Management of biliary stones in bariatric surgery

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Abstract: Morbidly obese and post-bariatric surgery patients are at increased risk for biliary stones formation. The complications related to biliary stones may impose complexity on their management. This study aimed to review the management of biliary conditions in obese and bariatric patients. In this study, a narrative review was performed of the medical, surgical, and endoscopic procedures for the management of biliary stones and their related complications. Knowing the main prophylactic and therapeutic interventions options is essential for clinicians to properly manage the biliary stones in patients candidates or submitted to bariatric surgery.

Plain Language Summary
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The complications related to biliary stones may imposed complexity on their management. Knowing the main prophylactic and therapeutic intervention options is essential for clinicians to properly manage the biliary stones in patient candidates or submitted to bariatric surgery. This study reviewed the main tools clinicians can handle to properly manage candidates for bariatric surgery or patients submitted to bariatric surgery.

Keywords: bariatric surgery, cholecystolithiasis, cholelithiasis, gallstones, gastric bypass, gastroplasty

Introduction
Cholelithiasis is a highly prevalent global disease and is one of the leading gastrointestinal causes of hospitalization and use of the health system. In the United States, it is estimated that gallstones stand for an annual billionaire budget in the national health systems.

The main risk factors for this disease are age, female gender, genetic susceptibility, pregnancy, diabetes mellitus, dyslipidemia, and nutritional and lifestyle factors. The prevalence of cholelithiasis increases with age reaches its plateau between the fifth and sixth decade of life and is rare in children. Obesity and rapid weight loss with diets less than 800 kcal a day are also significant risk factors. In this sense, patients submitted to bariatric surgery are at elevated risk for cholelithiasis. Most of the patients that decide for bariatric surgery have a plethora of risk factors for cholelithiasis, including female gender, adult age, diabetes, dyslipidemia, obesity, history of pregnancy, and rapid weight loss.

The increased risk for the development of gallstones following bariatric surgery is well known. However, the mechanism of occurrence is not yet fully understood. Changes in bile composition in patients with rapid weight loss when undergoing a low-calorie diet or any bariatric procedure are important factors in the formation of cholelithiasis. Shiffman et al., in an old study with morbidly obese patients, collected bile directly from the gallbladder in 11 patients without gallstones.
during the bariatric surgery. Later, the bile was collected again after gallstone formation during cholecystectomy. The concentration of bile salts increased significantly from an average of 83 to 158 mmol/L, and the mean mucin concentration in the gallbladder increased from 62 to 1110 mg/mL. Free calcium and total calcium changed from mean values of 1.1 and 5.1 mmol/L to 1.9 and 8.6 mmol/L, respectively. Besides, the cholesterol concentration in the gallbladder bile increased, leading to the supersaturation of cholesterol and increasing the risk for cholesterol precipitation. These results showed that the imbalance among the gallbladder mucin, calcium, bile salts, and cholesterol after weight loss might lead to gallstones formation. Impaired motility of the gallbladder is another mechanism for stones formation. The motility disorder may be related to the surgery manipulation and vagal branches section or due to low-fat diet content during the postoperative period. A fat intake lower than 7–10 g per day is associated with inefficient gallbladder emptying.

After bariatric surgery, 28.9% of the patients will develop gallstones, and 15.7% will be symptomatic within a 3-year median follow-up. The most common symptom is biliary colic, but, a small amount will develop more severe complications, such as acute cholecystitis, acute cholangitis, choledocholithiasis, and acute pancreatitis.

Obesity not only increases the chance of developing acute gallstones complications but also predicts a poor prognosis for their evolution and frequently imposes a high level of difficulty in these complications' management. The diagnosis of cholelithiasis complications may be challenging. Transabdominal ultrasonography in morbidly obese patients loses accuracy in diagnosing cholecystolithiasis, missing 27–36% of stones. A significant percentage of obese individuals present normal ultrasound at first, sometimes requiring more sensitive diagnostic tests, such as endoscopic ultrasound. Besides, the use of the conventional magnetic resonance cholangiopancreatography is hedged to the gantry size and the table weight limit.

Cholecystolithiasis is a major challenge in patients with Roux-en-Y gastric bypass or bilio-pancreatic diversion, given the anatomical changes caused by such procedures. This condition imposes an important limitation to diagnosis and mainly to treat biliary tree obstruction in these patients.

This study aims to discuss the management of biliary stones in morbidly obese patients candidates or submitted to bariatric surgery.

Materials and methods
This study is a narrative review. The following search terms were used: ‘cholelithiasis’, ‘biliary stones’, ‘gallstones’, ‘cholecystectomy’, ‘choledocholithiasis’, ‘jaundice’, ‘pancreatitis’, ‘cholecystitis’, ‘biliary colic’, ‘bariatric surgery’, ‘gastroplasty’, ‘sleeve gastrectomy’, ‘gastric bypass’, ‘ursodeoxycholic acid’, and ‘cholangiopancreatography’. The main databases searched were PubMed, Lilacs/BVS, Embase, Cochrane Central, and Google Scholar. The included study designs were any observational or experimental human study and animal models, from the inception of the databases to July, 2021. An overview of the current available research evidence regarding the management of biliary stones and bariatric surgery treatment was gathered, aiming to provide an evidence-based orientation for clinicians.

The SANRA, the scale for the assessment of narrative review articles, was followed.

Results
The management of biliary stones along bariatric surgery can be subdivided into prophylactic and therapeutic interventions.

Therapeutic interventions are usually indicated if the patient develops any gallstone-related symptom. The symptoms are due to any complication of the biliary stones, such as biliary colic, acute cholecystitis, jaundice, and acute pancreatitis. After bariatric surgery, the incidence of biliary colic is 3.04 per 1000 patient-year; acute cholecystitis is 1.44 per 1000 patient-year; choledocholithiasis is 0.34 per 1000 patient-year; and acute pancreatitis 0.11 per 1000 patient-year. Compared with the general population, the incidence of cholecystitis and gallstones-related complications is 5.5 times higher in bariatric patients than the general population.

The therapeutic interventions should be adapted to each bariatric technique. Medical, surgical,
and endoscopic interventions are among the arsenal that clinicians can use, and they will be discussed along with this manuscript.

Prophylaxis may be indicated in asymptomatic cholelithiasis patients or patients with no cholelithiasis. The prophylaxis can be performed before bariatric surgery, including the pre-bariatric cholecystectomy; concomitant to bariatric surgery, such as the simultaneous bariatric surgical surgery and cholecystectomy; and post-bariatric surgery, such as the use of ursodeoxycholic acid (UDCA) or the cholecystectomy in asymptomatic gallstones after bariatrics.

A suggested flow diagram for biliary management in patients submitted or candidates for bariatric surgery is present in Figure 1. However, it is important to note that this flow diagram should only guide management and not be inflexible. The management of biliary gallstones in bariatric patients should follow a tailored decision focused on the shared decision-making.

**Prophylactic interventions**

**Prophylactic cholecystectomy before bariatric surgery.** To date, there is no consensus in the literature regarding prophylactic cholecystectomy in cases of diagnosis of cholelithiasis before bariatric surgery. It is reasonable to consider cholecystectomy before bariatric surgery if the patient manifests any cholelithiasis-related symptom as a therapeutic procedure (not prophylactic). The advantage of performing cholecystectomy before bariatric surgery is that the trocars disposition is directed to the gallbladder, and there is a reduction in operation time compared with simultaneous cholecystectomy and bariatric procedure.32 However, the main doubt relies on asymptomatic patients with gallstones diagnosed before the bariatric procedure. Elective cholecystectomy in morbidly obese patients is associated with a higher risk for complications, such as wound seromas, hematomas, and infections.33 Consequently, a prophylactic cholecystectomy before bariatric surgery could be avoided if the patient is asymptomatic. Simultaneous bariatric and cholecystectomy is an option. If simultaneous cholecystectomy is not performed, the bariatric technique should be carefully pondered, and gastric bypass or biliopancreatic diversion procedures could be put aside due to the risk for gallstones obstruction of the biliary tract during follow-up. Small gallstones (microlithiasis) may easily migrate into the common bile duct (choledocholithiasis), where they may cause biliary obstruction. Owing to alterations of the anatomy by bariatric bypass or biliopancreatic diversion, the conventional treatment with endoscopic retrograde choledochopancreaticography is no longer possible.

**Prophylactic cholecystectomy simultaneous to the bariatric surgery.** Prophylactic cholecystectomy has been proposed as a preventive strategy simultaneous to bariatric surgery.34 Prophylactic cholecystectomy concomitant with bariatric surgery could avoid gallstones formation and stone-related complications. In addition, concomitant cholecystectomy could theoretically reduce hospitalization-related costs due to additional surgery. In this sense, patients with cholelithiasis diagnosed before bariatric surgery could benefit from simultaneous cholecystectomy and bariatric procedure if the gallbladder removal was not performed before bariatics. In these patients, if the surgeon and patient decide not to perform the cholecystectomy at the time of bariatric surgery, gastric bypass and biliopancreatic diversion should be avoided, as pointed in section 'Prophylactic cholecystectomy before bariatric surgery'.

There is a lack of solid evidence regarding the safety of concomitant cholecystectomy. Kim and Schirmer,36,37 in a prospective cohort of 752 patients, pointed out that simultaneous cholecystectomy at Roux-en-Y gastric bypass could be safely performed with experienced surgeons, with no increase in postoperative morbidity (18.3% vs. 18.5%, \( p = 0.1 \)) or mortality (0% vs. 0.6%; \( p > 0.99 \)). Besides, in their study, no difference was noted in the length of hospital stay between gastric bypass with and without cholecystectomy (3.3 vs. 2.9 days; \( p = 0.56 \)). On the contrary, Wanjura et al.38 reported that there would be a higher chance of postoperative complications in concomitant cholecystectomy [odds ratio (OR): 1.35; 95% confidence interval (CI): 1.1–1.7]. Doulamis et al.,39 in a meta-analysis, suggest a higher rate of anastomotic leak and stricture in simultaneous cholecystectomy with gastric bypass, despite the lack of high quality of evidence in the
loss rate and bariatric technique.29 Surgery, which may vary according to the weight bladder-related complications after bariatric strategy. However, the primary variable to deter- ultrasonography findings was the least-expensive selective cholecystectomy based on preoperative effectiveness of simultaneous cholecystectomy Hamad surgery alone (95% CI: 14.8–50.9). In a cohort by bariatric surgery was 32 min higher than bariatric surgery alone, and the mean operative time for cholecystectomy and bariatric surgery was 32 min higher than bariatric surgery alone (95% CI: 14.8–50.9). In a cohort by Hamad et al.,40 the addition of cholecystectomy to laparoscopic gastric bypass increased the operative time by nearly 50 minutes and the hospital stay by 2 days. Although no cholecystectomy-specific complica- tions were observed, patients who underwent cholecystectomy had more overall complications than the rest of the cohort. The prolonged operation time imposed due to cholecystectomy during bariatric surgery may favor rhabdomyolysis. Rhabdom- olysis can lead to renal injury and increase the risk for postoperative mortality.41

In this context, simultaneous bariatric and cholecystectomy should not be indicated for all mor- bidly obese patients, and any decision should be shared with the patient and family. Simultaneous cholecystectomy should be particularly avoided for patients with a higher risk for complications related to prolonged operation time. In morbidly obese patients, hypertension, diabetes, and micro-circulation disorders are risk factors for complica- tions related to rhabdomyolysis.42

If a patient does not show any sign of gallstones before bariatric surgery, the risk for developing complications related to cholelithiasis is low. The incidence of overall biliary complications after bariatric surgery is 5.5 per 1000 patient-year.29 These patients could be followed, and in case they mani- fest any gallbladder-related symptom, cholecystectomy could be indicated. At this point, these patients probably would have a lower amount of visceral obesity, reduced liver steatosis, and the sub-optimal ports would not be a problem anymore.

Benarroch-Gampel et al.43 evaluated the cost-effectiveness of simultaneous cholecystectomy and Roux-en-Y gastric bypass. By their model, selective cholecystectomy based on preoperative ultrasonography findings was the least-expensive strategy. However, the primary variable to determine cost-effectiveness is the incidence of gall-bladder-related complications after bariatric surgery, which may vary according to the weight loss rate and bariatric technique.29

The use UDCA following bariatric surgery. The UDCA is increasingly being used for cholestatic diseases. The efficacy of UDCA has been used for the treatment of primary biliary cirrhosis,44–47 sclerosing cholangitis,48 intrahepatic cholestasis of pregnancy,49 liver disease in cystic fibrosis,50 pediatric liver diseases such as progressive familial intrahepatic cholestasis,51 Alagille syndrome,52 biliary atresia,53 total parenteral nutrition-associated liver diseases,54 chronic graft-versus-host disease of the liver,55 and some forms of drug-induced liver disease.56 In addition, UDCA has been used for the treatment of cholesterol gallstones in patients that refused or were not fitted to surgery57–59 and for gallstone prophylaxis in obese patients undergoing rapid weight reduction.60–62

UDCA is a secondary bile acid, and like all bile acids, it is a choleretic agent63 that can be used to prevent gallstone formation in obese patients, who are expected to experience rapid weight loss. UDCA is slowly absorbed in the small intestine, follows the enterohepatic circulation, and in bile, decreases the lithogenicity.64 Besides, UDCA inhibits the absorption of endogenous bile acids in the small intestine by competitive action.65 This effect leads to decreased cholesterol absorption, increased bile acid biosynthesis, and decreased biliary cholesterol secretion.53,65

Several studies, including randomized controlled trials, have shown that UDCA can effectively pre- vent cholelithiasis and the risk of the need for cholecystectomy after bariatric procedures.66,67 Miller et al.68 showed that 500 mg UDCA daily prevents gallstone formation at 12 months follow-up (placebo: 22%; UDCA: 3%; \( p = 0.001 \)) and at 24 months follow-up (placebo: 30%; UDCA: 8%; \( p = 0.002 \)) in patients submitted to vertical banded gastroplasty and adjustable gastric banding.

UDCA is usually well-tolerated and has few side effects. The most common adverse event is diar- rhea, which occurs in 2% to 9% of the patients.69

UDCA is administered orally in its unconju- gated form. The pharmacokinetics of UDCA is determined by the dosage, absorption, endolum- inal \( \text{pH} \) distribution, binding to tissues, bio- transformation, and excretion.63,70 UDCA is partially absorbed in the small bowel, and in the colon, UDCA undergoes microbial conversion to lithocholic acid, which remains mostly insoluble within the colonic content.71 In this sense, probably each bariatric surgical technique presents different UDCA pharmacokinetics. However, no experimental study has been
directed to assess bariatric surgical technique UDCA pharmacology.

With these data, in patients without contraindications, the postoperative oral administration of UDCA can be considered during the period of rapid weight loss to decrease the incidence of symptomatic cholelithiasis. The American Clinical Practice Guidelines for Perioperative, Metabolic and Non-Surgical Nutritional Support for Bariatric Surgery Patients recommends oral administration of UDCA, at least 300 mg per day, following the bariatric surgery.72

Besides, patients with cholelithiasis diagnosis before bariatric surgery that decide not to remove the gallbladder before or concomitant the bariatric procedure may also benefit from the use of UDCA. UDCA can be a safe and effective agent for dissolving cholesterol gallstones in patients with a preoperative diagnosis of cholelithiasis.58,73

However, UDCA may impose additional costs to the treatment and may be a non-cost-effective strategy.43 Currently, a randomized trial investigating the cost-effectiveness, cost-utility, and budget impact analyses of UDCA for the prevention of symptomatic gallstone disease after Roux-en-Y gastric bypass and sleeve gastrectomy is ongoing.74

The routine ultrasonography for screening biliary stones. The routine use of postoperative ultrasound can be used for searching for cholelithiasis development in patients who were submitted to bariatric procedures. Ultrasonography is inexpensive, with no radiation, and can be repeated at any time necessary.75 However, to date, there is a lack of consensus on the optimum practice.76 There is no consensus on investigating asymptomatic patients for cholelithiasis at their post-bariatric period.

Post-bariatric symptomatic gallstone disease has been observed in 6–16% of patients after a mean of 10 to 12 months.77–79 In this sense, it is reasonable to recommend that patients who show a high rate of weight loss, and mainly those patients submitted to gastric bypass or biliopancreatic diversion, the use of endoscopic retrograde cholangiopancreatography (ERCP) limited in case of choledocholithiasis formation, should be at surveillance for cholelithiasis. Transabdominal ultrasound should be performed as soon as the patients become symptomatic or within 6 to 12 months of surgery to screen for new gallstones.

Pineda et al.80 propose that conservative management of any asymptomatic cholelithiasis (pre-existing or de novo) is safe in post-bariatric patients but that these patients should be carefully monitored. This recommendation is based on the low rate (3.4%) of cholecystectomy after bariatric surgery in their cohort. However, if surgery is not performed, despite most gallbladder problems occurring during the first year after bariatric surgery, a longer follow-up is required.

Several patients with gallstones will not develop symptoms or complications, and there is no consensus on whether we should offer cholecystectomy in the asymptomatic phase. Shiffman et al.81 found that only 40% of those patients with asymptomatic cholelithiasis will develop symptoms. Şen et al.62 also advocate no intervention for asymptomatic gallstones after weight loss surgery. There will not exist a definitive answer and the suggested flow diagram for biliary management in patients submitted or candidates for bariatric surgery (Figure 1) is far from a definitive guideline. The choice for cholecystectomy should be based on a shared decision with the patient. Patients should be aware of the risks and benefits of a prophylactic cholecystectomy while asymptomatic. Patients submitted to Roux-en-Y gastric bypass and biliopancreatic diversion should be advised for the risk of choledocholithiasis and the limited use of the traditional ERCP for stones extraction. In these patients, prophylactic cholecystectomy due to cholelithiasis diagnosed after bariatric surgery should be strongly considered, avoiding the risk for stones migration.

Therapeutic interventions

Obesity and bariatric surgery may impose a high level of difficulties in the therapeutic interventions of biliary gallstone complications.

Acute cholecystitis. Acute cholecystitis is one of the most common gallstone biliary complications. The incidence of acute cholecystitis after bariatric surgery is 1.44 per 1000 patient-year.29 The increased systemic inflammatory response in morbidly obese patients prone to a higher severity for any infection and sepsis, including acute cholecystitis and cholangitis.22 Besides, laparoscopic cholecystectomy for acute cholelithiasis in obese patients has an inherently higher level of difficulty and is associated with a significantly longer operating time.23

In this sense, an early acute cholecystitis diagnosis and intervention are necessary for bariatric
Figure 1. A suggested flow diagram for biliary management in patients submitted or candidates for bariatric surgery. It should be noted, however, that no consensus exists for the management of asymptomatic gallstones, and every decision should be shared between patients and physicians.
patients. Extra-caution should be used, avoiding iatrogenic lesions. The surgeons should foresee a longer operating time, and intraoperative measures should be taken, including the use of intermittent pneumatic compression, operating room temperature control, and ensure adequate circulatory volume and blood glucose.82,83

**Acute pancreatitis.** Patients with body mass index (BMI) greater than 30 kg/m² are at risk for severe complications related to pancreatitis and a higher chance for mortality.20 This higher chance for mortality may be explained through several mechanisms, including a higher risk for necrosis infection due to local microcirculation impairment and a higher amount of peripancreatic fat. Lipolysis and unsaturated fatty acid toxicity also have a role in systemic injury.21

On the contrary, if acute pancreatitis occurs following bariatric surgery after a significant weight loss, the evolution may be milder. Kröner et al.,84 in a population-based study, showed that acute pancreatitis following bariatric surgery has lower mortality odds (OR: 0.42; 95% CI: 0.28–0.63), lower risk for complications (acute kidney injury, shock, and multiorgan failure), and lower resource use (mean difference: -$2805; 95% CI: -$3401 to -$2208). The post-bariatric surgery improvement in metabolic syndrome and comorbidities may impact acute pancreatitis development. Besides, Kröner et al.84 hypothesized that anatomical and hormonal changes after bariatric surgery might contribute to milder pancreatitis.

The incidence of acute pancreatitis following bariatric surgery is 0.11 per 1000 patient-year.29 The sleeve gastrectomy is associated with a chance for acute pancreatitis 2.3 times greater than gastric bypass.85

As a general rule, the management of acute biliary pancreatitis in obese and bariatric patients is no different from the remaining population. However, patients with a BMI greater than 30 kg/m² should be treated as high risk for complications. Besides, all bariatric patients should be considered as a high nutritional risk due to the catabolic state of pancreatitis, frequent long fasting periods, and restrictive and disabsortive nature of bariatric surgeries,86 and early nutritional attention should be taken.

**Choledocholithiasis.** The incidence of choledocholithiasis following bariatric surgery is 0.34 per 1000 patient-year.28 The gold-standard treatment for choledocholithiasis is the ERCP for most cases.87

In sleeve gastrectomy, ERCP may be performed similarly to the non-bariatric patients. However, this procedure may be challenging in Roux-en-Y reconstructions. The endoscopic route includes a 100 to 150 cm length alimentary limb after pouch in gastric bypass, following an 80 to 100 cm length biliopancreatic limb up to reaching the duodenal papilla.88 Besides, the sharp angulation at the jejunoojejunostomy hampers traversing the anastomosis, and papilla catheterization is inverted from the habitual procedure.89 Consequently, conventional ERCP devices are frequently not helpful in these cases.90 The management of choledocholithiasis following biliopancreatic diversion or gastric bypass should be customized, and decisions should be based on the institutional expertise and surgical and endoscopic resources availability.

We can group the therapeutic options for reaching the papilla of Vater in the options ERCP per oral, ERCP through alternative ways, transhepatic cholangioscopy, and surgical treatment.

**Transluminal ERCP** is technically demanding, and the success rate is low, with 33–54% success rate.91,92 A pediatric colonoscope (164 cm) or conventional enteroscope (240 cm) may be used in short-limb bypass.93

Several advanced endoscopic techniques have been described to facilitate the progress of the endoscope along the Roux-en-Y route. The device-assisted enteroscopy includes the double-balloon enteroscopy, the single-balloon enteroscopy, and spiral (rotational overtube) enteroscopy. In these techniques, an overtube helps the progression of the enteroscope through an anchoring mechanism.94 These procedures have similar success rates, and spiral enteroscopy has a shorter procedural time.95 In a systematic review, these overtube-assisted enteroscopies’ success was 70% in gastric bypass patients.96

**Transmural ERCP:** An artificial gastrointestinal orifice can be used for ERCP access to the papilla. A laparoscopic gastrostomy or jejunostomy may be performed at the moment of the ERCP procedure, and thus, the laparoscopic view and instrumentalization may also facilitate the enteroscope progression. Choi et al.97 compared ERCP via transmural
gastrostomy with double-balloon enteroscopy. The authors showed that the success rate of accessing the papilla was higher with the ERCP via transmural gastrostomy (97% vs. 78%) but with a higher risk for complications (14.5% vs. 3.1%). The main complications are related to both ERCP and operation procedures.98

Endoscopic ultrasound-directed transgastric ERCP was recently described.99 With this technique, the remnant stomach is achieved with the help of a lumen-apposing metal stent. The technical success is over 95%, but with a 21% risk for complications.100 The most common adverse event is stent migration.100

Percutaneous transhepatic cholangioscopy: Percutaneous transhepatic access to the biliary tree is another option in the unavailability or failure of the endoscopic approaches.101 The success rate is over 95%,102 The rate of major complications is 7% and includes bleeding, pseudoaneurysm, biliary lesion, cholangitis, and liver abscess,101,103

Surgical treatment: The last option for choledocholithiasis treatment is surgical intervention.102 The surgical procedure, both open and laparoscopic, allows simultaneous cholecystectomy combined and bile duct exploration. Lithotripsy, flushing, basket, balloon, or a flexible choledochoscope can be used for stone extraction. The retained stones after a primary intervention are <1% for surgical intervention.104 The first option is transcystic access, and if unsuccessful, the choledochotomy may be used. The choledochal may be primarily sutured, or a T-tube can be used.105 Duodenotomy could be used for obstinate choledocholithiasis.106

Conclusion
Morbidly obese and post-bariatric patients are at increased risk for biliary stones formation and related complications, such as biliary colic, acute cholecystitis, acute pancreatitis, and choledocholithiasis. Knowing the main prophylactic and therapeutic interventions options is essential for clinicians to properly manage the biliary stones in patients candidates or submitted to bariatric surgery.

Availability of data and material
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contribution(s)
Francisco Tustumi: Conceptualization; Supervision; Validation.
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Leonardo Carvalho Serigiolle: Data curation; Writing – original draft.
Thiago Nogueira Costa: Conceptualization; Supervision.
Denis Pajecki: Investigation; Methodology; Validation; Visualization.
Marco Aurélio Santo: Conceptualization; Writing – review & editing.
Sérgio Carlos Nahas: Conceptualization; Supervision; Validation.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

Conflict of interest statement
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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