Pharmacological prophylaxis versus none-pharmacological prophylaxis in prevention of clinical venous thromboembolic complications in morbid obese patients following bariatric surgery: a retrospective observational case-control study

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Research article

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Abstract

Background: Venous thromboembolism (VTE) is a serious complication that may occur after bariatric surgery. This study aims to report the rate of clinically evident VTE using pharmacologic versus non-pharmacologic prophylaxis among morbid obese patients undergoing laparoscopic bariatric surgery who were at low risk for VTE.

Methods: The laparoscopic research center database from 2017 to 2018 was queried to identify patients undergoing laparoscopic bariatric surgery. Retrospectively, each patient who met the inclusion and exclusion criteria was clinically evaluated for the presence of symptomatic VTE (DVT and PTE) during the postoperative period. VTE prophylaxis regimens were pharmacological prophylaxis or non-pharmacological prophylaxis.

Results: We identified 794 patients who underwent bariatric surgery.110 patients excluded from the study based on the VTE risk factor. 371 (54.4%) patients had non-pharmacological, 313 (45.9%) patients had pharmacological prophylaxis. In the non-pharmacological group, the overall rates of DVT, and PTE were 1 (0.26%) and 1 (0.26%), respectively. In the pharmacological group, the overall rates of PTE and DVT were 2 (0.63%) and 0, respectively. Patients without pharmacological prophylaxis had no significant difference in DVT and PTE rate compared to the group which received pharmacological prophylaxis (P>0.5).

Conclusions: Adequate VTE prophylaxis is achieved without pharmacological thromboprophylactic agents for lower-risk patients. Thus, an individualized prophylaxis regimen that balances efficacy and safety is suggested for each patient, based on various risk factors.

Background

Obesity is known as a risk factor for venous thromboembolism (VTE) including deep venous thrombosis (DVT) and pulmonary embolism (PE) [1]. However, morbidly obese individuals undergoing bariatric procedure appear to be less prone to VTE than morbidly obese individuals undergoing major operations for other indications [2]. This is reported that the incidence of VTE among patients undergoing laparoscopic bariatric surgery is lower than 1% [2].

In addition to obesity, several factors can increase risk of VTE including advanced age, male gender, major orthopedic operation, malignancy, prolonged operations, immobilization and estrogen medication [3]. On the other hand, there is some evidence suggesting that VTE complications are relatively less common amongst Asians as compared to their Western counterparts [4]. Therefore, due to ethnic variations in VTE risk, Asian patients may, possibly, require a lower dosage of thromboprophylaxis but the risk–benefit ratio needs to be determinate [5]. There is no agreement on the standard of care for prophylactic regiment [6], which some surgeons advocating chemoprophylaxis, some mechanical prophylaxis, and some using both. Standardization of the prophylaxis based on individually VTE risk factor and ethnic variations is an important issue, because the under treatment may lead to increased incidence of VTE and overtreatment may lead to bleeding-related complications and higher financial

burden on the health-care system [5]. Because of the lack of uniform guideline, we reviewed our experience since changing our postoperative protocol from routine chemoprophylaxis with clexan or heparin to mechanical measures including whole leg compression stockings (LCS), an emphasis on early ambulation, adequate hydration and short operation time to avoid the VTE incidence and potential risk of anticoagulant medication adverse effects.

Method

Study design

Using hospital registry data, we conducted a retrospective observational study of patients who underwent laparoscopic bariatric surgery for morbid obesity. The registry was implemented at Ghadir mother and child hospital from April 2016 to December 2018. Data collection was within an implemented best clinical practice protocol and data were gathered in a registry. The study was in adherence to the Declaration of Helsinki and written, informed consent was obtained from all patients before initiating the study.

Patients

All patients 18 years or older undergoing laparoscopic bariatric surgery (i.e., laparoscopic Roux-en-Y gastric bypass, laparoscopic single anastomosis gastric bypass, or laparoscopic sleeve gastrectomy) were included. The high risk patients for thrombosis events were excluded as following: patients with aged > 65 years, BMI > 50, history of cerebrovascular accident (CVA) and VTE, smoking, those medically diagnosed with congestive heart disease, malignancy, chronic liver disease, a high preoperative platelet (PLT) count, uncontrolled diabetic patients with FBS>180 mg/dL and patients underwent second operation due to leakage or Re-Do surgery due to weight regain.

Treatment regimens

The 454 patients who underwent surgery did not receive pharmacological prophylaxis after surgery (group A), whereas 343 patients who underwent surgery by another surgeon were administered clexane 60 mg subcutaneously once daily or heparin 5000 IU three times daily subcutaneously for 2 weeks postoperatively (group B).

For all the patients, a therapeutic whole leg compression stocking (LCS) was applied for 6 weeks after surgery. Furthermore, hydration (4000 mL) was done pre and post-operatively and ambulation was encouraged within 4 to 6 hours of the operation. Nurses on the floor were educated and trained on the importance of LCS use and early ambulation. All patients were seen in follow-up at 1 week, 1 month, 3 months, 6 months and 12 months thereafter.

Outcome measures

The primary outcomes were the rate of symptomatic DVT and pulmonary embolism (PE) up to 1 year after surgery. Patients presenting clinical signs of DVT (swelling, pain, and/or rigidity of the limb) and/or

PE (desaturation, dyspnea, tachypnea, tachycardia, hypo- or hypertension) were investigated with duplex Doppler ultrasound imaging and computed tomography angiography, respectively.

The secondary outcomes were the incidence of major bleeding events registered post operation. Major bleeding referred to the following: fatal bleeding; clinically overt bleeding in excess, associated with ≥2 g/mL fall in hemoglobin and/or leading to transfusion of ≥2 units of packed cells or whole blood; and bleeding requiring treatment cessation and/or operation.

Statistical Analysis

Continuous variables are expressed as means±standard deviations and discrete variables as frequencies and percentages. Independent sample *t*-tests were applied to evaluate differences between group means. The chi-square test, Fisher's exact test or Mann-Whitney *U*-test were used to compare continuous variables. Statistical significance was accepted for *P*-values <0.05. The statistical analysis was performed using SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA).

Results

The study population included 794 patients. Based on the VTE risk factor, 80 patients from 451 patients in group A and 30 patients from 343 patients in group B excluded from the study. Indeed, group A had 371 patients with a mean BMI of 42.94 ± 6.4 (range, 36.5 to 49.34), while 313 patients were in Group B with a mean BMI of 42.88 (range, 35.88 to 49.9). Demographics were similar between the 2 groups. Mean age at group A and B were 37.31 years (range, 26 to 48.6) and 40.44 years (range, 25.3 to 48.5), respectively. In group A, 20.1% and in group B, 22.7% were females. Mean operating times were 165 min and 175 min in groups A and B, respectively (Table 1).

In group A, 1 (0.26%) developed PE and 1 (0.26%) developed DVT 14 and 45 days respectively after surgery, none were fatal. In group B, however, only 2 (0.63%) patients developed PTE in 5 and 50 days after surgery. There were 1 non-VTE related mortalities, in group A (Figure 1). There was not any incidence of Intraluminal bleeding defined as melena and/or hematemesis in both groups but one case of intraabdominal bleeding in the group A and two cases in the group B occurred postoperatively which all of them required the second operation in the first 24 hours post-primary surgery (Figure 1).

Discussion

Obesity has traditionally been considered an increased risk factor for the development of VTE, which is preventable [7]. However, a meta-analysis of more than 5,500 patients, undergoing bariatric surgery failed to demonstrate any indisputable correlation between the presence of obesity and a higher incidence of postoperative DVT [8]. Actually, there are several VTE risk factors including poor glycemic control, dyslipidemia, inflammation, oxidative stress, endothelial dysfunction and impaired venous return that may intensify the risk of VTE in morbid obese patients[2]. Therefore, in the present study, in addition to

patients with history of VTE, we excluded patients with higher risks including older age, super obesity (BMI>50), inflammatory related disease, cardiovascular disease and uncontrolled diabetes (FBS>180).

Although , the American Society for Metabolic and Bariatric Surgery acknowledges the importance of early ambulation and sequential compression device use and recommends the use of chemoprophylaxis in all bariatric surgery patients unless contraindicated [9], the ideal method of prophylaxis for VTE in bariatric surgery has yet to be elucidated. There is no generally accepted guidance regarding the type, dose, or duration of prophylactic method in bariatric surgery [10]. The present retrospective study with 12 months follow up and controlled confounders by excluding and matching between groups, showed no greater effect of chemical prophylaxis in VTE prevention.

Although pharmacologic prophylaxis against postoperative DVT is more used in bariatric surgery [11], its use may increase the incidence of hemorrhagic, cost, hospital stay and allergic complications associated with the use of chemical agents [12–15]. In a recent systematic review and meta-analysis of 19 studies by using a standardized definition of hemorrhage, indicated that there was 2% incidence of bleeding complications. They concluded that the incidence of major bleeding seems to increase using weight-adjusted doses of heparin with no advantage in terms of VTE reduction [16]. Therefore, it indicated that bleeding complications associated with chemoprophylaxis, are an important problem, which have to be considered for pharmacologic agent prescription in VTE prophylaxis.

To the best of our knowledge, only 3 studies have investigated the efficacy of mechanical prophylaxis in VTE prevention of patients underwent bariatric surgery. Frantzides et al. studied 1692 patients undergoing laparoscopic Roux-en-Y gastric bypass. This study compared the using of twice daily routine enoxaparin and using of only mechanical methods including SCD and early ambulation in the patients. They found that there was no difference in incidence of DVT and PE in the two groups but the incidence of intraluminal bleeding was higher in group who had used anticoagulant than the group who only was on mechanical prophylaxis [17]. Another study, which was done on 957 patients without a history of VTE who underwent a laparoscopic Roux-en-Y gastric bypass reported that the use of mechanical prophylaxis with SCDs, early ambulation, and short operative times were as effective as chemical prophylaxis in the prevention of VTE. They reported that incidence of DVT and PE was 0.31 and 0.10%, respectively, on postoperative day 30 and the bleeding complication rate was 0.73% [18]. Gonzalez et al investigated the rate of DVT in morbid obese patients underwent laparoscopic Roux-en-Y gastric bypass when a pneumatic compression stocking is used as the only prophylaxis against DVT instead of anticoagulants. In addition, Patients were encouraged to be mobilized on the evening of the operation. The incidence of DVT was as low as 0.8% [8]. Likewise, in agreement with our results, these previous studies indicated that mechanical prophylaxis, early ambulation and hydration made not only the incidence of VTE lower postoperative, but also the bleeding rates significantly lower than chemical prophylaxis. It is worth noting that the incidence of DVT and PE in our study is well within the range reported by the previous studies, which used mechanical or chemical or both. This shows both the efficacy and benefit of the mechanical measures that we used. The possible explanation is that in the present study firstly, we avoided hemoconcenteration by intravenously hydration pre and post operation. Secondly, we used LCS for at

least 2 months post operation, which avoids placing the knee in acute angulation, preventing venous pooling in the lower extremities. Third, we enforced patient for early ambulation after surgery. It has to be noted that early ambulation is the most important factor in the prevention of VTE [18]. Forth, although in our procedure we put the patients on Liyod davis position and short operating times, which might have beneficial effect on reducing the risk of VTE, because pneumoperitoneum and the reverse trendelenberg position used in laparoscopic gastric bypass can increase the risk of VTE by lowering venous return to the heart.

Furthermore, Bhattacharya et al. in a web-based survey investigated the DVT prophylaxis measures amongst 11 surgeons from high-volume centers in Asia in patients undergoing bariatric surgery. In this published systematic review, it has been indicated that the VTE incidence reported by Asian surgeons ranged from 0% to 0.2% [5]. This incidence is considerably lower than what is reported in Western literature that ranged from 0.5 and 2% [19, 20]. Therefore, according to Bhattacharya study, bariatric surgery can be safely performed without pharmacologic VTE prophylaxis in Asian morbid obese patients. Therefore, the variations in VTE prophylaxis have to be considered because of its effect on postoperative complication such as VTE and bleeding. Actually, an individualized prophylaxis regimen that balances efficacy and safety is suggested for each patient, based on various risk factors.

The most important strength of this study among the few studies, which assess mechanical prophylaxis in VTE prevention in morbid obese patients underwent bariatric surgery, is that this is the first study, which compares VTE incidence rate after excluding the high-risk patients and matching them between groups.

This study has also some limitations. Firstly, the weakest point of this study is an inadequate sample size for a complication with as low an incidence as less than 1% the sample size of 300 odd patients in each group is definitely insufficient to draw a solid conclusion as the study is not adequately powered. Secondly, we did not use PCD as a mechanical device for PTE prevention. Therefore, we suggest using PCD for ideal VTE mechanical prophylaxis in future studies. Moreover, we only evaluate clinically evident VTE, however it would be more valuable if we had performed Duplex and multi-slice computed tomographic scan for all patients to recognize also subclinical cases of VTE. Furthermore, we did not measure active clotting times and factor X levels, which are the coagulation biomarkers.

Conclusion

In the present study, we have showed the beneficial effects of LCS, early ambulation, short operation time and adequate hydration as a relatively natural method in the prevention of VTE in selected morbid obese patients underwent bariatric surgery. Pharmacologic anticoagulation is not mandatory in morbid obese patients without additive VTE risk factor and an individualized prophylaxis regimen based on risk factor may be a safe way to achieve appropriate thromboprophylaxis after bariatric surgery. However, further studies need to investigate thromboprophylaxis methods in bariatric surgery.

Abbreviations

VTE: venous thromboembolism

DVT: deep venous thrombosis

PE: pulmonary embolism

LCS: leg compression stockings

Declarations

- **Ethics approval and consent to participate**

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The Ethics Committee of Shiraz University of Medical Sciences approved the present study. The written informed consent was obtained from all patients before initiating the study.

- **Consent for publication**

All author *approved the manuscript* to be published in BMC surgery.

- **Availability of data and materials**

Not applicable

- **Competing interests**

Drs. Masoud Amini, Nader Moeinvaziri, Babak Hosseini, Leila Vafa and Neda Haghighat have no conflicts of interest or financial ties to disclose.

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- **Authors' contributions**

All authors were involved in the concept and design of the study. MA contributed to study conception and design. NM, BH, and LV participated in data collection. NH and NM contributed data analysis, interpretation and preparation of the manuscript. . NH supervised the conduct of the study and data collection, provided advice and edited the manuscript. All authors have read and approved the manuscript.

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Tables

Table 1- Characteristics and preoperative comorbidities of patients

P^1	Group B (n=313)	Group A (n=371)	Variables
0.709	40.44 ± 50.97	37.31± 11.38	Age, years
0.445			**Gender, No. (%)**
	244 (78.0%)	296 (79.8%)	Female
	69 (22.0%)	75 (20.2%)	Male
0.374	160.99 ± 21.98	116.33 ± 13.08	Weight , kg
0.756	161.7 ± 10.1	163.36 ± 8.0	Height , cm
0.533	42.98 ± 7.1	42.94 ± 6.4	BMI, kg/m^2
			Comorbid conditions, No. (%)
			Diabetes mellitus
	61 (19.6%)	65 (17.6%)	Arterial hypertension
	63 (20.4%)	72 (19.6%)	Hyperlipidemia
	62 (20.0%)	68 (18.4%)	Obstructive sleep apnea
	3 (6.6%)	3 (6.6%)	Infertility
	53 (1.7%)	16 (4.5%)	Gastrointestinal disorder
	53 (17.1%)	45 (12.9%)	Thyroeid disfunction
	50 (16.1%)	53 (14.4%)	Liver disease
	83 (26.1%)	87 (23.7%)	
0.89	175 ± 30	165 ± 30	Operative time (min)

BMI, body mass index; Mean ± SD for quantitative and frequency (%) for qualitative variables. Using chi-square.

Figures

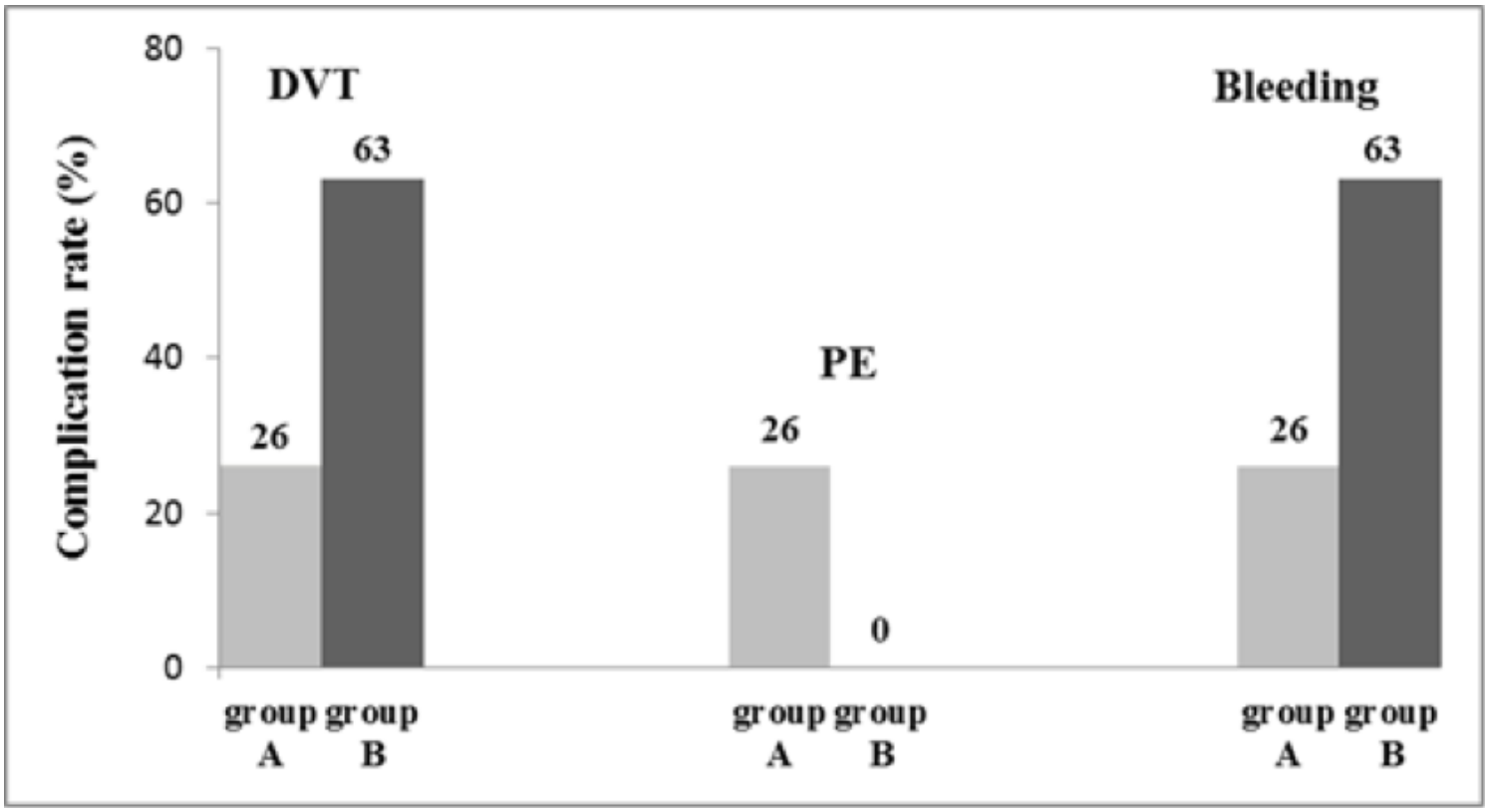

Figure 1

Comparison of DVT, PE and bleeding incidence between group A (pharmacological prophylaxis) and group B (none-pharmacological prophylaxis). DVT, deep venous thrombosis; PE, pulmonary embolism