Assessment of rivaroxaban as venous thromboembolism prophylaxis after gastric bypass surgery

Original Article

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ABSTRACT

Background: Bariatric surgery is increasingly utilized to manage and prevent health issues related to obesity and the associated high incidence of venous thromboembolism (VTE). This work aimed to evaluate the effectiveness of a prophylactic dose of rivaroxaban against the development of VTE after bariatric surgery.

Patients and Methods: This prospective cohort study was carried out on 40 morbid obese patients aged 18–60 years old, both sexes, with BMI) greater than or equal to 40 or greater than 35 kg/m^2 with obesity-related co-morbidities who underwent gastric bypass surgery. Patients received rivaroxaban 10 mg once a day orally 24 h postoperation for 1 month.

Results: After 30 days, thrombosis did not occur in any patient. Intra luminal bleeding occurred in 3(7.5%) of the patients who were presented with melena, tachycardia, and hypotension and readmitted and all managed conservatively. The mean red blood cells transfused was 2.7 units, plasma transfused was 3.3 units, and the mean hospital stay was 2.3 days.

Conclusion: Prophylactic oral rivaroxaban 10 mg once daily 24 h after gastric bypass surgery for 1 month is effective against VTE development.

Key Words: Bariatric, prophylaxis, rivaroxaban, venous thromboembolism.

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INTRODUCTION

The global surge in severe obesity, coupled with the proven efficacy and safety of bariatric procedures, has contributed to a significant elevation in the frequency of bariatric surgeries over recent decades[1].

Patients undergoing bariatric surgery (BS) are categorized as having a moderate to high risk for venous thromboembolism (VTE), including conditions such as deep venous thrombosis (DVT) and pulmonary embolism (PE), due to various factors associated with severe obesity and related comorbidities, the use of laparoscopic techniques, and reduced mobility during the perioperative period[2,3].

Severe obesity and BS were identified as significant contributors to the risk of VTE. However, VTE is a rare complication following BS. VTE is linked to substantial morbidity and mortality in the postoperative period, with the majority of incidents occurring after hospital discharge, within the initial 30 days following the procedure[4].

Numerous approaches have been employed to mitigate the risk of VTE in individuals undergoing BS, encompassing both drug-based and physical methods of thromboprophylaxis. Yet, determining the most effective thromboprophylaxis strategy, including the specific regimen to be used, is still a field of further investigation[5].

Low-molecular-weight heparin (LMWH) is frequently chosen for VTE prevention and treatment because of its proven effectiveness and reliable outcomes. However, its use is not without challenges, such as the requirement for subcutaneous control risk of major bleeding events. The absence of a quick antidote to reverse its effects adds complexity to its management. Moreover, the expense associated with LMWH might be onerous, and their prolonged use is associated with an increased risk of developing osteoporosis[6].

Rivaroxaban presents an alternative as an orally administered medication that directly blocks Factor Xa. Rivaroxaban is rapidly absorbed upon ingestion, reaching maximum plasma concentrations within two to four hours. Rivaroxaban demonstrates excellent oral bioavailability, with absorption rates of 80% to 100% for a 10 mg dose, and unaffected by food intake. This high level of absorption is also maintained for doses of 15 mg and 20 mg when taken with food[7].

Depending on the estimated VTE risk and country-specific recommendations, recommendations for VTE prophylaxis after BS range from 7 days to 4 weeks[8].

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Additionally, the medical community has yet to reach an agreement on the best chemoprophylactic drug form, dosage, and, notably, the duration of drug-based prophylaxis following BS[9]. Thus, this study aimed to evaluate the effectiveness of a prophylactic dose of rivaroxaban 10 mg once daily for 1 month against the development of VTE after gastric bypass surgery.

PATIENTS AND METHODS:

This prospective cohort study was carried out on 40 morbidly obese patients aged 18–60 years old, both sexes, with BMI greater than or equal to 40 or greater than 35 kg/m^2 with obesity-related co-morbidities who underwent gastric bypass surgery. Informed written consent was obtained from the patient.

Exclusion criteria were previous BS, surgically unfit patients with compromised cardiopulmonary function, chronic decompensated diseases (renal or hepatic), incurable cancer, major psychological disorders, secondary obesity (hormonal disturbances), and drug and/or alcohol abuse patients.

All patients were subjected to full history taking (with special concern to dietary, and obesity history, and medical disorders), clinical examination, anthropometric measurements, full laboratory investigations [complete blood count (CBC), coagulation profile, lipid profile, fasting and 2 h postprandial blood glucose and HbA1c, virology screening, hormonal profile, and liver and renal function tests], imaging [pelvic-abdominal ultrasound to assess the liver status and gallbladder, chest radiography and respiratory function tests to assess respiratory status, echocardiogram, and ECG for cardiac assessment, and pulmonary function tests], and upper GIT endoscopy when indicated to ensure healthy stomach.

In this study, a uniform laparoscopic procedure was employed. The operation involved an antecolic antegastric Roux-en-Y gastric bypass, with both the alimentary and biliopancreatic limbs measuring 100 cm in length. The formation of the gastric pouch began with the application of a first blue 60 mm linear stapler, positioned 5 cm beneath the angle of His, perpendicular to the lesser curvature. To complete the small proximal pouch, 60 mm staplers were utilized alongside a 40 French gastric tube, concluding 1 cm to the side of the angle of His. The larger pouch extension was initiated 10 cm below the angle of His, extending horizontally, and finalized with vertical blue 60 mm stapler firings adjacent to a 40 French gastric tube, also finishing 1 cm beside the angle of His.

Following this, the duodenojejunal (DJ) junction was located, and a segment of the jejunum, 100 cm in length, was identified and marked with a metal clip. The construction of the gastrojejunostomy involved the use of a blue 60 mm linear stapler for the initial join, with the anterior part being sealed with barbed sutures. An additional 100 cm of the small intestine was measured from the site of the gastrojejunostomy, after isolating the biliopancreatic limb using a white 60 mm linear stapler. The enteroenteric anastomosis was then performed with a white 60 mm linear stapler and similarly finalized anteriorly with barbed sutures. The integrity of the gastrojejunostomy was verified intraoperatively through an air leak test, and any mesenteric openings were sutured closed with 2/0 proline pierce string sutures.

All patients received postoperative IV fluids, started oral clear fluids 6 h postoperative, and were discharged home from 24 to 48 hours after drain removal, toleration of clear oral fluids, and vital stability. All patients were discharged home and received prophylactic anti-coagulants against VTE (rivaroxaban), antibiotics, proton pump inhibitors, and prokinetics.

Patients received rivaroxaban 10 mg once daily orally 24 h postoperation for 1 month. After 1 month, the incidence of intraluminal bleeding, and thrombosis were recorded.

Statistical analysis

SPSS V26 (IBM Inc., Chicago, IL, USA) was employed for statistical analysis. Mean and SD were used to display quantitative variables. Frequency and percentage were used to display qualitative variables.

RESULTS:

The mean value (±SD) of age was 41.2±9.86 years of weight 131.3 (±21.1) kg, and 27 (67.5%) patients were females. The mean value (±SD) of height was 1.66 (±0.08) m, and BMI was 47.81 (±8.4) kg/m^2 (Table 1).

Type II diabetes mellitus was present in 27 (67.5%) patients. Hypertension was present in 21 (52.5%) patients. Osteoarthritis was present in three (7.5%) patients. Hyperlipidemia was present in 15 (37.5%) patients. Respiratory complications were present in three (7.5%) patients. (Table 2)

Intra luminal bleeding occurred in three (7.5%) patients. Thrombosis did not occur in any patient (Table 3).

Intra luminal bleeding patients were presented with melena, tachycardia, and hypotension and they were readmitted. The mean value (±SD) of red blood cells transfused was 2.7 (±58) units. The mean value (±SD) of plasma transfused was 3.3 (±58) units. The mean value (±SD) of hospital stay was 2.3 (±58) days (Table 4).

All readmitted patients were managed conservatively without re-operation of further endoscopic interventions.

Table 1: Demographic data of the studied patients

	(*n*=40) [n (%)]
Age (years)	41.2±9.86
Sex	
Male	13 (32.5)
Female	27 (67.5)
Weight (kg)	131.3±21.1
Height (m)	1.66±0.08
BMI kg/m^2	47.81±8.4

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

Table 2: Comorbidities of the studied patients

	(*n*=40) [n (%)]
Type II DM	27 (67.5)
Hypertension	21 (52.5)
Osteoarthritis	3 (7.5)
Hyperlipidemia	15 (37.5)
Respiratory complications	3 (7.5)

Data are presented as frequency (%).
DM, diabetes mellitus.

Table 3: Early postoperative complications of the studied patients

	(*n*=40) [n (%)]
Intra luminal bleeding	3 (7.5)
Thrombosis	0

Data are presented as frequency (%).

Table 4: Characteristics and conservative management of the intra luminal bleeding patients

	(*n*=3)
Presented with melena	3 (100%)
Tachycardia	3 (100%)
Hypotension	3 (100%)
Readmission	3 (100%)
RBCs transfused (units)	2.7±0.58
Plasma transfused (units)	3.3±0.58
Hospital stay (days)	2.3±0.58

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

DISCUSSION

Following BS, thromboembolic complications are a significant clinical and economic issue, as they are the leading cause of morbidity and mortality. However, the best chemoprophylactic drug for VTE and the duration of prophylaxis are subjects of ongoing debate[10].

Direct oral anticoagulants (DOACs) have significantly broadened the range of anticoagulation therapy options in recent years, thanks to their advantages such as ease of oral administration, minimal potential for interaction with other drugs, absence of food-related effects, and standardized dosing schedules[11].

Rivaroxaban, a DOAC administered orally once a day, is recognized for its efficacy in both primary and secondary prevention of thrombosis in patients undergoing hip or knee replacement surgery, including those with severe obesity, without the need to adjust the dosage[12]. However, there is a notable lack of clinical evidence regarding the application of DOACs in obese patients. Research conducted in vitro on such individuals showed that the effectiveness of rivaroxaban in inhibiting thrombin generation in the body is correlated with its concentration[13]. The advantages of DOACs over vitamin K antagonists include fewer food and drug interactions, fixed dosing, and no requirements for routine monitoring[14].

Yet, specific guidelines for the use of DOACs in the context of BS are still absent.

The influence of BS, which results in significant anatomical changes, on the pharmacokinetics and pharmacodynamics of a single preventative dose of rivaroxaban has been the subject of two trials. These trials concluded that modifications in anatomy and weight reduction following BS do not significantly alter the pharmacokinetic and pharmacodynamic profiles of rivaroxaban[15,16].

Rivaroxaban is an orally administered anticoagulant that directly targets factor Xa and demonstrates a high oral bioavailability of 80–100%. It reaches peak plasma levels within – 3 h after intake. The drug's absorption improves with food intake, hence the recommendation for taking 15 or 20 mg doses with meals. In healthy adults, the elimination half-life of rivaroxaban ranges from 5 to 9 h, which increases to 11–13 h in the elderly. About one-third of the drug is eliminated unchanged through the kidneys, while the liver processes the rest. Of the metabolized portion, half is excreted by the kidneys and the other half through the bowels. The pharmacokinetic and pharmacodynamic responses to rivaroxaban differ based on the administered dose, though they are not influenced by the patient's age, sex, or body mass[17].

In our study, intra-luminal bleeding occurred in three (7.5%) of patients. None of the patients experienced thrombosis. All intra-luminal bleeding patients exhibited signs of melena (black, tarry stools indicative of gastrointestinal bleeding), tachycardia, and hypotension, which led to their readmission.

Kröl *et al*.[18] demonstrated that after receiving an oral dose of 10 mg of rivaroxaban for 28 days following

Roux-en-Y gastric bypass, bleeding occurred in 4.3% of patients. Postoperative complications following bariatric surgeries included asymptomatic VTE in 0.8% of the patients, DVT in 0.8%, and readmission in 3.1% of the patients.

Rodríguez *et al*.[19] reported that after laparoscopic sleeve gastrectomy, no one exhibited venous thrombosis after receiving thromboprophylaxis with rivaroxaban.

LMWH is commonly used as the primary pharmacological prevention for VTE in patients undergoing BS[20]. Nonetheless, the major complication of LMWH therapy is bleeding.

Li *et al*.[21] reported that bleeding incidence ranged between 0 and 6.4% after using LMWH following BS. Also, Imberti *et al*.[22] noticed that the incidence rate of bleeding after using LMWH following BS was 5.6%. Additionally, Pengo *et al*.[23] noted that the incidence rate of bleeding after using LMWH following BS was 1.2%. Moreover, Bechtel *et al*.[24] demonstrated that the incidence of bleeding after using warfarin after gastric bypass was 16%.

Based on the existing literature, the reported risk of major bleeding ranges from 1 to 33% in patients receiving LMWH. Thus, rivaroxaban is a promising drug in the context of VTE prophylaxis with a lower incidence of bleeding.

Limitations of this study included the sample size, the study being in a single center, the absence of a control group, and the comparison with LMWH. Further studies to compare DOACs other than rivaroxaban are required.

CONCLUSION

Prophylactic oral rivaroxaban 10 mg once daily 24 h after gastric bypass surgery for 1 month is effective against VTE development with better patient compliance and less financial cost than LMWH.

CONFLICT OF INTEREST

There are no conflicts of interest.

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