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Original article

Assessment of the procoagulant potential after laparoscopic sleeve gastrectomy: a potential role for extended thromboprophylaxis

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Abstract

Background: Bariatric surgery is associated with increased thromboembolic risk, which may extend well beyond hospital stay. The hemostatic mechanisms implicated in this risk are not well established.

Objectives: We aimed to determine the dynamics of hemostatic changes and procoagulant potential among patients undergoing laparoscopic sleeve gastrectomy, during both the early and late postoperative periods.

Setting: A university hospital.

Methods: Patients who underwent laparoscopic sleeve gastrectomy were recruited consecutively to this study. Blood samples were taken preoperatively, before discharge (postoperative day [POD] 3), and at the first follow-up visit (POD10). All samples were tested for complete blood count, C-reactive protein, von Willebrand factor, factor VIII, fibrinogen, and thrombin generation.

Results: The median preoperative body mass index of the 26 participants was 41.3 (38.7–43.3) kg/m^2. Compared with preoperative evaluation, fibrinogen, von Willebrand factor antigen and activity, and factor VIII levels were significantly higher at POD3 and POD10 ($P < .0001$ for all comparisons). Peak thrombin levels and endogenous thrombin potential (ETP) were higher at POD3 ($P = .005$ for both comparisons) and POD10 ($P = .0009$ and $< .0001$) compared with baseline. ETP and peak thrombin, as well as fibrinogen, von Willebrand factor, and factor VIII levels, were comparable between POD3 and POD10. Multivariate analysis showed that the only predictor of postoperative ETP was the preoperative ETP level ($\beta = .55$, $P = .007$).

Conclusions: As determined by thrombin generation, laparoscopic sleeve gastrectomy was associated with hypercoagulability, which persisted during POD10. This finding suggests a possible benefit of extended thromboprophylaxis. Nevertheless, our results should be interpreted with caution due to the lack of a control group. (Surg Obes Relat Dis 2017;▮:00–00.)

Keywords: Bariatric; Laparoscopic sleeve gastrectomy; Thrombin generation; Hypercoagulability; Obesity

Obesity is recognized as a global epidemic. Its worldwide prevalence has more than doubled in the last 2 decades, including 35% of the U.S. population [1]. Bariatric surgery has become the mainstay of treatment for morbid obesity,

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due to its demonstrated efficacy in achieving significant weight loss and in improving obesity-related co-morbidities [2]. Despite the dramatic increase in the utilization of bariatric surgery in the management of obesity, postoperative complications are not uncommon and were reported to occur in up to one third of patients [3].

Obesity and abdominal surgery are both established risk factor for thrombotic complications due to multifactorial mechanisms including platelet activation, elevated levels of fibrinogen, coagulation factors VIII, IX, XI, and XII, and impaired fibrinolysis [4,5]. Hence, patients undergoing bariatric surgery are at particularly high risk for venous thromboembolism (VTE) events, including pulmonary embolism, deep vein thrombosis, and portal-splenic-mesenteric venous thrombosis, with an overall incidence of up to 3% [6,7]. This increased thrombotic risk extends well beyond the hospitalization period, with 70% to 80% of VTE events occurring after discharge [8–10].

There is no consensus regarding the optimal thromboprophylaxis regimen for preventing the occurrence of VTE after bariatric surgery. This is highlighted by the wide variability of recommendations espoused by professional society guidelines [11–13]. Moreover, while most guidelines support the administration of perioperative thromboprophylaxis, the role of an extended course of anticoagulation beyond hospital stay is inconclusive [11–13].

As the prothrombotic tendency among obese patients undergoing bariatric surgery may result from several hemostatic mechanisms, the assessment of a particular component of the coagulation system might not suffice to evaluate the overall hypercoagulable state. In vitro thrombin generation is a well-accepted tool in the assessment of procoagulant potential, as it describes the potential of a given plasma sample to generate thrombin; and thus, may quantify the composite global effects of the multiple parameters of the coagulation system [14,15]. Moreover, enhanced thrombin generation was found to correlate with VTE occurrence [16–19].

In this study, we aimed to investigate the dynamics of hemostatic and thrombin generation alternations, during both the early and late postoperative periods, among patients who underwent laparoscopic sleeve gastrectomy (LSG) and to evaluate whether hypercoagulability is sustained beyond hospital stay.

Methods

Patients

This clinical trial was designed as an observational, cross-sectional cohort study. Patients who underwent LSG from December 2016 to May 2017 were assessed consecutively for eligibility to participate. Exclusion criteria were age <18 years, revisional surgery, pregnancy, known bleeding or thrombotic disorders, recent thrombotic or bleeding events, hepatic or renal failure, active inflammatory condition (other than the metabolic syndrome), endocrine disorders (i.e., thyroid dysfunction, Cushing syndrome), current or recent (<7 d) use of any antiplatelet therapy or anticoagulants, nonsteriodal anti-inflammatory drug use, and heavy alcohol consumption. Indications for LSG were those according to the National Institute of Health guidelines and included a history of repeated failures of nonsurgical weight loss techniques and body mass index $\geq$40 kg/m^2, or body mass index 35 to 39.9 kg/m^2 with at least one severe obesity-associated co-morbidity.

VTE prophylaxis

Routine prophylaxis included the application of a thigh-length pneumatic compression device at the time of surgery and until the patient recovered normal mobility; and early ambulation, within the first few hours after the procedure. In addition, routine anticoagulation in the form of 40-mg enoxaparin daily was given, starting 12 hours after surgery until 1 week after discharge.

Surgical procedure

We use a standardized surgical technique for LSG. Briefly, mobilization of the stomach greater curvature begins 5 cm proximal to the pylorus and continues to the angle of His. Gastric resection involves using a 42-Fr bougie. The resection is performed using an endoscopic staple device.

Data collection

Blood samples were taken at 3 successive time points: (1) at baseline before induction of anesthesia, (2) on the third postoperative day (POD3), (3) and at the first follow-up visit (POD10). Blood samples were collected in the morning, from an antecubital vein, by using a 23-G needle without stasis. Sampling was performed at least 12 hours after the last enoxaparin dose to obtain heparin-free plasma and to preclude the effect of prophylactic anticoagulation therapy. For coagulation assays, blood was collected in vacutainer tubes containing trisodium citrate (final concentration .32%; Becton Dickinson and Company, Franklin Lakes, NJ). All analyses were performed immediately, except for thrombin generation assay, which was carried out using plasma samples stored at -80°C. In addition to the laboratory evaluation performed, in each patient the following data were extracted: sex, current age, preoperative anthropometric parameters, preoperative laboratory evaluation (lipid profile, fasting glucose, liver enzymes), co-morbidities, and operative time. Hypertension was defined as systolic blood pressure >140 mm Hg and/or diastolic pressure >90 mm Hg (diastolic) or the use of antihypertensive medications. Diabetes was defined as