

## Management of gallstones and gallbladder disease in patients undergoing gastric bypass

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### Abstract

The appropriate management of gallstones and gallbladder disease in patients undergoing gastric bypass remains unknown. Several therapeutic modalities are used and include performing cholecystectomy on all patients at the time of gastric bypass, performing concomitant cholecystectomy only when patients have gallstones and performing cholecystectomy only in the presence of both symptoms and gallstones. Some groups administer ursodeoxycholic acid for gallstone prevention in the postoperative period. All treatment modalities are analyzed and their results and rationality are discussed.

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### INTRODUCTION

Rapid weight loss after bariatric surgery is one of many known risk factors for gallstone development, along with age, female gender, parity, race, obesity, genetics, very-low-calorie diets, short bowel syndrome, gallbladder motor dysfunction, diabetes, drugs and gastrointestinal surgery, among many others<sup>[1-25]</sup>.

Traditionally cholecystectomy was indicated only in the presence of both gallstones and symptoms, but recently some have advocated elective cholecystectomy in selected cases in the absence of symptoms and even in the absence of gallstones<sup>[26-29]</sup>.

Sustained weight loss after gastric bypass is achieved by a combination of gastric restriction and a variable degree of malabsorption<sup>[30-32]</sup> and has therefore a greater risk for gallstone development than purely restrictive procedures like adjustable gastric banding<sup>[33-35]</sup>. The appropriate management of gallstones and gallbladder disease in these patients is still under debate and several therapeutic modalities are used<sup>[36]</sup>, including simultaneous cholecystectomy to all patients at the time of gastric bypass, regardless of the presence or absence of gallstones and/or symptoms (prophylactic approach)<sup>[37]</sup>, simultaneous cholecystectomy only to patients with gallstones (elective or selective approach)<sup>[38]</sup> and expectant management with or without the prophylactic administration of ursodeoxycholic acid until symptoms develop (conventional approach)<sup>[39]</sup>.

The objective of the paper is to discuss the rationale and the results obtained with these therapeutic modalities.

## PROPHYLACTIC APPROACH

This consists of performing simultaneous cholecystectomy on all patients at the time of gastric bypass, regardless of the presence or absence of gallstones and/or symptoms.

The rationale behind this approach is based on the elevated incidence of gallstone development after gastric bypass compared to the normal population and the low sensitivity and specificity of ultrasonography for detecting gallstones in patients with morbid obesity<sup>[37,40-42]</sup>. A minimal morbidity rate with the addition of cholecystectomy is required.

In the series of Fobi *et al.*<sup>[37]</sup> abnormal findings in the gallbladder were found in 75% of surgical specimens despite a negative preoperative ultrasound. Most of these patients had gallstones but other findings include cholesterosis and cholecystitis. The addition of cholecystectomy to open gastric bypass added only an average of 15 min and the authors report no specific morbidity related to it.

Nougou *et al.*<sup>[43]</sup> found some pathology in nearly 82% of specimens after simultaneous cholecystectomy with laparoscopic gastric bypass. 8.3% of patients did not undergo simultaneous cholecystectomy because it was judged to be dangerous. In the remaining patients, cholecystectomy added only 19 min on average to the procedure, with no extra ports addition. The authors do not report specific morbidity related to cholecystectomy.

Guadalajara *et al.*<sup>[41]</sup> performed simultaneous cholecystectomy on 89 patients undergoing open gastric bypass and found a postoperative incidence of gallstones of 24% while the preoperative ultrasound incidence was only 16%.

Liem *et al.*<sup>[44]</sup> performed simultaneous cholecystectomy on all patients undergoing open gastric bypass and found an incidence of gallbladder pathology of 80%.

A summary of these results is presented in Table 1.

## ELECTIVE/SELECTIVE APPROACH

This consists of performing simultaneous cholecystectomy only on patients with asymptomatic gallstones diagnosed pre or intraoperatively.

The rationale behind this approach is based on an assumed higher incidence of symptomatic gallbladder disease in patients with gallstones in comparison to those without them. Some groups administer prophylactic ursodeoxycholic acid to patients without gallstones and therefore not submitted to concomitant cholecystectomy. A low morbidity rate is also required to support this approach.

Hamad *et al.*<sup>[38]</sup> performed simultaneous cholecystectomy on 16.9% of patients at the time of gastric bypass. Operative times were significantly longer for patients undergoing simultaneous cholecystectomy and total hospital stay was almost doubled in comparison to gastric bypass without concomitant cholecystectomy. A significantly higher major morbidity rate was observed for

patients undergoing simultaneous cholecystectomy but no specific morbidity was directly related to it. The most common pathological finding in the specimens was cholecystitis (99% of the cases). All patients without simultaneous cholecystectomy received 300 mg of ursodeoxycholic acid twice a day orally for a 6 mo period. During follow up 2.3% of these patients developed symptomatic gallstone disease and required cholecystectomy after an average of 12.4 mo.

Villegas *et al.*<sup>[45]</sup> performed simultaneous cholecystectomy on 14% of patients after intraoperative diagnosis of gallstones or sludge with the aid of laparoscopic ultrasound. The global need for a subsequent cholecystectomy was 7%. Patients completing prophylactic ursodeoxycholic acid treatment had a significantly lower need of subsequent cholecystectomy.

In the series of open gastric bypass of Caruana *et al.*<sup>[46]</sup> the diagnosis of gallstones was made by intraoperative palpation of the gallbladder. The authors did not report significant morbidity related to the addition of cholecystectomy. A subgroup of 125 patients that did not undergo simultaneous cholecystectomy was followed for at least 16 mo, requiring 8% of them to have a subsequent cholecystectomy for symptomatic gallstone disease.

Ahmed *et al.*<sup>[47]</sup> retrospectively analyzed a series of 400 consecutive patients and found only significant differences in terms of operative times, which were 29 min longer for patients undergoing simultaneous elective cholecystectomy. No information about the incidence of symptomatic gallstone disease in the population without simultaneous elective cholecystectomy is given.

The group of the Universidad Católica de Chile reports a rate of simultaneous elective cholecystectomy of 10.9%<sup>[48]</sup>. The only significant differences were found for operative times, which were higher for the population undergoing simultaneous elective cholecystectomy. No information regarding the incidence of symptomatic gallstones in the population without simultaneous elective cholecystectomy was given.

Taylor *et al.*<sup>[49]</sup> performed simultaneous cholecystectomy on 15% of patients. They reported the lowest need for subsequent cholecystectomy without the administration of prophylactic ursodeoxycholic acid, with only 3% of patients requiring it.

Tucker *et al.*<sup>[50]</sup> performed simultaneous cholecystectomy on 7.2% of patients. A subgroup of patients was not submitted to this approach although they had gallstones present at the time of gastric bypass. The need for subsequent cholecystectomy in these patients was 17.6% whereas for patients without gallstones at the time of gastric bypass it was 6%.

A summary of these results is presented in Table 1.

## CONVENTIONAL APPROACH

This consists of performing cholecystectomy only in the presence of both gallstones and symptoms, following the present guidelines for gallstone disease management<sup>[51,52]</sup>. The rationale behind this approach is to

Table 1 Results for cholecystectomy

Author	Yr	Indication for cholecystectomy	Increased morbidity	Ursodesoxicolic acid administration	Need for subsequent cholecystectomy
Fobi <i>et al</i> <sup>[37]</sup>	2002	Prophylactic open	No	NA	NA
Nougou <i>et al</i> <sup>[43]</sup>	2008	Prophylactic laparoscopic	No	NA	NA
Guadalajara <i>et al</i> <sup>[41]</sup>	2006	Prophylactic open	No	NA	NA
Liem <i>et al</i> <sup>[44]</sup>	2004	Prophylactic open	No	NA	NA
Hamad <i>et al</i> <sup>[38]</sup>	2003	Selective laparoscopic	Yes	Yes	2.30
Villegas <i>et al</i> <sup>[45]</sup>	2004	Selective laparoscopic	NR	Yes	7.00
Caruana <i>et al</i> <sup>[46]</sup>	2005	Selective open	No	No	8.00
Ahmed <i>et al</i> <sup>[47]</sup>	2007	Selective laparoscopic	No	No	NR
Escalona <i>et al</i> <sup>[48]</sup>	2008	Selective laparoscopic	No	No	NR
Taylor <i>et al</i> <sup>[49]</sup>	2006	Selective open	NR	No	3.00
Tucker <i>et al</i> <sup>[50]</sup>	2008	Selective laparoscopic	No	NR	11.80
Swartz <i>et al</i> <sup>[53]</sup>	2005	Conventional	NA	Yes	14.70
Fuller <i>et al</i> <sup>[54]</sup>	2007	Conventional	NA	Yes	7.69
Ellner <i>et al</i> <sup>[55]</sup>	2007	Conventional	NA	No	9.00
Portenier <i>et al</i> <sup>[56]</sup>	2007	Conventional	NA	No	8.10
Papasavas <i>et al</i> <sup>[39]</sup>	2006	Conventional	NA	No	7.83
Patel <i>et al</i> <sup>[57]</sup>	2006	Conventional	NA	No	6.00
Patel <i>et al</i> <sup>[58]</sup>	2009	Conventional	NA	No	4.90
Cosme Argerich Hospital	2010	Conventional	NA	No	9.84

NA: Not applicable; NR: Not reported.

indicate cholecystectomy only for the patients requiring it and since most of the subsequent cholecystectomies are performed when a significant weight loss is achieved, the operation is done in a leaner and healthier patient.

Swartz *et al*<sup>[53]</sup> found an incidence of subsequent cholecystectomy of 14.7%, with a significant lower incidence for patients completing prophylactic ursodeoxycholic acid treatment. In Fuller and coworker's experience, the need for subsequent cholecystectomy in patients completing prophylactic ursodeoxycholic acid treatment was 7.69%<sup>[54]</sup>.

Ellner *et al*<sup>[55]</sup> and Portenier *et al*<sup>[56]</sup> did not administer prophylactic ursodeoxycholic acid treatment and found an incidence of subsequent cholecystectomy of 9% and 8.1%, respectively.

Papasavas *et al*<sup>[39]</sup> did an interesting study in which they retrospectively reviewed the records of 644 patients undergoing gastric bypass without simultaneous cholecystectomy. All of them received postoperative prophylactic ursodeoxycholic acid treatment. The need for a subsequent cholecystectomy in patients with gallstones present at the time of gastric bypass was 8.3%, which is similar to the incidence observed for patients without gallstones (6.9%) and to the incidence for patients without preoperative ultrasound screening (8.3%). After obtaining these results, this group no longer screens for gallstones preoperatively. Similarly, Patel *et al*<sup>[57]</sup> at the UCLA School of Medicine found an incidence of subsequent cholecystectomy without preoperative screening and without postoperative ursodeoxycholic acid administration of 6%. A subsequent analysis by the same group with a longer follow up showed an even lower rate of subsequent cholecystectomy of 4.9%<sup>[58]</sup>.

In our experience at Cosme Argerich Hospital from Buenos Aires, the global need for cholecystectomy after gastric bypass, without prophylactic ursodeoxycholic

acid treatment, was 9.84% (unpublished data). For patients with gallstones present at the time of surgery a subsequent cholecystectomy was needed in 5% and for patients without gallstones in 10.71% (*P*: not significant). Based on our own data, the natural history of patients with asymptomatic gallstones undergoing gastric bypass is very much like the natural history of asymptomatic gallstones in the general population<sup>[59-61]</sup>.

A summary of these results is presented in Table 1.

## URSODEOXYCHOLIC ACID TREATMENT

The preventive administration of ursodeoxycholic acid proved to be significantly better than placebo in preventing gallstone formation in a double blind, prospective and randomized study conducted by Sugerman *et al*<sup>[62]</sup>. A daily dose of 600 mg was associated with the lowest rate of gallstone formation and the lowest incidence of adverse events. Patients that developed gallstones showed a lower compliance rate. The effect of the 6 mo treatment seems to last for at least 1 year, since at that moment patients were reevaluated with ultrasonography and the incidence of gallstones was significantly less compared to the placebo arm. Unfortunately, there is no mention in the study regarding how many of those patients that developed gallstones were actually symptomatic and therefore required cholecystectomy, since the actual standard of care for non-obese patients indicates a cholecystectomy only when both symptoms and gallstones are present (SSAT NIH). A true benefit for ursodeoxycholic acid would be a lower rate of delayed cholecystectomy over the placebo group.

Wudel *et al*<sup>[63]</sup> compared, in a randomized double-blind fashion, a cohort of 60 patients without gallstones at the time of open gastric bypass and prescribed them

a 6-mo course of ursodeoxycholic acid, ibuprofen or placebo. 71% of the patients subsequently developed gallstones and no benefit of the two therapies investigated could be demonstrated because of an extremely low compliance rate of 28%.

A recently published meta-analysis by Uy *et al*<sup>[64]</sup> concluded that ursodeoxycholic acid administration prevents gallstone formation after bariatric surgery, but no meta-analysis of symptomatic gallstones could be done, since only one paper addressed this topic and unfortunately did not include patients undergoing gastric bypass<sup>[65]</sup>.

## CONCLUSION

Prophylactic and selective management can be safely performed and the only significant difference with patients not submitted to concomitant cholecystectomy is mostly observed in operative times that are higher in those who do undergo cholecystectomy. Data obtained from conventional management studies, with or without ursodeoxycholic acid administration, show that most of the patients remain asymptomatic even when they develop gallstones and therefore do not require a subsequent cholecystectomy, so that the risks of performing a concomitant cholecystectomy might be unwarranted. Treatment with ursodeoxycholic acid prevents gallstone formation after gastric bypass but most of the studies conducted show a low compliance rate and do not mention the true benefit of the treatment, which would be a lower cholecystectomy rate.

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