG	3 (100.0)	36 (76.6)	1.000
MGB	0 (0.0)	11 (23.4)	

Data are presented as mean±SD or *n* (%); DVT, deep vein thrombosis; LSG, laparoscopic sleeve gastrectomy; MGB, mini-gastric bypass.

continued alone for 6 months to keep the international normalized ratio at 2–3. There were no complications recorded in the two studied groups in the form of bleeding, hematoma, wound leak, wound infection, or cardiopulmonary complications.

Discussion

This study demonstrated that combined mechanical and chemothromboprophylaxis is suggested to be superior to mechanical methods only for prevention of silent DVT in patients undergoing laparoscopic bariatric surgery. The difference between mechanical only and combined groups was not statistically significant (*P*=0.235); however, the RR of combined therapy was 0.47 (95% CI: 0.35–0.64).

Prevention of VTE is a priority to improve patient safety in hospitals especially after surgical procedures that carry a significant risk of developing thrombotic complications, such as bariatric surgery. On the basis of the results of previous studies, we extended the thromboprophylaxis for 2 weeks as it was reported that DVT can occur after discharge from the hospital and within 1 month [11,12].

In the current study, asymptomatic DVT occurred in 6% of patients. Most of the studies in the literature reported the incidence of clinical VTE while rates of potential asymptomatic patients were not included. The Bariatric Outcomes Longitudinal Database [13] reported an incidence of VTE of 0.42% in a data set of 74 000 patients; the risk was 1.5% after open surgery and 0.34% after laparoscopic procedures. A comparable figure (0.4%) was reported by the Longitudinal Assessment of Bariatric Surgery (LABS) study [14], whereas the Michigan Surgery Collaborative (MBSC) [15] reported a DVT rate of 0.21%.

The main restraints in thromboprophylaxis in bariatric surgery focus on the risk of significant postoperative bleeding that may require blood transfusions and reoperation with subsequent increased hospital stay and costs. This is of course linked to pharmacologic anticoagulants. Nevertheless, many studies have reported effective thromboprophylaxis with LMWH and unfractionated heparin with variable incidence of significant bleeding.

LMWH in general or abdominal surgery was reported to reduce the risk of clinical Pulmonary Embolism (PE) and clinical VTE by about 70% with an approximate doubling of the risks of major bleeding and wound hematoma (RR: 1.88; 95% CI: 1.54–2.28) [16]. Similar results were reported in studies of gastrointestinal, gynecologic, urological, and thoracic surgery [17].

In fact, the optimal dose of prophylactic heparin in bariatric surgery patients is not clear. LMWH dose is calculated according to body weight. Thus, many studies used an adjusted dose higher than the standard prophylactic dose. Scholten *et al.* [18] concluded that high dose of enoxaparin (40 mg/12 h) can reduce the incidence of DVT without an increase in bleeding complications following bariatric surgery. However, a prospective nonrandomized study that compared unfractionated heparin with 40 mg of subcutaneous enoxaparin twice daily reported that enoxaparin was associated with more frequent postoperative blood transfusion and reoperation for bleeding [19]. These high doses of enoxaparin carry the risk of significant bleeding complications.

In a multicenter pilot study, Imberti *et al.* [20] compared two prophylactic doses of LMWH in bariatric surgery: a standard dose and a 150% of the standard dose. The rates of VTE in the adjusted-dose group was lower (0.8 vs. 1.5%), but not significantly different. The rates of bleeding were 5% for the adjusted-dose group compared with 6.1% for the standard-dose group. Another study reported no VTE events with a standard dose and 167% of the standard dose. Major bleeding rate was 3% in the higher-dose group compared with none in the standard-dose group. Scholten *et al.* [18] compared enoxaparin 30 mg twice daily with 40 mg twice daily. The higher-dose group had a significantly lower incidence of VTE events (0.6 vs. 5.4%), with no significant difference in bleeding. Other studies used different doses with different regimens.In the current study, we used 40 mg of enoxaparin 12 h preoperatively and once a day for 2 weeks. This extended chemoprophylaxis regimen combined with bilateral above-knee graduated compression stockings effectively prevented symptomatic and asymptomatic DVT. The practice of postdischarge prophylaxis was based on the possibility of VTE after discharge. Froehling *et al.* [11] reported increased incidence of VTE from 0.3 to 1.9% between 7 and 30 days postoperatively after bariatric surgery. Postdischarge prophylaxis is used in abdominal or pelvic cancer surgery and in major orthopedic surgery [21,22].

An important finding in the current study is that the three patients who developed silent DVT do not have special characteristics to be considered a significant risk factor for the development of thromboembolism. This emphasizes our point of view of the necessity of combined prophylaxis regardless of the presence or absence of known risk factors.

We can conclude that the perioperative use of the LMWH enoxaparin in a dose of 40 mg daily for 2 weeks postoperatively combined with graduated compression stockings is safe and effective for the prevention of DVT following laparoscopic bariatric surgery.

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Conflicts of interest
There are no conflicts of interest.

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