

Portal Vein Thrombosis a Rare but Life-threatening Complication after Laparoscopic Sleeve Gastrectomy: A 5 Years Study in a Bariatric Center of Excellence

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Abbreviations:

PVT - Portal vein thrombosis;
LAGB - laparoscopic adjustable gastric band;
LRYGB - laparoscopic Roux-en-Y Gastric Bypass;
LSG - laparoscopic sleeve gastrectomy;
DVT - deep vein thrombosis;
LMWH - low molecular weight heparin;
aPTT - activated partial thromboplastin time;
TPA - Tissue Plasminogen Activator;
BMI - body mass index;
BPD - biliary pancreatic diversion;
ER - emergency room.

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Rezumat

Tromboza portală o complicație rară dar primejdioasă după gastrectomie longitudinală laparoscopică: un studiu pe 5 ani într-un Centru de Excelență Bariatrică

Introducere și scop: Gastrectomia longitudinală laparoscopică (GLL) este actualmente cea mai populară intervenție bariatrica în lume. Tromboza portală (TP) a fost raportată cu o incidență din ce în ce mai mare ca o complicație rară dar serioasă asociată cu GLL. Algoritmul de prevenire și tratament al TP este încă discutabil. Scopul acestui studiu este de a explora incidența și prognosticul PT după GLL într-un Centru de Excelență în Chirurgie Bariatrică (CE-CB) și elaborarea unui algoritm eficient de diagnostic și tratament.
Metodă: Toți pacienții operați electiv pentru GLL în ultimii 5 ani între 1 noiembrie 2014 și 30 octombrie 2019 în Ponderas Academic Hospital, au fost revizuiți retrospectiv. Toți pacienții cu GLL au primit un protocol extins și cu doze ajustate de HGMM pentru profilaxia trombozei venoase profunde. În ultimii 2 ani am introdus măsurarea concentrației factorului anti X activat pentru monitorizarea activității HGMM la pacienții cu risc. Pacienții cu suspiciune de TP care s-au prezentat la camera de gardă au fost diagnosticati prin tomografie computerizată cu contrast intravens. Pacienții diagnosticati cu TP au primit tratament anticoagulant sistemic initial, ulterior considerandu-se necesitatea altor terapii - tromboliză sau intervenție chirurgicală. Dupa faza acută, pacienții au fost externați cu tratament anticoagulant pe termen lung.

Rezultate: Dintre cei 3861 pacienți care au efectuat GLL electiv,

trei (0,077 %) au fost readmiși pentru TP la 7-60 zile de la intervenția bariatrică. Vârsta media a fost 40 ani (SD 11,97), indicele de masa corporală a avut media de 40,34 Kg/m². (SD 7,994). Toți pacienții au urmat același protocol de GLL. Doi pacienți au primit tratament conservator sistemic cu heparină și au ramas pe tratament anticoagulant pe termen lung. Nu a fost nevoie de tratament chirurgical. Al 3 lea pacient a avut o evoluție fulminantă în terapie intensivă, datorită unei TP extensive, soldată cu deces în două ore de la admisia în spital în ciuda tuturor măsurilor de resuscitare luate.

Concluzii: Este necesară o atitudine de suspiciune înaltă clinică pentru pacienții cu TP după GLL și un diagnostic și tratament rapide. Protocolul preventive extins cu doze ajustate de HGMM aplicat în CE-CB și-a dovedit eficiența reducând semnificativ incidenta TP după GLL.

Cuvinte cheie: tromboza portală, protocol de preventive, gastrectomia longitudinală laparoscopică, centrul de excelență, chirurgie bariatrică

Abstract

Background and Aim: Laparoscopic sleeve gastrectomy (LSG) is actually the most performed bariatric procedures in the world, and porto-mesenteric vein thrombosis (PVT) has been increasingly reported as a rare but serious complication. The best algorithm for PVT's prevention and therapy is still under discussion. The aim of this study is to explore the incidence and the outcomes of the PVT after LSG in a Bariatric Surgery Center of Excellence (BS-CoE) and elaborate a diagnostic and therapeutic algorithm for PVT after LSG.

Methods: We retrospectively reviewed all the consecutive patients who underwent elective LSG within the last five years, between November 2014 and October 30th 2019, in Ponderas Academic Hospital, Bucharest, Romania. All the patients received an extended DVT prophylaxis protocol with adjusted doses of LMWH. Anti-factor Xa concentrations measurement to monitor the activity of LMWH in all the high-risk patients was used for the last two years. The patients suspected of PVT were scanned by computed tomography using IV contrast. All PVT patients were initially treated with systemic anticoagulation (Heparin), further interventions, such as systemic thrombolysis or surgery, being considered. After the acute stage, the PVT patients received long-term anticoagulation.

Results: Of the 3861 patients who underwent elective LSG, three were readmitted 7-60 days after the bariatric procedure for PVT, equating to an incidence of 0.077%. The average age of the patients developing PVT was 40 years (SD 11.97), the average body mass index (BMI) was 40.34 (SD 7.994) kg/m² and all of them underwent the same protocol for LSG. Two patients underwent conservative therapy with heparin anticoagulation and no surgery was needed. The third patient had a fulminant evolution in ICU, due to an extensive PVT, with death within two hours from his admission despite all resuscitation measures taken. The two patients remained on long life anticoagulant therapy.

Conclusion: A high clinical suspicion of PVT after LSG is required with prompt diagnosis and treatment. The BS-CoE protocol with adjusted doses of LMWH and extended prophylaxis proved to be very efficient showing a very low incidence of PVT.

Key words: Portal vein thrombosis, preventive protocol, Sleeve gastrectomy, center of excellence, bariatric surgery

Introduction

Portal vein thrombosis (PVT) is a rare complication of laparoscopic gastro-intestinal operations, that involve the portal or mesenteric venous territory. It may be potentially life threatening due to mesenteric ischemia and small intestine infarction if the PVT is occlusive (1-5).

Laparoscopic bariatric surgery proved to be an efficient treatment for morbid obesity by inducing sustained weight loss, controlling the obesity-related co-morbidities, and improving the patients' quality of life (4,6). However, the bariatric procedures have some complications, the most significant being sepsis, bleeding and pulmonary embolism (7).

All severely obese patients are at increased risk of thromboembolic events and ischemia secondary to vessel wall damage and hypercoagulability (7,8), thus bariatric surgery teams should be aware by the danger of the venous thrombosis. The reported incidence is up to 3% (1,7,9). The portal vein thrombosis (PVT) occurs less frequently (0,3-1 %) and has been reported after laparoscopic adjustable gastric band (LAGB), laparoscopic Roux-en-Y Gastric Bypass (LRYGB), and laparoscopic sleeve gastrectomy (LSG) (1,2,7,9,10). However, with the actual extensive use of sleeve resections, PVT has been increasingly reported over the last 10 years (5). It appears to be more often associated to LSG as compared with other bariatric procedures (7).

Besides its aggressive evolution, the best algorithm for PVT's prevention and therapy is still under discussions. Most centers use heparin anticoagulation to treat PVT, even though heparin alone has a significant failure rate, approaching only 65% for the non-surgical cases (12).

Being challenged by several complex cases of PVT, we have introduced 10 years ago a protocol of preventing the venous thrombosis in the current bariatric surgery practice. The protocol's outcomes were evaluated in 2012 and the rate of PVT was calculated at 0.19% (13). The algorithm was further improved when our hospital became Center of

Excellence in Bariatric Surgery, designated by Surgical Review Corporation (SRC) (USA) and the European Chapter of International Federation of Surgery of Obesity (IFSO-EC).

The aim of this study is to explore the incidence and the outcomes of the PVT after laparoscopic sleeve gastrectomy in a Center of Excellence in Bariatric Surgery. As a result of the study a diagnostic and therapeutic algorithm for PVT after LSG is proposed.

Method

We retrospectively reviewed all the consecutive patients who underwent elective, primary or revisional laparoscopic sleeve gastrectomy within the last five years, between November, 1st 2014 and October 30th 2019, in Ponderas Academic Hospital, a high volume Centre of Excellence for Bariatric and Metabolic Surgery, yearly approaching 1000 primary and revisional surgery procedures.

The institutional ethics committee approval was obtained for the study and all the patients signed an informed consent. As an observational study, no intervention in medical protocols was applied.

All the cases are prospectively registered in BOLD, the bariatric outcomes longitudinal database, as per required by SRC accreditation program. (14)

All the obese patients who received any other primary or revisional bariatric procedure were excluded from the present analysis.

A preoperative work-up addressed to all patients with American Society of Anesthesiologists (ASA) physical status I-IV, was applied 3-4 weeks prior to surgery by a multidisciplinary team, which included a cardiologist and an anesthetist who prescribed the DVT prophylaxis or anti-coagulation preoperative regimen. All patients received deep vein thrombosis (DVT) prophylaxis according to the patient body weight as per the protocol of our hospital. The protocol, described below, included perioperative LMWH and sequential compression devices intraoperatively.

As a standard of attitude in our hospital, all

the bariatric patients were treated according to a low opioid anesthesia and a multimodal non-opioid postoperative analgesia protocol. (15)

All patients underwent LSG in reverse Trendelenburg with carbon dioxide insufflation pressure of 12-15mm Hg. Adequate dissection of the posterior aspect of the fundus and active search of the hiatal hernia are steps of our current surgical protocol for LSG. A 35 F bougie catheter was used for calibration and the stomach's division started 1-2 cm proximal to the pylorus to be ended 1cm lateral to angle of His. The stapled line was entirely oversewn in all the cases. Performing the methylene blue test, verifying the local hemostasis while the blood pressure is elevated up with 30% of the preoperative status and specimen removal are the last steps of LSG.

All the patients received a prophylactic antibiotic regimen (from the first generation cephalosporines) and postoperative fluids to maintain a proper hydration. Early mobilization was actively recommended and monitored. Patients were discharged on the second postoperative day or, later, when they were able to drink adequate quantities of clear liquids, thus avoiding any risk of dehydration.

Venous Thrombosis Prophylaxis

The patient's discharge summaries indicated that all the patients received DVT prophylaxis which continued 21 days post-operatively or anticoagulation treatment followed by bridging to oral therapy when indicated.

In 2011, we have introduced a LMWH prophylaxis protocol applied to all surgical patients irrespective the risk, with dose adjustment on body weight, for 21 days post-discharge, based on the recommendation of the UK Hemostasis, Anticoagulation and

Thrombosis (HAT) Committee, published on April 2010. (16,17) (*Table 1*). Our protocol proved to be in agreement with the recent guidelines of the European Society of Anesthesiology, published by in 2018 (18).

The patients with preoperative anticoagulation therapy were bridged from oral therapy five days preoperative. The postoperative bridging to oral therapy is recommended after 21 days of LMWH based on a specific recommendation of our cardiologist.

In the last two years (since January 2018) we have introduced Anti-factor Xa (anti-Xa) (18) concentrations measurements to monitor either prophylactic or therapeutic dose of LMWH in challenging bariatric cases, especially in patients with extreme obesity, associated thrombotic risk factors or history of DVT. The first evaluation of the plasma level of anti-Xa is performed four hours after the third dose of LMWH.

Therapy of PVT

The patients presented to the emergency room with the suspicion of PVT are screened for laboratory testing including DDimers and are scanned by computed tomography (CT) using IV contrast to confirm the venous thrombosis (*Fig. 1*). An abdominal Doppler ultrasound of the PV and its mesenteric branches is part of the evaluation protocol, too. Subsequent thoraco-abdominal CT-angiograms are performed during therapy to evaluate the status of the thrombi and to investigate other potential sites of evolutive thrombosis.

All PVT patients are initially treated with systemic therapeutic heparin with intravenous bolus followed by continuous infusion to achieve a therapeutic range of activated partial thromboplastin time (aPTT) 2-3 times baseline). Further interventions are

Table 1. LMWH dose adjustment on body weight for perioperative DVT/PVTprophylaxis protocol (16)

Weight	50-100 kg	100-150 kg	Over 150 kg
Dalteparine	5000UI	5000 UI BID	7500 UI BID
Enoxaparine	40 mg/day	40 mg BID	60 mg BID

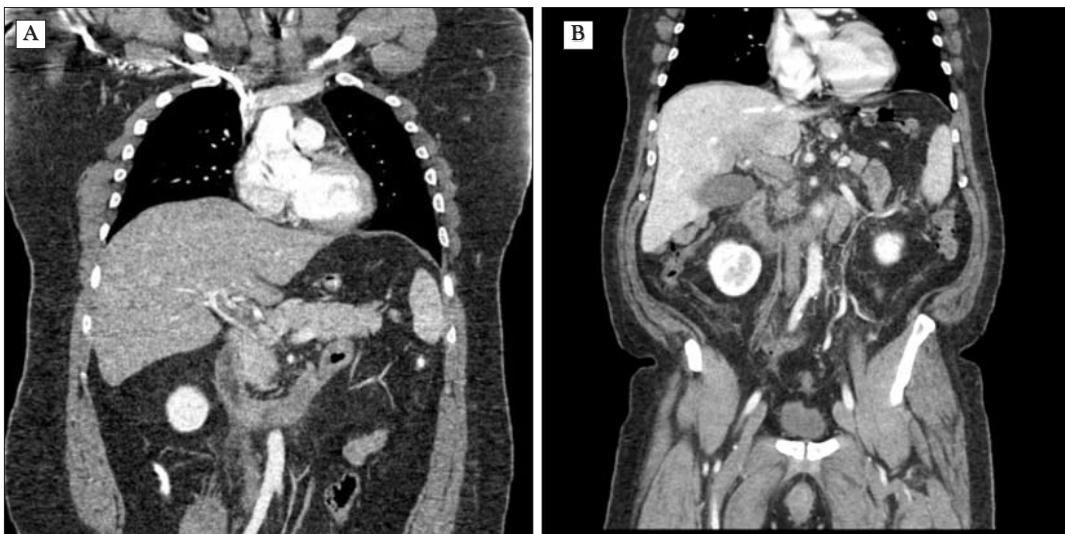


Figure 1. Portal Vein Thrombosis – CT aspect. **(A)** massive thrombosis The thrombi occluded the PV, mesenteric and splenic veins. **(B)** partial mesenteric thrombosis

determined by the severity of disease, progressing from high-grade nonocclusive to occlusive thrombosis. Patients with occlusive disease may be treated with perioperative heparin followed by systemic Tissue Plasminogen Activator (TPA) infusion. Surgery aims to remove the thrombi from the porto-mesenteric tree or to resect the ischemic bowel loops. Diagnostic laparoscopy is not anymore indicated of a first step, as the accuracy of the imaging examinations is so high. However, if for any reason the diagnostic is not offered by other investigations,

laparoscopy may reveal cyanotic bowel loops, ascites, enlarged, dark-blue spleen (*Fig. 2*). As a consequence, immediate therapy of PVT will be introduced.

After the acute stage of thrombosis, all the PVT patients received long-term anticoagulation with warfarin or, preferably, a factor Xa inhibitor (rivaroxaban, apixaban). We maintain the subsequent anticoagulation therapy for at least six months but most of the patients remained with long life therapy.

All patients with PVT diagnosis were further investigated for thrombophilia.

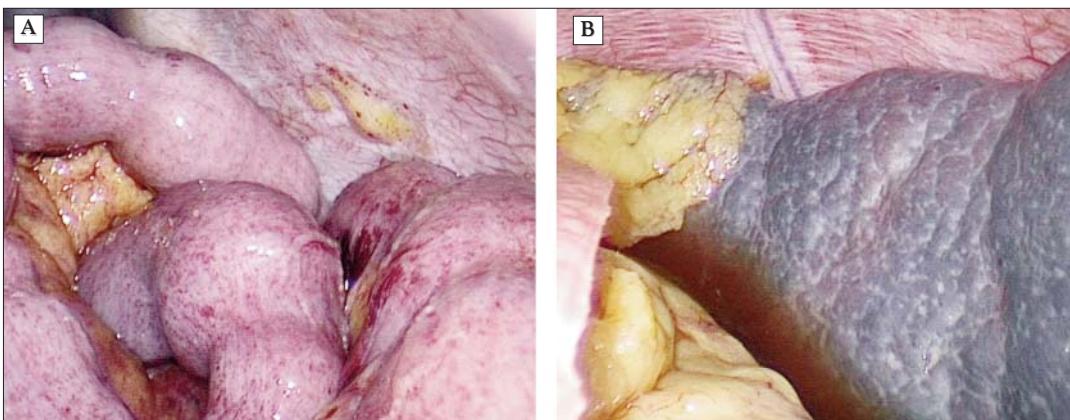


Figure 2. Portal Vein Thrombosis – The laparoscopic view reveals: **(A)** cyanotic bowel loops; **(B)** ascites, enlarged, dark-blue spleen

Statistical Method

Statistical analysis was performed with SPSS version 22 (Chicago, IL, USA), and the level of significance was set at $p \leq 0.05$. Categorical data were reported as frequencies and percentages and continuous data as average (mean) and standard deviation.

Results

3861 patients underwent elective LSG within the studied interval, 3759 primary LSG and 108 revisional sleeve resections, performed after other bariatric operation. Of them, three were readmitted 7-60 days after the bariatric procedure for PVT, equating to an incidence of 3/3861 -0,077%. The most important post-operative complications associated with LSG in the studied cohort were bleeding (7, 0.18%), fistula and sepsis (5, 0.13%) DVT 2, 0.052%).

The average age of the patients complicated with PVT was 40 years (SD 11,97), the average body mass index (BMI) was 40,34 (SD 7,994) kg/m² and all of them underwent the same protocol for LSG as described above performed by our surgical team.

The initial complaints in the PVT patients were nonspecific, including malaise, nausea, abdominal or back pain; one patient had fever.

All patients had at least one systemic predisposition toward venous thrombosis. These included prothrombotic factors, such as morbid obesity, personal or family history of deep vein thrombosis, current smoker.

The average time of LSG surgery was 96 minutes (range 60-135). The standard intra-abdominal pressure used by all surgeons was 15 mm Hg. All patients underwent conservative therapy for PVT and no surgery was needed in this series of PVT patients. The treatment was initiated on a heparin bolus followed by continuous infusion.

The patients remained on long life anti-coagulant therapy because of their history. No patient in this series received thrombolysis. No PVT was identified in the group of revisional sleeve (108 patients).

We describe below the clinical presentation,

management, and outcome of the three cases of PVT after laparoscopic sleeve gastrectomy (LSG), treated at our center (*Table 2*).

Case 1

A 29-year-old man presented 12 days post LSG as an emergency with central abdominal pain, nausea, and vomiting. The body mass index (BMI) of the patient was 50,5 kg/m², with W=160 kg. The duration of surgery was 135 min. He left the hospital in the postoperative day 2 after LSG with thromboprophylaxis at home for 3 weeks LMWH (Dalteparine 5000 ui BID as per our protocol. He had a personal medical history of smoking, hypertension under treatment obstructive sleep apnoea for what he was recommended with positive pressure therapy at home at the preanesthetic assessment and familial history of thrombosis.

The laboratory findings were minimal at readmission, with only an increase in white cell count. Doppler ultrasound (US) and computerized tomography (CT) of the abdomen confirmed the diagnosis of nonocclusive portal vein thrombosis on the posterior right branch and partial to superior mesenteric vein. Therefore, the patient was treated conservatively with anticoagulation therapy, started with heparin with a target of APTT 2-2.5 times baseline (60-90s) for 12 days. A subsequent CT scan found clot regression. The patient was discharged on therapeutic dose of anticoagulant (Apixaban 5mg BID). He has had no symptom or CT image of recurrence during his follow-up until present.

Case 2

A 40-year-old obese man (BMI=38 kg/m², W=115 kg) presented with diffuse abdominal pain (more prominent at the epigastrium), nausea, and constipation 2 months post-LSG. He had a personal medical history of smoking, hypertension, inferior myocardial infarction with angioplasty and stent on right coronary artery with double antiplatelet therapy before LSG and suspicion of thrombophilia.

The abdominal Doppler US findings

Table 2. The LSG patients presenting PVT in a BS-CoE with in five years (0.077%): demographics, medical and intraoperative characteristics, diagnosis , treatment and outcomes

Patient	1	2	3
Age	29	38	37
Sex	M	M	M
BMI (Kg/m ²)	50.2	38	44
Weight (Kg)	160	115	127
Time of Surgeryfor LSG (min)	135	95	60
Intra-abdominal presure (mmHg)	15	15	15
History of Thrombophilia/ DVT	yes	suspicion (No)	Yes
LMWH prophylaxis for 3 weeks	yes	yes	yes
Days after LSG	12	60	8
Clinical signs	abdominal pain	abdominal pain, nausea	altered general state, diffuse abdominal pain
D DIMERs at admission	5400	7500	100000
Doppler Ultra-sound	partial PVT	partial PVT	complete PVT
CT scan	partial PVT	partial PVT	extensive, occlusive portal thrombosis
Heparin infusion	yes	yes	yes
Thrombolysis (TPA)	No	No	No
Surgery (lap/open)	No	No	No
Hospital stay (days)	13	6	2 hours
Mortality	No	No	Yes
Lost of Follow-up	NO	No	-

BMI=Body Mass Index; TPA- Tissue Plasminogen Activator; DVT – Deep Venous Thrombosis

revealed non-occlusive portal vein thrombosis on the right branch and partial to superior mesenteric vein.

Therapeutic heparin was started and continued for 3 days, overlapped by warfarin with a therapeutic international normalized ratio. The patient was discharged on day 6 with good recovery, and clot regression on CT angiograms. He has had no symptom or CT image recurrence at his follow-up until present.

Case 3

A 37-year-old male patient with obesity (BMI=44 kg/m²). presented with altered general state, with severe tachycardia, BP 100/60, fever, cold sweating, diffuse abdominal pain and tenderness in left and right hypochondrium and lumbar, nausea, and vomiting with the onset 18 hours before the presentation. He was admitted directly in ICU at his presentation because of the gravity of

his symptoms. His past medical history revealed DVT with bilateral PE with anti-coagulation - warfarin and antiplatelet therapy at home, dyslipidemia, but not proven thrombophilia.

He underwent LSG 8 days before the index hospitalization with 60 min duration of operation, without incidents. Before LSG he switched warfarin with LMWH, Dalteparine 15000 UI daily. He left the hospital in the post-operative day 2 after LSG with therapeutic LMWH (Dalteparine 7500 UI BID).

At actual presentation the laboratory findings showed an increase in white cell count and D-Dimer 100000 ng/ml with very slight increase of liver function tests. The CT scan showed extensive, occlusive, portal, splenic and mesenteric thrombosis, ascites and evidence of small bowel hypoperfusion but not clear ischemia. D – Dimer 100000 ng/ml. Unfortunately, in one hour after admission, the patient had a fulminant deterioration, in shock with serum lactate level >15 mmol/L. In

ICU it was started immediately after his admission volemic resuscitation, then cardio-respiratory support with double vasoactive drugs, heparin bolus 10000 ui followed by continuous infusion, antibiotherapy, hemofiltration. It was considered thrombolysis or surgery but the exitus occurred in two hours from his ICU admission not letting room for other medical or surgical intervention due to the uncorrected hemodynamic instability.

Discussion

Portal vein thrombosis may be identified with increasing frequency as the number of laparoscopic bariatric operations continues to extend. The need for a high index of suspicion to allow early diagnosis and management of this rare but life-threatening complication is reinforced.

Our interest on PVT incidence and outcomes started much earlier than the current study. We retrospectively analyzed a cohort of patients operated between January 2008-September 2012 by the same team before the appointment of the hospital as Centre of Excellence for Bariatric and Metabolic Surgery (13). Moreover during that period we worked to develop and implement specific protocols that were evaluated in the process of accreditation for center of excellence in bariatric surgery by SRC and IFSO-EC. During that period 2220 patients underwent LSG, the incidence of PVT was 0,19% and all the patients had a favorable outcome after conservative treatment (13). All the PVT cases in that series were treated with heparin only, except a woman, BMI 41 kg/m², with complete obstruction of PV, who received systemic thrombolysis with intravenous TPA followed by heparin infusion. She had a favorable outcome and further was diagnosed with Leiden V factor thrombophilia.

The challenges of the first series of patients raise us the awareness of this possibly underestimated but life-threatening complication. We acknowledged this complication post LSG as being relatively rare and often little-known, while its early diagnosis can alter the outcome in a favorable way.

We have introduced a protocol of prophylaxis of thrombotic events with adjusted doses of LMWH, for 21 days post discharge as described in method. Accordingly, all the patients were discharged when they were able to drink 1500 ml clear fluids a day, to reduce the risk of dehydration. At the first index of suspicion for PVT diagnosis the patient is admitted and adequately investigated with CT scan, D Dimers for an early diagnosis and a prompt therapy.

In the actual study, we have analyzed all the obese patients who underwent LSG during the last 5 years, in a high-volume Centre of Excellence in Bariatric Surgery, aiming to evaluate the incidence of PVT and the outcomes of the mentioned preventive protocol and specific therapy.

Also, we have evaluated what changes could be applied to the protocol used for prophylaxis and treatment of venous thrombosis especially PVT, due to its potential lethal outcome.

The incidence of PVT post-LSG found in our actual study was very low (0,077%) and 2.5 times lower than our previous cohort (0,19%), lower than in other studies (7,19) and definitely did not reach the 1% mentioned elsewhere in the literature (9).

It appears that the incidence of PVT in LSG is higher than that with other bariatric operations. In two different large retrospective studies that had investigated PVT in patients undergoing bariatric surgery by Goitein et al. (5706 patients) (7), and Rottenstreich et al. (4386 patients) (20) no events of PVT were encountered following laparoscopic Roux-en-Y gastric bypass or biliary pancreatic diversion (BPD). Each study has described a PVT following LSG with a incidence of 0,37% and 0,55%. James (1) reported 7 cases of PVT post-laparoscopic Roux-en-Y gastric bypass though.

We found no PVT in the 108 patients who underwent revisional sleeve gastrectomy, after gastric plication, gastric banding or LSG.

A precise explanation for the increased risk of a PVT associated with LSG is still unclear (7,19). There are described some theories

about intraoperative and postoperative factors. Intraoperative factors include:

1. The thermal effect of energy devices used for ligation of the right gastroepiploic and short gastric vessels in close proximity to the splenic vein could potentially initiate thrombosis (1,9,21,22).
2. Prolonged liver retraction may potentially cause congestion, stasis within the liver and the clots' formation (23).
3. Effects of the pneumoperitoneum. Kotzampassi et al. (24) suggested that a pressure of 14 mmHg of carbon dioxide could decrease the mucosal blood flow in an experimental animal model. There are other studies that show the increase in intra-abdominal pressure more than 14 mmHg reduces the portal venous flow by 50% (10) that is more decreased by the prolonged reverse-Trendelenburg position (25).
4. Hypercapnia may cause mesenteric vasospasm which eventually reduces venous blood flow and increases the risk of thrombosis (26-29).

All of these conditions could reduce portal flow; but the same conditions exist for many other laparoscopic procedures which are not associated with an increased PVT risk (30).

Several postoperative factors including dehydration and hypovolemia, are known as risk factors for developing thrombosis, including DVT, PE, and PVT (29,31-33). We have observed that the LSG patients have a reduced fluid intake as compared with other laparoscopic bariatric procedures, potentially due to the reduction of gastric capacity and its' diameter. Further studies should investigate if the geometry and function of the LSG may explain why patients after LSG are at an increased risk for PVT. However, considering that dehydration can significantly influence the PVT risk we have decided to include in the post-discharge summary for all the patients the recommendation to avoid the exposure to heat or sun for the first 6 months, and to present to the emergency room (ER) whenever they are not able to be properly hydrated (drink at least one liter of clear liquids per day).

Amongst the predisposing factors, overall

obesity is a hypercoagulable state by reduction of fibrinolysis, elevation of clotting factor levels, and release of proinflammatory mediators and is associated with increased thrombotic events (34,35) but all patients undergoing bariatric surgery have this risk. A prospective cohort study reported a linear relationship between increased weight and venous thromboembolism. (36) For this reason in our center the thromboprophylaxis protocol is applied to all patients. In a recent multicenter case-control study about the assessment of risk factors for PVT 2 patient factors significantly impacted the risk of PVT after LSG including personal history of malignancy and type 2 diabetes compared with controls. Thrombophilia was not found amongst these factors (37).

Contrary, a systematic review of portomesenteric vein thrombosis after sleeve gastrectomy evaluated 28 studies enclosing 89 patients, found thrombophilia present in at least 56% of PVT patients. Heritable thrombophilia workup was done in 77.5% of patients with LSG, and 30.43% of them had a positive result (5).

The two cases with PVT included in the present study having the suspicion of thrombophilia did not commit to be screened again for thrombophilia, thus we cannot confirm this status for them. The genetic coagulation disorder screening may be worth proposing at least in high risk patients, but their acceptance remains an issue. To conclude relative to etiopathology, several predisposing and risk factors can be responsible for the development of PVT after LSG.

The clinical features of acute PVT are poorly defined in the literature (38). Notably, patients present with non-specific symptoms abdominal pain, malaise, fever and, less commonly, with nausea, vomiting, diarrhoea, or gastro-intestinal tract bleeding (1,7,9,19,38-40). The severity of symptoms varies significantly and may be associated with the extent of mesenteric venous thrombosis because of bowel ischemia (30) and can be fulminant with septic shock and organ failure as described in our third case. The symptoms onset of this patient with massive intra-abdominal organ

infarction that ended by death without having time to perform thrombolysis or surgical intervention were 18 hours before his admission and he had a full treatment with LMWH. The prompt diagnosis could be done if the patient has been presented earlier to ER and maybe we have had time to attempt a thrombolysis despite all risks. At this point, insisting to the po recommendations and further patients' education may be considered.

After laparoscopic surgery, the literature suggests that symptoms appeared on average 12 to 15 days postoperatively (1,7,9,19). The onset of symptoms from the day of LSG ranged from 7 to 60 days in our series.

The clinical diagnosis of PVT is often difficult and it can be confirmed by a combination of color Doppler ultrasound, contrast-enhanced CT, or magnetic resonance angiography (41). The contrast CT is recommended to be the first line with a sensitivity of 90%. (41,42) All our patient had a CT scan evaluation and, during the therapy imaging control by angio-CT, Doppler US or IRM angiography to appreciate the PVT evolution under treatment.

The PVT medical treatment consists in reversing the thrombus progression, preventing the acute and chronic complication while surgery aims thrombectomy or resection of ischemic bowel (5).

It has been recommended that subjects with acute PVT should be treated with anticoagulation therapy as early as possible, which enhances the recanalization of the portal venous system and reduces the risk of further thrombotic events (43,44).

All of our patients were treated with heparin- therapy with good outcome except the case with fulminant evolution. The adequate doses for heparin are important for prophylaxis to prevent the developing of PVT or prevent the complication. The patient with fulminant bad evolution was already on a maximal dose of LMWH when he developed the massive PVT. The question we need to answer to is, if the LMWH was effective. Consequently, in the last two years, following that dramatic case, we have introduced anti-

factor Xa (anti-Xa) concentrations measurement to monitor the activity of LMWH in all the high risk and difficult cases.

There is no consensus regarding the optimal duration and extent of anticoagulation. Ghandet al. (10) recommended 3–6 months of anticoagulation, in another study it was recommended a longerduration of oral anti-coagulants, between 6 and 12 months (45). However, patients with a systemic aetiology and extensive thrombosis are required to be on lifelong anticoagulation therapy (46). All our diagnosed and treated patients remained on lifelong anticoagulant therapy.

Studies have shown that anticoagulation may result in recanalization in 48% of cases (38).

In conservative management, we associated as other authors supportive measures to our patients to help the anticoagulation therapy such as bowel rest, adequate fluid infusion and in some cases nasogastric suction (45).

There is some evidence to suggest the treating of acute PVT with early thrombolysis, as there are higher rates of recanalization compared with either conservative management or heparin infusion (47-49). These studies are not specifically looking at post-operative patients, but rather at patients with cirrhosis and malignancies.

We found one study mentioning a successful thrombolysis occurred in a PVT patient (7). Upon laparotomy, the patient was found to have edematous, ischemic bowel. The patient underwent percutaneous transhepatic thrombolysis of the portal vein with a continuous infusion for 2 days. On second and third relook laparotomies, the patient had viable bowel, and no resection had to be performed (7).

The systemic thrombolytic therapy was initially used in PVT after liver transplantation. TPA can be used safely, even in patients with recent bleeding, if there is no evidence of active bleeding during the treatment period. However, during the TPA therapy, bleeding is the most important, sometimes life threatening complication, affecting central nervous system, gastrointestinal, or liver, (50).

We have experienced only one case that

was treated with systemic thrombolysis TPA due to its occlusive aspect of PVT and its severity in a young women diagnosed consequently with Leyden factor thrombophilia (13). No use of systemic thrombolysis TPA was needed for the patients included in the present study.

Thrombolytic therapy was applied by other authors, locally, in mesenteric or portal veins by percutaneous or transhepatic approach. This method was recommended when systemic anticoagulation did not show favorable response in severe presentations, or when clinically and/or radiologically signs of bowel ischemia were present and an non-operative approach was indicated (1, 7, 19, 51).

In the postoperative setting, thrombolytic therapy must be considered very carefully before being initiated, as there is a possibility of further surgery with the potential for bowel resection. Further research in this area is recommended.

The role of laparoscopic exploration for the diagnosis of PVT is still controversial. However, Swartz et al. (2) suggested that the extent of bowel ischemia could not be determined only by CT scan and he suggested a combination approach which involves both radiological investigation and laparoscopic exploration to determine its magnitude. Eventually, the decision for diagnostic laparoscopy should be based on the clinical course of the patient and CT findings (10). Moreover, if CT findings are uncertain and the patient clinically deteriorates, laparoscopic exploration is highly indicated. No patients included in the present study required diagnostic laparoscopy. This exploration was included in the previously communicated series and rapidity drove us to the correct diagnostic of an acute abdomen (*Fig. 2*).

Prevention

To our knowledge, there are no protocols or guidelines for the specific prevention of PVT in patients who underwent bariatric surgery, due to the rare presentation (11) or scarce reporting of such complication. DVT and PE

remain among the leading causes of mortality after bariatric procedures (31). In a small series of 10 autopsies performed on patients who died after bariatric procedures, although only 20% of patients were clinically suspected to have died from PE, up to 80% of patients had microscopic evidence of pulmonary emboli, despite being on appropriate prophylaxis (52).

So it sounds to be reasonable that prophylaxis would likely be guided by that of deep venous thrombosis as we did with our patients. After we introduced the DVT protocol the frequency of PVT in the first cohort was 0,19 % and after the protocols and follow-up were better conducted the frequency decreased to 0,077%.

At this point, the literature shows insufficient evidence regarding the utility of prophylactic thromboprophylaxis after discharge for prevention of PVT. Prospective, controlled trials are recommended to assist in developing guidelines.

Our Algorithm of prevention and therapy for PVT is shown in *Fig. 3*.

The present study has some limitations related to its retrospective design and the results may require further validation on prospective studies or RTC. However, all the data presented in the study was prospectively collected in BOLD. Moreover, we have analyzed a large cohort of LSG patients, who received a standardized management and follow up, in high-volume Centre of Excellence for Bariatric Surgery, supporting the very low incidence of PVT. Another important aspect of this study is related to the PVT prevention and management algorithm that can be a very useful tool to reduce the incidence and improve the outcomes for patients with PVT.

Conclusions

Portal vein thrombosis is a rare but serious complication after LSG.

Previous history of venous thromboembolic events in obese patients with hypercoagulable state, smoking, predisposing factors such as thrombophilia and postoperative dehydration

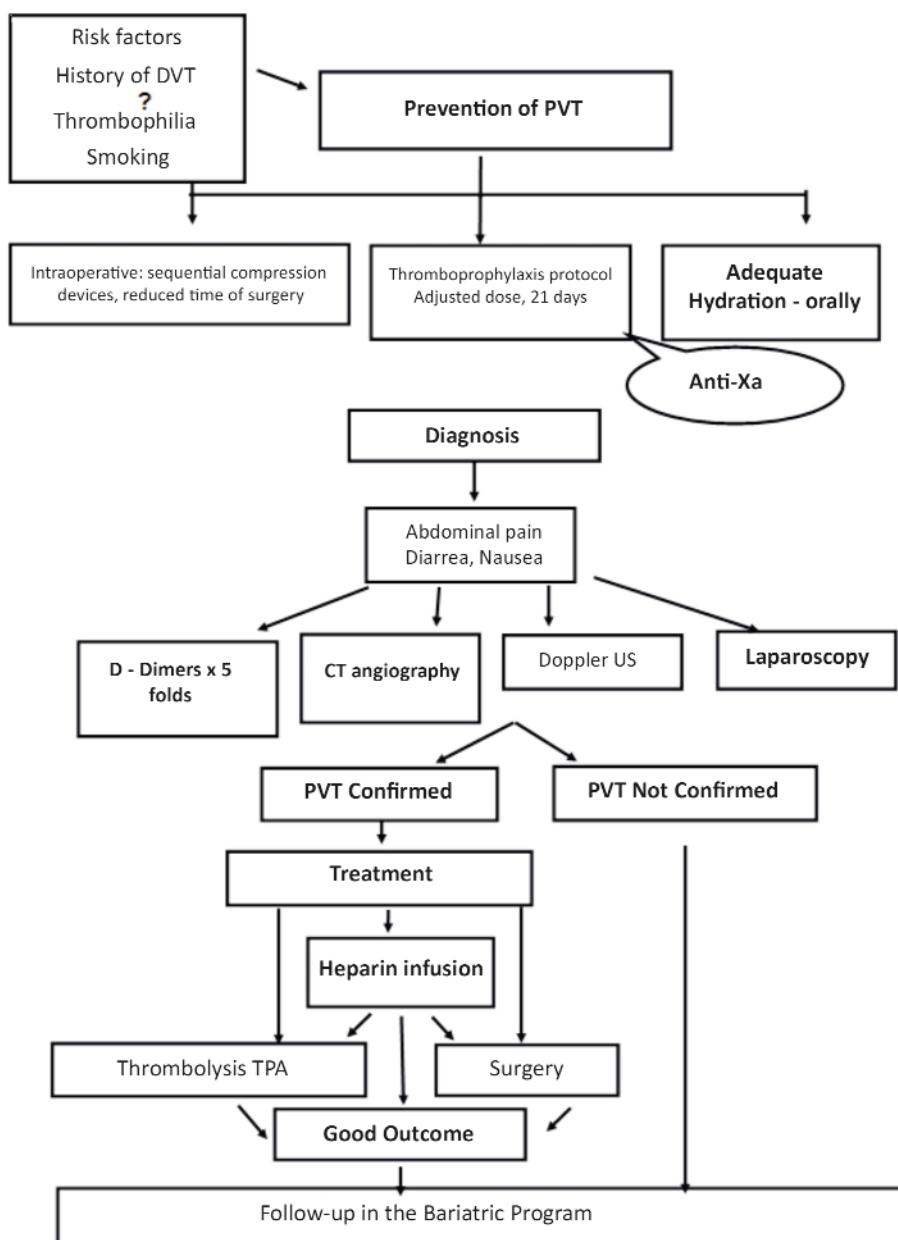


Figure 3. Algorithm for Prevention and Management of PVT in LSG Patients

are the most important risk factors for the development of PVT after bariatric surgery.

A high clinical suspicion of PVT is required during the postoperative period after LSG. The prompt diagnosis and treatment can produce favorable outcomes. Following the acute event, long-term monitoring is necessary to prevent PVT chronic complications.

Prevention of PVT by a thromboprophylaxis

protocol is of paramount importance. Although strong evidence data about PVT anticoagulant prophylaxis plan is still lacking our protocol with adjusted doses of LMWH and extended prophylaxis to 3 weeks proved to be very efficient. The anti Xa factor measurement can improve the outcomes by identifying the most efficient ranges of therapy.

Conflict of Interest

The authors declared no conflict of interest.

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