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Fátima Raquel Vieira Gomes

Portomesenteric Venous Thrombosis after Bariatric Surgery: a case series and a systematic review comparing LSG and LRYGB

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Mestre André Manuel Costa Pinho

E sob a Coorientação de:

Professor Doutor Bernardo Manuel de Sousa Pinto

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Cirurgia

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Portomesenteric Venous Thrombosis after Bariatric Surgery: a case series and a systematic review comparing LSG and LRYGB

ORIENTADOR

André Manuel Costa Pinho

COORIENTADOR (se aplicável)

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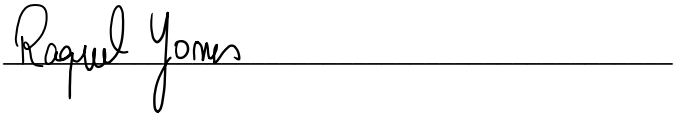
Assinatura conforme cartão de identificação: 

UC Dissertação - DECLARAÇÃO DE TRANSPARÊNCIA RELATIVAMENTE À UTILIZAÇÃO DE FERRAMENTAS DE CHATBOT GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, Fátima Raquel Vieira Gomes, abaixo assinado, nº mecanográfico 201807501, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

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Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

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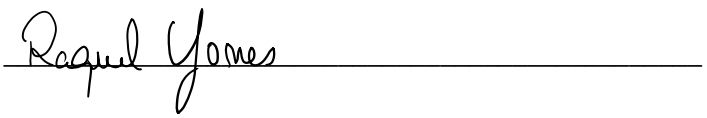
Assinatura conforme cartão de identificação: 

Dedicatória

"É necessário sair da ilha para ver a ilha. Não nos vemos se não saímos de nós."

José Saramago

Gostaria, em primeiro lugar, de expressar a minha profunda gratidão ao Dr. André, que prontamente aceitou o convite para ser meu orientador. Agradeço-lhe sinceramente pela ajuda, apoio e disponibilidade para ouvir todas as minhas questões ao longo destes dois anos. Tenho uma enorme admiração pelo profissional e médico exemplar que é, considerando-o um verdadeiro exemplo a seguir.

Aos meus pais, quero agradecer por me terem dado asas e por me terem permitido voar, sempre acreditando cegamente em mim e apoiando-me incondicionalmente. O mérito também é vosso. Mesmo à distância, nunca me deixaram sentir só e deram-me força para enfrentar cada dia.

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Portomesenteric Venous Thrombosis after Bariatric Surgery: a case series and a systematic review comparing LSG and LRYGB

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Abstract

***Introduction**:* Portomesenteric Venous Thrombosis (PMVT) is a rare but serious complication of Metabolic Bariatric Surgery (MBS). Although more frequently reported after laparoscopic sleeve gastrectomy (LSG), risk factors for PMVT remain unclear. This study aims to compare the incidence and determinants of PMVT between LSG and laparoscopic Roux-en-Y gastric bypass (LRYGB).

Methods: A retrospective analysis of 5235 MBS conducted at our institution between 2015 and 2023, identified five cases of PMVT. Additionally, a systematic review in March 2023, covering PubMed, Web of Science and Scopus, was performed. Several data was analyzed regarding risk factors.

***Results**:* In our case series, the incidence of PMVT was 0,1%. The five cases described involved four females, BMI between 39,7-56,0 kg/m^2. Comorbidities were associated with metabolic syndrome, all women used oral contraceptive and two patients were diagnosed with thrombophilia or pulmonary embolism. Thromboprophylaxis per-protocol was administered to all patients. Diagnosis was made at a median of 16 days post-surgery, with abdominal pain as main presenting symptom. Acute cases were managed with enoxaparin, unfractionated heparin and fibrinolysis. One patient required surgery.

Ten studies were included in the systematic review and 205 patients with PMVT were identified: 193 (94,1%) post-LSG and 12 post-LRYGB. The most common comorbidities were dyslipidemia, hypertension, diabetes, sleep apnea and liver disorders.

***Conclusion**:* PMVT is a potentially life-threatening complication after MBS, requiring preventive measures, timely diagnosis and several treatments. Our findings suggest a higher occurrence in women, with elevated BMI and post-LSG. Tailored thromboprophylaxis for MBS patients at risk for PMVT may be warranted.

Keywords

Bariatric Surgery, Laparoscopic Sleeve Gastrectomy, Laparoscopic Roux-en-Y Gastric Bypass, Venous Thromboembolism, Portomesenteric Venous Thrombosis

Authors' Contributions: Study conception and design and drafting of manuscript: RG, ACP. Acquisition of data: RG, FV. Analysis and interpretation of data: RG, ACP, BSP. Critical revision of manuscript: RG, ACP.

Introduction

Obesity is defined as excessive fat accumulation with a body mass index (BMI) equal to or exceeding 30 kg/m^2. It is a significant global health concern with increasing prevalence. In 2022, 43% of adults aged 18 and above were overweight and 16% were obese [1]. Obesity is associated with elevated risk of mortality and various chronic conditions, including diabetes, cardiovascular diseases, gastro-esophageal reflux disease, musculoskeletal pain, depression and several forms of cancer [2, 3].

Metabolic bariatric surgery (MBS) has emerged as a viable treatment for individuals with a BMI≥35 kg/m^2, regardless of obesity-related comorbidities, offering sustainable long-term results. Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are the predominant procedures, accounting for approximately 90% of surgeries. [4] These surgeries have a high safety profile and are increasingly performed worldwide to address the obesity epidemic, yielding consistent and favorable short and long-term outcomes.

Severe obesity and laparoscopic surgery are recognized risk factors that increase the risk of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). Consequently, patients undergoing MBS face a moderate to high risk, which is further exacerbated by their comorbidities. Other high risk comorbidities for VTE include venous stasis, BMI≥60kg/m^2, truncal obesity and sleep apnea [5].

A severe complication of MBS is portomesenteric venous thrombosis (PMVT), a rare life-threatening event, involving the portal vein (PV), its intrahepatic branches and potentially extending to the superior mesenteric vein (SMV) and splenic vein (SV). PMVT is associated with intra-abdominal inflammatory conditions causing injury to the portal system [6]. A recent systematic review reports that PMVT incidence after MBS is 0,419% and mortality of 1,33% [7], although other studies suggest higher mortality rates (3,6%) [8]. Risk factors for PMVT remain unclear, although factors such as surgical technique, patient's comorbidities and thrombophilia history likely contribute to increased risk [9].

Perioperative thrombophylactic guidelines for patients MBS are not well established. The European Society of Anesthesiology (ESA) [10] and the American College of Chest Physicians (ACCP) [11, 12] recommend mechanical prophylaxis with intermittent pneumatic compression (ICP) during and after bariatric procedures, along with anticoagulation therapy, preferably using low molecular weight heparin (LMWH). General thromboprophylaxis measures such as early ambulation and optimal hydration are also recommended [10]. However, considering potential differences in pathophysiology, it remains unclear whether these recommendations effectively prevent PMVT, as they are primarily aimed for VTE prevention.

Patients with PMVT typically present with diffuse abdominal pain, nausea, vomiting, leukocytosis and fever. The gold-standard exam for diagnosis is an abdominal contrast-enhanced computer tomography (CT). Pharmacologic anticoagulation with LMWH, unfractionated heparin (UFH) or vitamin K antagonist is the preferred initial treatment, but further treatments such as fibrinolysis through percutaneous vascular access or surgery may be warranted [8].

This study was prompted by a critical case of PMVT observed in our hospital, in 2022. This event conducted us to further research similar cases. We analyzed all patients with PMVT after MBS in our institution and conducted a systematic literature review. The primary objective was to compare the incidence, patient characteristics and risk factors for PMVT after LSG and RYGB, the two most common MBS worldwide.

Methods

Retrospective analysis of all MBS performed in a single high volume center between 2015 and 2023, to identify patients diagnosed with PMVT. A total of 5235 surgeries were performed and five cases of PMVT were identified.

Search Strategy

The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines statement [13]. A comprehensive electronic literature search was performed on PubMed, Web of Science and Scopus on March 9, 2023. Search items are listed in the Supplementary Information. A manual screening of the list of references regarding relevant papers was also performed to supplement the literature search.

Study Selection

The study selection was composed of two phases. In the screening phase, two authors (RG, FV) independently screened abstracts obtained from the data base search. Afterwards, the full texts of potentially relevant articles were retrieved for further assessment and disagreements were resolved by consensus-based discussion or by consultation with a third reviewer (ACP).

Eligibility Criteria

The inclusion criteria were studies reporting thrombosis in any branch of the porto-mesenteric-splenic axis after LSG and LRYGB, in adults (18-65 years). The exclusion criteria were studies not reporting PMVT, robotic surgery and open surgery (laparotomy). Meeting abstracts, commentaries, editorials, letters, case reports, systematic reviews and meta-analysis and animal studies were also excluded.

Data Extraction

Relevant data were extracted by two independent authors, and conflicts were resolved by consensus. We extracted available data regarding study characteristics (authors name, year of publication, study period, sample size, type of study and country), patients characteristics (age, sex), BMI, history of thrombosis and/or thrombophilia, comorbidities (diabetes, hypertension, dyslipidemia, sleep apnea, liver disorders), oral contraceptive use, type of surgery, operative time, length of hospital stay, antithrombotic prophylaxis and characteristics of PMVT (time until event, symptoms and type of treatment).

Quality Assessment

Methodological quality assessment of included studies was performed independently by two authors (RG and FV) and disagreements were resolved by consensus or by consultation with a third reviewer (ACP). The included studies were assessed by the NHLBI quality assessment tool [14].

Results

Our single-center case series of patients with PMVT after MBS is summarized in Table 1. As per-protocol, all patients underwent evaluation by a multidisciplinary team preoperatively and had a minimum follow-up period of 3 years. Thromboprophylaxis measures included ICP during surgery, as well as compression stockings, before and 24 hours after surgery. Fast-track surgery protocols involving early mobilization and early oral hydration were implemented. Additionally, all patients received chemoprophylaxis with LMWH (Enoxaparin 40-60mg) the day before surgery and continued for 2-4 weeks postoperatively.

Case 1:

A 43-year-old female, with BMI of 40,4 kg/m^2 underwent LSG in August 2015. Eleven days post-LSG, she presented to the emergency room (ER) with diffuse abdominal pain and fever. She had no relevant comorbidities and was taking oral contraceptive (OC). Abdominal CT-scan revealed complete thrombosis of the SMV and partial thrombosis of the PV. She was treated with Enoxaparin 100mg, twice daily, with favorable clinical evolution and discharged home after twelve days. Factor II G20210A heterozygote gene mutation was detected and long-term anticoagulation with Warfarin 5mg was recommended.

Case 2:

A 23-year-old female with a BMI of 45,9 kg/m^2, underwent LSG in December 2016. Thirteen days post-LSG, she presented to the ER with abdominal pain, vomiting and hematochezia. She had diabetes, treated with metformin, asthma, and was on OC. Abdominal CT-scan demonstrated extensive thrombosis involving the SMV, PV and SV. She was hospitalized, and received treatment with UFH 1980 UI/h, guided by activated partial thromboplastin time (aPTT). She developed severe hematemesis, leading to discontinuation of anticoagulation in the following day. Despite best medical treatment, her condition evolved rapidly with multiple organ failure, and the patient died three days later.

Case 3:

A 42-year-old male with a BMI of 39,7 kg/m^2, with hypertension (HTN), dyslipidemia and sleep apnea, underwent LSG in November 2019. Nine days after surgery, the patient developed PE and was treated with Enoxaparin 100mg. After discharge, he maintained anticoagulation with Warfarin 5mg, for three months. In August 2021, nearly two years latter, an abdominal CT performed for unrelated reasons revealed thrombosis of PV and SV. The patient was referenced to Immuno-hemotherapy consultation: as PMVT was asymptomatic, no treatment

was instituted. Thrombophilia study was negative and thromboprophylaxis was recommended before high risk situations. Warfarin was not maintained due to the absence of identifiable risk factors other than the risk associated with the surgery.

Case 4:

A 23-year-old female with a BMI of 48,2 kg/m^2 underwent LSG in July 2022. Sixteen days post-LSG, she presented to the ER with abdominal pain, fever, nausea and vomiting. She had sleep apnea and was on OC. Abdominal CT diagnosed complete thrombosis of SMV and partial occlusion of PV. Despite optimal treatment with UFH, there was progression to intestinal ischemia, necessitating surgical intervention with bowel resection twenty-five days post-LSG. The patient hospitalization extended beyond one year, marked by multiple complications, including infectious, pulmonary and nutritional issues. Dehiscence of LSG staple line was detected three months post-LSG. More than one year after, the patient died because of a gastro-pleural fistula uncontrolled by several treatments.

Case 5:

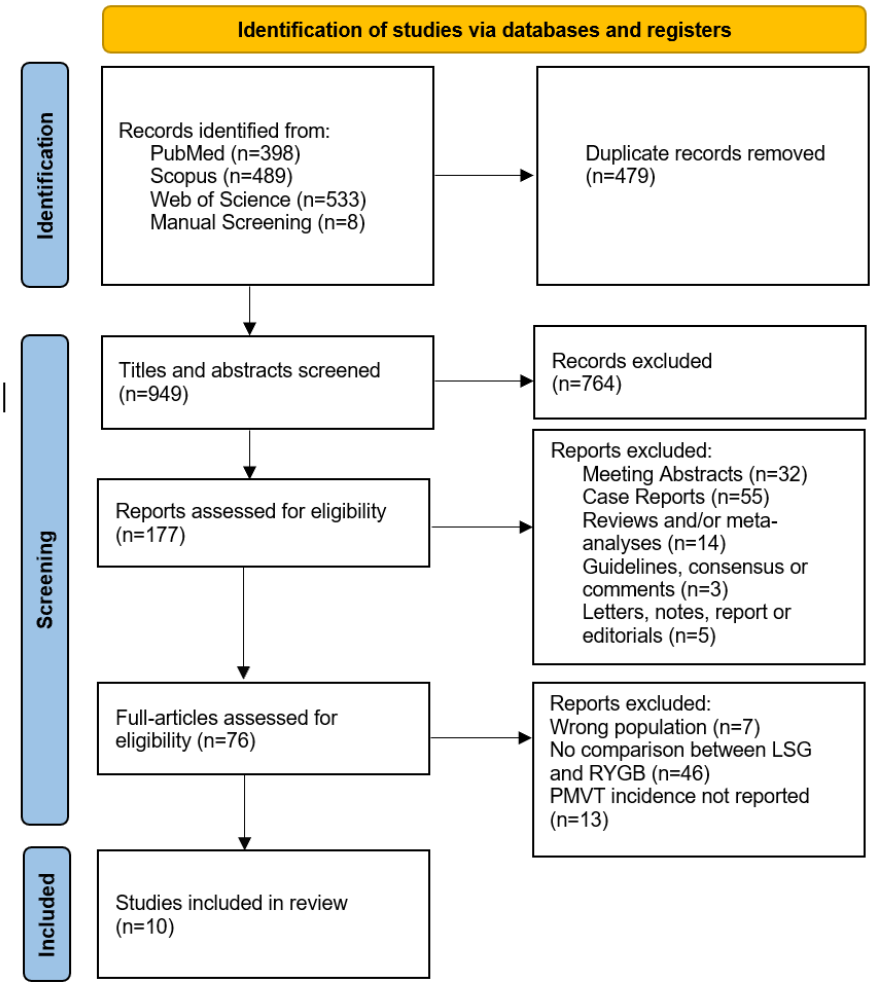
A 32-year-old female with a BMI of 56,0 kg/m^2, with a history of polycystic ovarian syndrome treated with OC, underwent LSG in June 2023. Thirty-nine days post-LSG, she presented to the ER with abdominal pain and nausea. Abdominal CT revealed complete thrombosis of SMV and partial thrombosis of PV. Initial treatment included UFH (adjusted to aPTT, administered for five days), followed by fibrinolysis using alteplase (0,5 mg/h) and UFH 500 UI for two days and then 1mg/h of alteplase for another three days. The patient showed favorable clinical evolution and was discharged after twenty-three days on Warfarin 5mg. Thrombophilia study yield negative results.

Systematic Literature Review:

The systematic review yielded a total of 941 studies: 398 from PubMed, 489 from Scopus and 533 from Web of Science. After full-text assessment for eligibility, 10 studies were included [15-25]. The PRISMA flowchart is shown in Fig. 1. The main reasons for exclusion were studies lacking a comparative analysis between LSG and LRYGB, omission of PMVT incidence data and inclusion of study populations not meeting predefined inclusion criteria.

The NHLBI quality assessment tool results are displayed in the Supplementary Table 1 to 3.

Figure 1. – PRISMA flow diagram.



The included studies, published between 2012 and 2022, comprised seven retrospective (six cohorts and one case-control study), one prospective cohort study, one cross-sectional study and one case series (Table 2). Despite documenting PMVT incidence following LSG and LRYGB, most studies lacked comprehensive information on patients characteristics and risk factors associated with each surgical procedure.

Patient characteristics and other variables studied are presented in Table 3. Among 104 867 patients undergoing MBS, LSG was the most frequently performed procedure, accounting for 69 338 (66,1%) cases. PMVT occurred in 205 cases reviewed, with 193 (94,1%) cases after LSG and 12 (5,9%) cases following LRYGB. Diagnosis of PMVT occurred within <30 days in most cases.

Common comorbidities among patients diagnosed with PMVT, included sleep apnea (50,0%), HTN (36,4%) and dyslipidemia (31,8%). OC use was reported in 45,5% of female patients. History of previous VTE was documented in 15,1% of cases. Hematologic conditions associated with higher thromboembolic risk were reported in five studies [16, 18, 21-23], with 15 cases positive for thrombophilia.

Presenting symptoms of PMVT cases were detailed in five studies [17, 18, 21-23], with abdominal pain being predominant (96,8%). Diagnosis was established mainly through abdominal CT in 71/73 cases, magnetic resonance imaging in 2/73 cases and two patients also required diagnostic laparoscopy. Doppler Ultrasound was utilized for follow-up in 32/38 cases.

Treatment included LMWH in 33/72 cases, UFH in 2/72 cases, a non-specific anticoagulant in 33/72 cases and 4/72 only required supportive treatment. Additionally, one patient received endovascular thrombolysis as part of their treatment.

Prophylactic anticoagulation measures were documented in six studies [16-18, 21-23]. LMWH was administered in 73 cases, with one case involving prior administration of UFH. Additionally, mechanical prophylaxis with compression stockings was reported in 76 cases.

Discussion

In our case series, all cases of PMVT occurred after LSG, with an incidence of 0,1% and a 30-day mortality rate of 20% (1/5). The mortality case occurring over a year post-LSG, was not directly attributed to PMVT, but to other complications. Thromboembolic events, though rare, are acknowledged as the most common cause of mortality after MBS [26].

The overall rate of VTE and PMVT following MBS is low but its incidence might be underestimated [27]. Our systematic review revealed a PMVT incidence of 0,17%, with 0,24% occurring after LSG and 0,03% after LRYGB. In contrast, a recent meta-analysis reported an incidence of 0,50% [28], but only included LSG. The lower incidence in our review may be attributed to our specific inclusion criteria, which accounted for studies reporting occurrences of PMVT in both LSG and LRYGB. In recent years, LSG has emerged as the most popular procedure for treating obesity [29, 30]. This preference is attributed to its perceived advantages, including simplicity, speed and lower invasiveness compared to other MBS, as it only modifies one organ. Studies have reported that LSG is associated with fewer post-surgical complications, including bleeding, serious morbidity, sepsis and reduced rates of 30-day readmission and reoperation [31-33]. However, it is crucial for both surgeons and patients to be aware that LSG is associated with a higher incidence of PMVT.

The pathophysiology of PMVT involves one or more components of Virchow's triad, including reduced portal blood flow, hypercoagulable state, or vascular injury [34]. Potential mechanisms, proposed by Goiten, *et al*. [22], contributing to the increased risk of PMVT after LSG include altered blood flow post-LSG, due to the division of the short gastric vessels, direct physical contact with the SV while working on the omental bursa (which can occur during both LSG and LRYGB), and early postoperative discharge leading to dehydration. Other factors such as pneumoperitoneum exceeding 14 mmHg, prolonged reverse Trendelenburg position (duration of surgery) and hypercapnia have also been identified as potential contributors to reduced portal blood flow. [35, 36].

Regarding other risk factors for PMVT, four cases in our case series involved young females with high BMI and who were taking OC. Comorbidities related to obesity were prevalent among most cases. Notably, PMVT developed despite adequate multi-level, per-protocol, thromboprophylaxis. These findings are consistent with our systematic review results, 45% of female patients with PMVT reported using OC, a factor that may need further investigation. Carlin, *et al*. [19] identified several independent predictors for PMVT following MBS, including LSG, prior history of VTE, liver disorders and serious postoperative complications such as obstruction, leaks and hemorrhage.

Hematologic abnormalities, including acquired and inherited thrombophilia, appear to be more prevalent in MBS patients. Parkin, *et al*. [37], reported a thrombophilia prevalence of 52,4% and verified that extended prophylactic anticoagulation reduced PMVT incidence in MBS patients. This finding suggests that screening for VTE history and hematologic abnormalities before surgery may be warranted, with consideration for extended thromboprophylaxis.

Abdominal pain consistently emerges as the primary presenting symptom in patients with PMVT, as noted by Naymagon, *et al*. [38]. The lack of specificity of abdominal pain underscores the importance of maintaining a high level of clinical awareness to achieve accurate and timely diagnosis. Post-MBS abdominal pain warrants attention from both patients and clinicians to avoid overlooking potential PMVT. The presence of concurrent symptoms, such as fever and bacteremia warrants consideration of septic thrombosis, which effects the treatment and prognosis [39]. The abdominal CT is paramount in the diagnosis of PMVT.

Clinically, PMVT can manifest as either acute or chronic, with no definitive timeframe for differentiation. A potential distinguishing factor is the absence of radiologic findings indicative of chronic PMVT, such as cavernoma or portosystemic collaterals and splenomegaly. In acute PMVT, liver function tests generally remain within normal ranges. Hepatic dysfunction is more likely in patients with prolonged portal hypertension resulting from PMVT [40], but may also arise consequently to multi-organ dysfunction due to septic shock, as observed in one patient described in our case series. The presence of portosystemic collaterals, although variable or inconsistent, may have an important role in the outcome of PMVT.

Most patients with PMVT present early (<30 days) after MBS, suggesting that delayed presentations may represent unrecognized or untreated acute cases, potentially underestimating the true prevalence of PMVT [23]. Early diagnosis, heightened clinical awareness, improved diagnostic techniques and prompt initiation of anticoagulation therapy have contributed to an improved 5-year survival rate of 85% for acute PMVT [34, 40].

The presence of bowel infarction and multi-systemic failure is associated with hospital mortality rates ranging from 20 to 50% [34]. High risk patients for bowel ischemia, infarction and death can be identified by abdominal CT, particularly by observing progressive thrombus extension into veins such as SMV and its smaller tributaries. Additionally, the presence of ascites can indicate increased risk [41]. Although predictors of survival rates remain unclear, advanced age and thrombosis involving the SMV appear to be significant determining factors [40].

The primary treatment modality for PMVT is anticoagulation, typically subcutaneous LMWH or

intravenous UFH, which have shown efficacy in promoting recanalization of the PV/SMV and its branches, reducing the risk of thrombosis progression. In severe PMVT cases, more invasive treatments might be necessary. While the utility of interventional radiology remains somewhat limited, there is growing evidence supporting its efficacy. Mechanical thrombectomy followed by local pharmacologic thrombolysis is recommended to enhance thrombus dissolution [42, 43]. Surgical intervention may also be necessary, particularly in instances where bowel segments are compromised [44].

Prophylactic anticoagulation measures, predominantly utilizing LMWH were documented in six studies, alongside with mechanical prophylaxis using compression stockings. Although compression stocking are standard for preventing DVT and PE and mandatory for patients undergoing MBS, their efficacy in preventing PMVT remains unclear. While guidelines from the ACCP recommend prophylaxis with LMWH, UFH or mechanical prophylaxis with ICP, there is a lack of consensus regarding the standard of care for prophylactic agents, dosing, timing or duration for patients undergoing MBS [5, 11, 12].

Hasley, *et al*. [45], evaluated the utility of the Caprini risk assessment model for LSG in selecting patients to receive extended courses of prophylaxis and found a low rate of VTE, no PMVT and no bleeding complications. A risk-adjusted approach for VTE prophylaxis in patients undergoing MBS has been proposed by Aminian *et al*. [46], utilizing their risk calculator. It categorizes patients into moderate, high and very high risk, with an escalating prophylactic approach. For moderate risk patients, they recommend early mobilization, pneumatic compression and in-hospital prophylaxis. For high risk patients, adding 2 weeks of post-discharge prophylaxis and for very high risk patients, adding 4 weeks of post-discharge prophylaxis [47]. Similarly, the ESA proposed a risk-adjusted approach, defining high risk patients based on age above 55 years, BMI above 55kg/m^2, history of VTE, venous disease, sleep apnea, hypercoagulability states and pulmonary hypertension [10].

After treatment of PMVT, it is important to prevent other thromboembolic events. Oral anticoagulation should be maintained for a minimum of 6 months post-discharge [44], considering more extensive duration based on thrombosis etiology [43].

There is limited evidence regarding the use of direct oral anticoagulants (DOACs) for prophylaxis and treatment in patients submitted to MBS [48]. While DOACs are used in non-bariatric patients with PMVT [49], their efficacy in MSB patients is controversial due to potential anatomical alterations affecting absorption. DOACs are primarily absorbed in the gastrointestinal tract, particularly the stomach and proximal small intestine [50]. Specifically, Apixaban is absorbed mainly in the small intestine offering advantages over other anticoagulants as it is unaffected by pH, does not need food restrictions, dose adjustment, monitoring or injections. Its absorption

appears unaltered in LSG patients [51]. Surve, *et al*.[52], reported favorable outcomes with thromboprophylaxis with Apixaban for thromboembolic events 30-day post-surgery, independently of MBS type. While current evidence discourage DOACs use in acute setting after MBS [53], conclusive data regarding this matter is lacking. Thus, further research is warranted to clarify DOACs efficacy and safety profile in this specific population.

Some limitations of this study should be acknowledge. The retrospective nature of most studies and the heterogeneity in the study designs may introduce bias. The lack of comprehensive information on patient characteristics and risk factors for PMVT impaired a more detailed comparison between cases of thrombosis post-LSG and post-RYGB, which was the primary objective of this study. This emphasizes the need for standardized reporting in future studies, regarding comorbidities and risk factors. We attempted to conduct a meta-analysis to compare the incidence of PMVT in LSG and LRYGB. However, it was unsuccessful, due to numerous studies reporting zero cases of thrombosis post-LRYGB and the limited occurrence of events, rendering statistical analysis unfeasible.

This systematic review provides valuable insights on PMVT incidence following different MBS, particularly noting higher frequency after LSG. These findings highlight the importance of implementing enhanced prophylactic measures, particularly in patients undergoing LSG with VTE risk factors. It also raises the question if patients undergoing LSG should receive prolonged anticoagulants compared to patients submitted to other MBS, namely LRYGB. The lack of specific thromboprophylaxis guidelines for MBS patients, emphasizes the need for further research to establish optimal anticoagulant choices, dosing regimens and duration for prophylaxis for PMVT, tailored to the unique considerations of each MBS patient.

Conclusion

PMVT is a rare yet potentially life-threatening complication after MBS. According to our case series and systematic review, the occurrence of PMVT appears to be higher in women taking oral contraceptives, with higher BMI and following LSG. Given the nonspecific nature of presenting symptoms, a high level of suspicion is necessary for accurate and timely diagnosis. Treatment involving prompt administration of anticoagulation is crucial. Notably, no consensus has been reached regarding the standard of care for thromboprophylaxis in MBS patients, therefore further research in this matter is necessary.

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Supplementary Information

Supplementary data is available in the following pages.

Statements

Conflict of interests: The authors declare that they have no conflict of interest.

Ethics Approval: For this study, ethical approval is not necessary.

Informed Consent: For this type of study, formal consent is not required.

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Tables

Table 1. – Characteristics of the patients in our case series.

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**	**Patient 5**
Age	43	23	42	23	32
Sex	Female	Female	Male	Female	Female
BMI	40,4 kg/m^2	45,9 kg/m^2	39,7 kg/m^2	48,2 kg/m^2	56,02 kg/m^2
Comorbidities	-	Diabetes, asthma	HTN, dyslipidemia, sleep apnea	Sleep apnea	PCOS
Medication	OC	OC, metformin	None	OC	OC
Surgery	LSG	LSG	LSG	LSG	LSG
Thromboprophylaxis	Enoxaparin 60mg/ 2 weeks	Enoxaparin 40 mg/ 2 weeks	Enoxaparin 40 mg/ 2 weeks	Enoxaparin 40mg/ 2 weeks	Enoxaparin 40mg/4 weeks
Thrombosis	SMV, PV	SMV, PV, SV	PV, SV	SMV, PV	SMV, PV
Time until event	11 days	13 days	646 days	16 days	39 days
Symptoms/sings	Abdominal pain, fever, leukocytosis, CRP elevation	Abdominal pain, vomit, hematochezia, leukocytosis, CRP elevation	Asymptomatic	Abdominal pain, nausea, vomit, fever, leukocytosis	Abdominal pain, nausea, CRP elevation
Treatment	Enoxaparin UFH	-	UFH; Bowel resection	UFH Alteplase	
Post discharge hypocoagulation	Warfarin -	Warfarin	Enoxaparin	Warfarin	
Thrombophilia	Factor II G20210A heterozygote gene mutation -	None	None	None	
Outcome	Partial resolution Deceased	Chronic thrombosis	Deceased	Partial resolution	

CPR, C-reactive protein; HTN, hypertension; LSG, Laparoscopic Sleeve Gastrectomy; OC, oral contraceptive; PCOS, polycystic ovarian syndrome; PV, portal vein; SMV, superior mesenteric vein; SV, splenic vein; UFH, unfractionated heparin.

Table 2. – Baseline characteristics of the included studies.

Author	Year	Study Period	Country	Design	N	Surgery	PMVT		Female (%)		Age (SD)		BMI	
							LSG	RYGB	LSG	RYGB	LSG	RYGB	LSG	RYGB
Aridi, et al.	2017	01/2008 – 12/2013	Lebanon	Retrospective cohort	575	LSG=400 RYGB=175	4	0	60.00	46.30	36.4 (12.7)	41.9 (10.3)	42.3 (6.6)	45.1 (7.5)
Barros, et al.	2020	N/A	Brasil	Case series	N/A	N/A	5	1	N/A	N/A	N/A	N/A	N/A	N/A
Bassiouny, et al.	2020	12/2014 – 03/2018	Egypt	Prospective cohort	129	LSG=84 RYGB=45	10	0	66.00	78.00	40.4 (7.1)	43.4 (7.6)	46.56 (6.27)	47.98 (5.76)
Boza, et al.	2012	01/2006 – 09/2009	Chile	Retrospective case-series	1597	LSG=811 RYGB=786	9	1	76.20	76.60	36.4 (11.7)	37.0 (10.3)	37.9 (4.6)	38.0 (3.4)
Carlin, et al.	2022	06/2006 – 11/2021	US	Prospective cohort	102869	LSG=59462 RYGB=32009	109	7	79.00		45.5		47.7	
Carrano, et al.	2021	N/A	Italy	Cross-sectional	26	N/A	22	2	N/A	N/A	N/A	N/A	N/A	N/A
Goitein, et al.	2013	01/2007 – 06/2012	Israel	Retrospective cohort	5706	LSG=4355 RYGB=966	16	0	N/A	N/A	45.0		44.4	
Rottenstreich, et al.	2016	01/2006 – 11/2015	Israel	Retrospective cohort	4386	LSG=2886 RYGB=762	16	0	N/A	N/A	N/A	N/A	N/A	N/A
Wysocki, et al.	2020	02/2014 – 03/2018	Poland	Retrospective cohort	1400	LSG=1192 RYGB=120	2	0	70.00	N/A	40.0 (35.0-39.0)	N/A	44.46 (39.31-49.84)	N/A
Tseng, et al.	2018	07/2009 – 12/2012	Canada	Retrospective cohort	819	LSG=148 RYGB=666	0	1	83.50		45.0 (31.0-59.0)		47.7 (38.2-57.2)	

Table 2. – (continued)

Operative time (SD)		Hospital Stay (SD)		Female PMVT (%)		Age PMVT (SD)		BMI PMVT (SD)		Operative time PMVT (SD)		Hospital stay PMVT (SD)	
LSG	RYGB	LSG	RYGB	LSG	RYGB	LSG	RYGB	LSG	RYGB	LSG	RYGB	LSG	RYGB
107.9 (20.6)	154.0 (19.1)	2.4 (1.2)	2.7 (1.5)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	100,0	0	35.4 (3.61)	29.0 (0)	37.2 (1.17)	39 (0)	45.04 (6.71)	91.00 (0)	1 (0)	1 (1)
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
76.6 (28.0)	106.2 (33.2)	2.8 (0.6)	3.4 (4.4)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
89.3		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	53.84		N/A	N/A	44.55 (5.32)		64,76 (27,6)		N/A	N/A
N/A	N/A	2.8		41.20	0	38 (9.9)	0	44.3 (3.9)	0	N/A	N/A	2.0 (0.5)	
N/A	N/A	N/A	N/A	56.00	0	35,1 (10.5)	0	41.8 (4.5)	0	85 (53-152)		3 (2-6)	
75 (60-105)	N/A	5 (4-7)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 3. – Characteristics of patients with PMVT

Variable	**N**	**(%)**
Female	33/62	53,3%
Diabetes	3/22	13,6%
Dyslipidemia	44/138	31,8%
HTN	8/22	36,4%
Sleep apnea	3/6	50,0%
Liver disorders	29/138	21,0%
History of VTE	26/172	15,1%
Thrombophilia	15/72	20,8%
FVLM	5	
FVIIIE	4	
PSD	4	
PCD	2	
FIIG20210AM	2	
MTHFRD	1	
JAK2M	1	
NSTS	1	
OC	10/22	45,5%
Symptoms		
Abdominal pain	61/63	96,8%
Fever	16/56	28,6%
Nausea	30/62	48,4%
Vomit	26/62	41,9%
Asymptomatic	2/16	12,5%
Time until event		
<30 days	182/203	89,7%
>30 days	21/203	10,3%

FIIG20210AM, Factor II G20210A gene mutation; FVLM, Factor V Leiden mutation; FVIIIE, Factor VIII elevation; HNT, hypertension; JAK2M, JAK2 mutation; MTHFRD, Methylenetetrahydrofolate reductase deficiency; NSTS, non-specific prothrombotic state OC, oral contraceptive; PSD, Protein S deficiency; PCD, Protein C deficiency.

Supplementary Information

Supplementary Table 1. – Search terms and queries.

	Keywords
PubMed	("Obesity/surgery"[Mesh] OR "Bariatric Surgery"[Mesh] OR "bariatric surger*"[Title/Abstract] OR "sleeve gastrectomy"[Title/Abstract] OR "gastric bypass"[Title/Abstract] OR "laparoscopic sleeve gastrectomy"[Title/Abstract] OR "laparoscopic gastric bypass"[Title/Abstract]) AND ("Venous Thrombosis"[Mesh] OR "Mesenteric Ischemia"[Mesh] OR "mesenteric vein"[Title/Abstract] OR "portal vein"[Title/Abstract] OR "portomesenteric vein thrombosis"[Title/Abstract] OR "vein thrombosis"[Title/Abstract])
Web of Science	TS=(bariatric surgery OR sleeve gastrectomy OR gastric bypass OR laparoscopic sleeve gastrectomy OR laparoscopic gastric bypass) AND TS=(mesenteric vein thrombosis OR portal vein thrombosis OR portomesenteric vein thrombosis OR mesenteric ischemia, OR venous thrombosis)
Scopus	TITLE-ABS-KEY(("bariatric surgery" OR "sleeve gastrectomy" OR "gastric bypass" OR "laparoscopic sleeve gastrectomy" OR "laparoscopic gastric bypass") AND ("mesenteric vein thrombosis" OR "portal vein thrombosis" OR "portomesenteric vein thrombosis" OR "mesenteric ischemia" OR "venous thrombosis"))

Supplementary Table 2. – Description of the answers in NHLBI quality assessment criteria tool for Observational Cohort and Cross-Sectional Studies

	Aridi et al.	**Bassiouny, et al.**	**Carlin et al.**	**Carrano et al.**	**Goitein, et al.**	**Naymagon et al.**	**Rottenstreich, et al**	**Wysocki, et al.**	**Tseng et al.**
1.	YES	YES	YES	YES	YES	YES	YES	YES	YES
2.	YES	YES	YES	YES	YES	YES	YES	YES	YES
3.	YES	YES	YES	NO	YES	YES	YES	YES	YES
4.	YES	YES	YES	YES	YES	YES	YES	YES	YES
5.	NO	NO	NO	NO	NO	NO	NO	NO	NO
6.	YES	YES	YES	NO	YES	YES	YES	YES	YES
7.	YES	YES	YES	NO	YES	YES	YES	YES	YES
8.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	YES
9.	YES	YES	YES	YES	YES	YES	YES	YES	YES
10.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	YES
11.	YES		YES	YES	YES	NO	YES	YES	YES
12.	NO	NO	NO	NO	NO	NO	NO	NO	NO
13.	NO	NR	NR	N/A	NR	NR	NR	YES	NO
14.	YES	YES	YES	NO	YES	YES	YES	YES	NO
YES/NO	9/3	8/2	9/2	5/6	9/2	8/4	9/2	10/2	10/4

1 - Was the research question or objective in this paper clearly stated?

2 – Was the study population clearly specified and defined?

3 – Was the participation rate of eligible persons at least 50%?

4 – Were all the subjects selected or recruited from similar populations? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?

5 - Was a sample size justification, power description, or variance and effect estimates provided?

6 - For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

7 - Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8 - For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome?
9 - Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10 - Was the exposure(s) assessed more than once over time?
11 - Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
12 - Were the outcome assessors blinded to the exposure status of participants?
13 - Was loss to follow-up after baseline 20% or less?
14 - Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Supplementary Table 3. – Description of the answers in NHLBI quality assessment criteria tool for Case-Control Studies

	Boza et al.
1 - Was the research question or objective in this paper clearly stated and appropriate?YES	YES
2 – Was the study population clearly specified and defined?	YES
3 – Did the authors include a sample size justification?	NO
4 – Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	YES
5 - Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	YES
6 - Were the cases clearly defined and differentiated from controls?	YES
7 - If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?	CD
8 - Was there use of concurrent controls?	NO
9 - Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	YES
10 - Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?	YES
11 - Were the assessors of exposure/risk blinded to the case or control status of participants?	NO
12 - Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?	YES
YES/NO	8/3

Supplementary Table 3. – Description of the answers in NHLBI quality assessment criteria tool for Case Series Studies.

	Barros et al.
1 – Was the study question or objective clearly stated?	YES
2 – Was the study population clearly and fully described, including a case definition?	YES
3 – Were the cases consecutive?	NO
4 – Were the subjects comparable?	YES
5 - Was the intervention clearly described?	YES
6 - Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	YES
7 - Was the length of follow-up adequate?	YES
8 - Were the statistical methods well-described?	N/A
9 - Were the results well-described?	YES
YES/NO	7/1

Apêndices:

1. PRISMA Reporting Guidelines;
2. Regras de formatação da revista *Langenbeck's Archives of Surgery*.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1: *"Portomesenteric Venous Thrombosis after Bariatric Surgery: a case series and a systematic review comparing LSG and RYGB."*
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2: (Abstract) *"**Introduction**: Portomesenteric Venous Thrombosis (PMVT) is a rare but serious complication of Metabolic Bariatric Surgery (MBS). Although more frequently reported after laparoscopic sleeve gastrectomy (LSG), risk factors for PMVT remain unclear. This study aims to compare the incidence and determinants of PMVT between LSG and laparoscopic Roux-en-Y gastric bypass (LRYGB)."*
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 5 (paragraph 7): *"This study was prompted by a critical case of PMVT observed in our hospital, in 2022. This event conducted us to further research similar cases. We analyzed all patients with PMVT after MBS in our institution and conducted a systematic literature review."*
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5 (paragraph 7): *"The primary objective was to compare the incidence, patient characteristics and risk factors for PMVT after LSG and RYGB, the two most common MBS worldwide."*
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6: *"The inclusion criteria were studies reporting thrombosis in any branch of the porto-mesenteric-splenic axis after LSG and LRYGB, in adults (18-65 years). The exclusion criteria were studies not reporting PMVT, robotic surgery and open surgery (laparotomy). Meeting abstracts, commentaries, editorials, letters, case reports, systematic reviews and meta-analysis and animal studies were also excluded."*
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6: "*A comprehensive electronic literature search was performed on PubMed, Web of Science and Scopus on March 9, 2023. Search items are listed in the Supplementary Information. A manual screening of the list of references regarding relevant papers was also performed to supplement the literature search.*"
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 24: "Supplementary Table 1. – Search terms and queries."
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6: *"The study selection was composed of two phases. In the screening phase, two authors (RG, FV) independently screened abstracts obtained from the data base search. Afterwards, the full texts of potentially relevant articles were retrieved for further assessment and disagreements were resolved by consensus-based discussion or by consultation with a third reviewer (ACP)."*
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6: *"Relevant data were extracted by two independent authors, and conflicts were resolved by consensus.."*
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6: "*We extracted available data regarding study characteristics (authors name, year of publication, study period, sample size, type of study and country), patients characteristics (age, sex), BMI, history of thrombosis and/or thrombophilia, comorbidities (diabetes, hypertension, dyslipidemia, sleep apnea, liver disorders), oral contraceptive*

Section and Topic	Item #	Checklist item	Location where item is reported
			use, type of surgery, operative time, length of hospital stay, antithrombotic prophylaxis and characteristics of PMVT (time until event, symptoms and type of treatment).”
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Not applicable.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7: *“Methodological quality assessment of included studies was performed independently by two authors (RG and FV) and disagreements were resolved by consensus or by consultation with a third reviewer (ACP). The included studies were assessed by the NHLBI quality assessment tool [14].”*
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Not applicable.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable.
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Not applicable.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Not applicable.
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable.
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable.
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable.
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 10: “Figure 1. – PRISMA flow diagram”
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not applicable.
Study characteristics	17	Cite each included study and present its characteristics.	Page 10: “*The included studies, published between 2012 and 2022, comprised seven retrospective (six cohorts and one case-control study), one prospective cohort study, one cross-*

Section and Topic	Item #	Checklist item	Location where item is reported
			sectional study and one case series (Table 2)."
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 9: "*The NHLBI quality assessment tool results are displayed in the Supplementary Table 1 to 3.*"
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 21: "Table 2. – Baseline characteristics of the included studies."
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 10: *"Despite documenting PMVT incidence following LSG and LRYGB, most studies lacked comprehensive information on patients characteristics and risk factors associated with each surgical procedure."*
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable.
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 12: *"The overall rate of VTE and PMVT following MBS is low but its incidence might be underestimated [27]. Our systematic review revealed a PMVT incidence of 0,17%, with 0,24% occurring after LSG and 0,03% after LRYGB. In contrast, a recent meta-analysis reported an incidence of 0,50% [28], but only included LSG. The lower incidence in our review may be attributed to our specific inclusion criteria, which accounted for studies reporting occurrences of PMVT in both LSG and LRYGB"*
	23b	Discuss any limitations of the evidence included in the review.	Page 15: *"The retrospective nature of most studies and the heterogeneity in the study designs may introduce bias. The lack of comprehensive information on patient characteristics and risk factors for PMVT impaired a more detailed comparison between cases of thrombosis post-LSG and post-RYGB, which was the primary objective of this study."*
	23c	Discuss any limitations of the review processes used.	Page 15: *"We attempted to conduct a meta-analyses to compare the incidence of PMVT in LSG and LRYGB. However, it was unsuccessful, due to numerous studies reporting zero cases of thrombosis post-LRYGB and the limited occurrence of events, rendering statistical analysis unfeasible."*
	23d	Discuss implications of the results for practice, policy, and future research.	Page 15: *"This systematic review provides valuable insights on PMVT incidence following different MBS, particularly noting higher frequency after LSG. These findings highlight the importance of implementing enhanced prophylactic measures, particularly in patients undergoing LSG with VTE risk factors. It also raises the question if patients undergoing LSG should receive prolonged anticoagulants compared to patients submitted to other MBS, namely LRYGB. The lack of*

Section and Topic	Item #	Checklist item	Location where item is reported
			specific thromboprophylaxis guidelines for MBS patients, emphasizes the need for further research to establish optimal anticoagulant choices, dosing regimens and duration for prophylaxis for PMVT, tailored to the unique considerations of each MBS patient."
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not applicable.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not applicable.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Not applicable.
Competing interests	26	Declare any competing interests of review authors.	Not applicable.
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not applicable.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Submission guidelines

Contents

Instructions for Authors

Types of Papers

• Brief reports (formerly rapid communications; cutting-edge findings in clinical or basic science research)

• Original research articles

• Controlled clinical trials

• Systematic reviews and meta-analyses

• Review articles

• Research Highlight articles (formerly “How-I-do-it” articles; articles presenting expert surgical techniques or clinical management)

• State-of-the-Art Clinical Surgery (should be submitted as Systematic Review)

Case reports are generally NOT accepted for publication.

Brief reports (rapid communications).

Manuscripts for this section should be strictly limited to no more than 3,000 words excluding references and up to 4 items (figures and tables). Rapid communications should be of timely relevance and address novel, cutting-edge findings with high impact or exceptional educational value. For manuscript preparation, please follow the guidelines for original articles. The Editor-in-Chief will promote a quick review process (within 2 weeks), but will very selectively accept manuscripts for this journal section.

Original research articles.

These manuscripts should represent original research in clinical, experimental or basic science. Consideration for publication is based on originality, novelty, scientific soundness, and appropriate analysis.

Controlled clinical trials.

The journal aims to encourage the submission of scientifically sound and relevant, well-conducted, randomized and controlled clinical trials. Manuscripts should be prepared according to the guidelines for original research articles and also submitted via this article type. Please state upon submission that this is a controlled clinical trial.

Systematic reviews/ meta-analyses/ review articles.

Langenbeck’s Archives of Surgery aims to publish paired expert reviews of up-to-date basic science and related clinical topics. On occasion, the Editor-in-Chief will invite additional clinical or basic science reviews on a specific topic, which are usually presented pair-wise. Exceptions include formal true systematic reviews with meta-analyses which are well-performed, and which are considered original articles.

Research highlight (formerly How-I-do-it articles).

These manuscripts illustrate surgical mastery in selective procedures or management of surgical diseases. The articles usually feature promising and interesting results of novel techniques, modifications or innovations of current surgical skills or tools. The manuscripts should be prepared according to the guidelines for original articles, and high-quality illustrations are very welcome. Individual case reports are NOT considered How-I-do-it articles.

State-of-the-Art Clinical Surgery

The topical collection State-of-the-Art Clinical Surgery intends to summarize state-of-the-art approaches for surgical intervention. The aim is to provide an evidence-based reference of surgical methodology that will aid decision making in everyday clinic and also guide readers toward further relevant in-depth clinical content. Please

submit through the article type "Systematic Review" and state that this is an article that should go into this topical collection. Techniques from the fields of general, visceral, and endocrine surgery are at the heart of this collection. We look forward to receiving and reviewing your cutting-edge clinical reviews, ideally consistently structured as outlined below in order to ensure ease of use and navigation for readers:

a. Quick Reference / Description

b. Overview

c. Differential Diagnosis

d. Indications for Surgery

e. Materials/Instruments

f. Surgical Techniques

g. Pitfalls & Complications

h. Further reading

Language

The manuscript should conform to the following order: title page, abstract and keywords, body of manuscript, acknowledgements, references, figure legends, tables, and figures. Manuscripts should be written in high-quality English suitable for effective communication to a professional medical audience. Authors who have difficulty writing in English may seek assistance with grammar and style to improve the clarity of their manuscript. Many companies provide substantive language editing via the Web. The Editor-in-Chief also reserves the right to reject manuscripts with inappropriate style or poor English.

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Manuscript Submission

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

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Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Online Submission

Please follow the hyperlink “Submit manuscript” and upload all of your manuscript files following the instructions given on the screen.

Source Files

Please ensure you provide all relevant editable source files at every submission and revision. Failing to submit a complete set of editable source files will result in your article not being considered for review. For your manuscript text please always submit in common word processing formats such as .docx or LaTeX.

Submitting Declarations

Please note that Author Contribution information and Competing Interest information must be provided at submission via the submission interface. Only the information submitted via the interface will be used in the final published version. Please make sure that if you are an editorial board member and also a listed author that you also declare this information in the Competing Interest section of the interface.

Please see the relevant sections in the submission guidelines for further information on these statements as well as possible other mandatory statements.

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Title Page

Please make sure your title page contains the following information.

Title

The title should be concise and informative.

Author information

- The name(s) of the author(s)
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Large Language Models (LLMs), such as ChatGPT, do not currently satisfy our authorship criteria. Notably an attribution of authorship carries with it accountability for the work, which cannot be effectively applied to LLMs. Use of an LLM should be properly documented in the Methods section (and if a Methods section is not available, in a suitable alternative part) of the manuscript.

Abstract

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusion

For life science journals only (when applicable)

- Trial registration number and date of registration for prospectively registered trials
- Trial registration number and date of registration followed by "retrospectively registered", for retrospectively registered trials

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Statements and Declarations

The following statements should be included under the heading "Statements and Declarations" for inclusion in the published paper. Please note that submissions that do not include relevant declarations will be returned as incomplete.

- **Competing Interests:** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication. Please refer to "Competing Interests and Funding" below for more information on how to complete this section.

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

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Text

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.

- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. We recommend using Springer Nature's LaTeX template.

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

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Manuscript Preparation

Manuscript length

Papers submitted should not exceed 15 manuscript pages including references, tables, and figure legends.

Arrange the **manuscript** as follows:

(1) title page

(2) abstract and keywords

(3) Authors' Contributions*

(4) body of the paper

(5) acknowledgements

(6) references

(7) tables

(8) figure legends

(9) figures

(10) permissions

Body of the Paper

Organize in the following manner:

(1) Introduction

(2) Material and methods

(3) Results

(4) Discussion

(5) Conclusion

* Authors' Contributions: Clarify the contributions of each author by adding a list of the following structure to your manuscript:

• Study conception and design

• Acquisition of data

• Analysis and interpretation of data

• Drafting of manuscript

• Critical revision of manuscript

For **systematic reviews** specific recommendations should be used as documented here.

For both **clinical controlled trials** and **systematic reviews** we encourage authors to report on the important quality issue of blinding as discussed here.

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Scientific style

Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

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References

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].

2. This result was later contradicted by Becker and Seligman [5].

3. This effect has been widely studied [1–3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

The entries in the list should be numbered consecutively.

If available, please always include DOIs as full DOI links in your reference list (e.g. “https://doi.org/abc”).

- Journal article

  Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

  Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

  Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

- Article by DOI

  Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

- Book

  South J, Blass B (2001) The future of modern genomics. Blackwell, London

- Book chapter

  Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

- Online document

  Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

- Dissertation

  Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal’s name according to the ISSN List of Title Word Abbreviations, see

ISSN.org LTWA

If you are unsure, please use the full journal title.

Authors preparing their manuscript in LaTeX can use the bibliography style file sn-basic.bst which is included in the Springer Nature Article Template.

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Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

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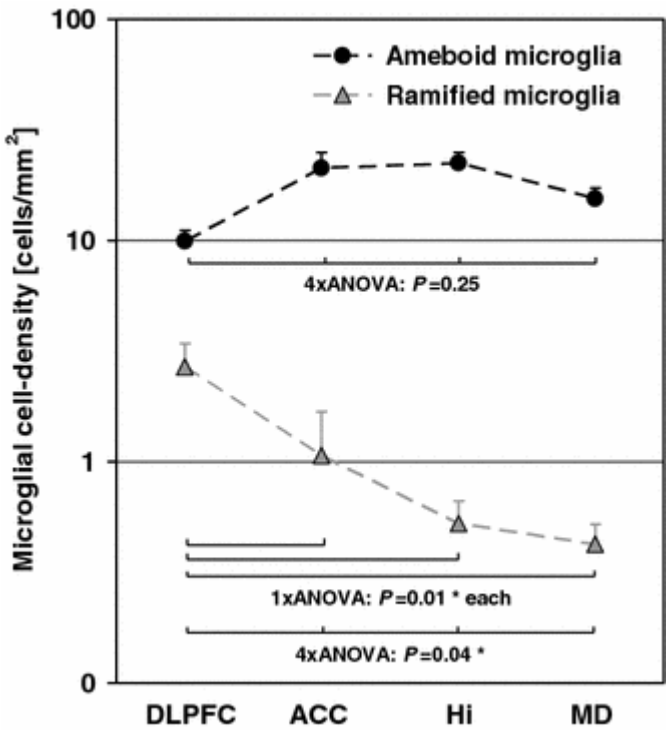
Artwork and Illustrations Guidelines

Electronic Figure Submission

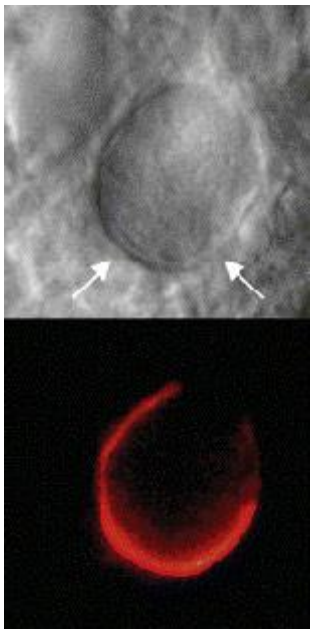
- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Line Art



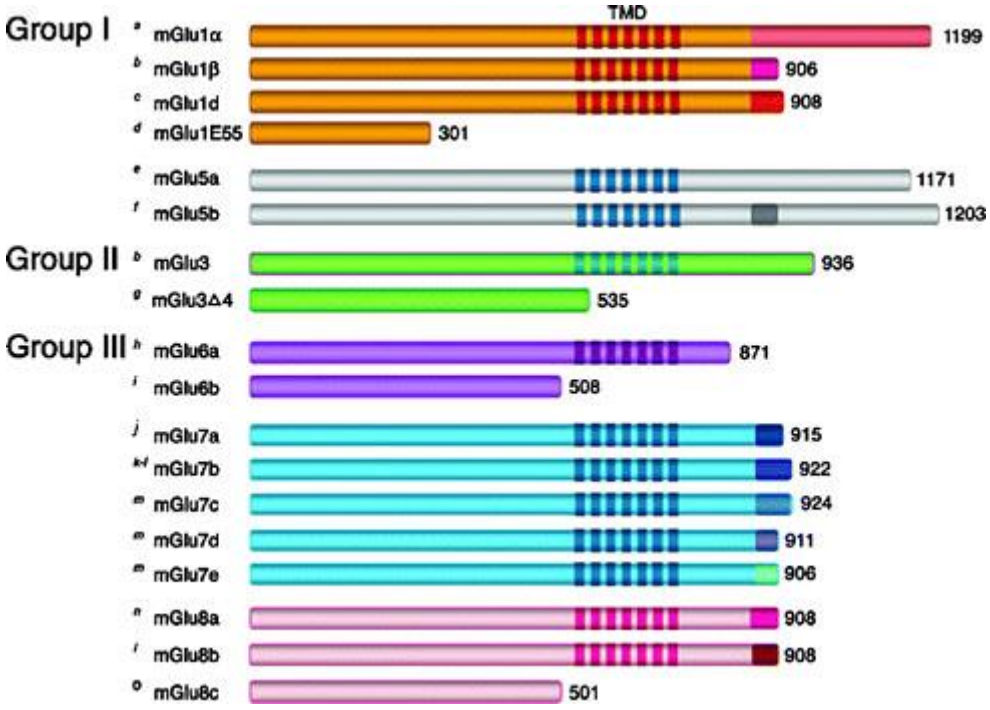
- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.
- Vector graphics containing fonts must have the fonts embedded in the files.

Halftone Art



- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

Combination Art



- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

Color Art

- Color illustrations should be submitted as RGB (8 bits per channel).

Figure Lettering

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

Figure Numbering

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures,"A1, A2, A3, etc." Figures in online appendices [Supplementary Information (SI)] should, however, be numbered separately.

Figure Captions

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ICMJE, Defining the Role of Authors and Contributors,

Transparency in authors' contributions and responsibilities to promote integrity in scientific publication, McNutt at all, PNAS February 27, 2018

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A Graduate Student's Guide to Determining Authorship Credit and Authorship Order, APA Science Student Council 2006

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• This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University B (Date.../No. ...).

• Approval was obtained from the ethics committee of University C. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

• The questionnaire and methodology for this study was approved by the Human Research Ethics committee of the University of D (Ethics approval number: ...).

Examples of statements to be used for a retrospective study:

• Ethical approval was waived by the local Ethics Committee of University A in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

• This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of XYZ who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of XYZ.

• This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University B approved this study.

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Informed consent

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For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

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Summary of requirements

The above should be summarized in a statement and placed in a 'Declarations' section before the reference list under a heading of 'Consent to participate' and/or 'Consent to publish'. Other declarations include Funding, Competing interests, Ethics approval, Consent, Data and/or Code availability and Authors' contribution statements.

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Sample statements for **"Consent to participate"**:

Informed consent was obtained from all individual participants included in the study.

Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

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The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

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