

## Overcoming the difficulties in laparoscopic management of contracted gallbladders with gallstones: possible role of fundus-down approach

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### Abstract

**Background** The aim of this study is to compare efficacy and complications between fundus-down and conventional laparoscopic cholecystectomy (LC) in treating contracted gallbladders with gallstones.

**Methods** Between January 1999 and May 2008, 64 patients with contracted gallbladders and gallstones were included in the study. Main outcome measures included conversion rate, complication rate, bile duct injury rate, operation time, and postoperative stay.

**Results** The average postoperative hospital stay for fundus-down technique was  $5 \pm 3$  days, and  $7 \pm 3$  days for conventional technique ( $P = 0.003$ ). The conversion rate and complication rate were 0% (0/33) and 3.00% (1/33) for fundus-down technique, and 32.3% (10/31) and 22.6% (7/31) for conventional technique ( $P = 0.0009$  and 0.02,

respectively). In subgroup analysis, fundus-down LC seemed to lower the bile duct injury rate from 2/31 (6.5%) to 0/33 (0%) compared with 6/1,468 (0.4%) ( $P = 0.01$  between 6.5% and 0.4% vs.  $P = 1.00$  between 0% and 0.4%).

**Conclusions** It appears that fundus-down laparoscopic cholecystectomy is associated with lower conversion and complication rates and shorter postoperative hospital stay as compared with conventional laparoscopic cholecystectomy when used to treat patients with contracted gallbladders and gallstones.

**Keywords** Contracted gallbladders · Gallstones · Fundus-down laparoscopic cholecystectomy · Conventional laparoscopic cholecystectomy

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Phillippe Mouret performed the first laparoscopic cholecystectomy (LC) on a human patient in 1987. Since then, this new advancement in the history of general surgery has gained wide acceptance and entered daily practice for general surgeons throughout the world [1–6]. Contracted gallbladders (GB) are known to result from long-standing chronic cholecystitis. Anatomic characteristics of contracted gallbladders include severe adhesions and complete coverage by greater omentum, severe pericholecystic fibrosis, thickening of gallbladder walls and loss of elasticity, obscure anatomy of triangle of Calot, and dense adhesions to duodenum, transverse colon, and common hepatic duct. The cystic artery is usually fibrosed and partially obliterated, and common bile duct is usually elevated by adhesions close to the cystic duct. These anatomic characteristics make this condition difficult to handle with laparoscopic approach. However, the difficulties in the laparoscopic management of contracted gallbladders are seldom addressed in the literature.

To complicate things further, anatomic variation of drainage of right posterior duct into cystic duct occurred in 2% of patients and drainage of a right sectoral duct into the left hepatic duct occurred in 6% of patients [7].

From reports in the literature, contracted gallbladder is the leading cause of conversion from laparoscopic cholecystectomy to open surgery due to obscure anatomy or increased risk for intraoperative hemorrhage from gallbladder bed [8, 9].

Some surgeons use fundus-down techniques routinely when performing laparoscopic cholecystectomy and claim to have lower incidence of bile duct injury than that of conventional techniques [10–16]. The reason was that the former adopted an operative strategy similar to the open techniques. The two techniques differ in the order of dissections. The former proceeds from fundus dissections towards the cystic duct and cystic artery, whereas the latter proceeds in reverse order. We conducted this study to examine which procedure can preserve the advantages of minimal invasiveness while simultaneously keeping the complication and conversion rates low.

The aim of this prospective randomized controlled trial is to compare efficacy and safety between fundus-down laparoscopic cholecystectomy and conventional laparoscopic cholecystectomy in treating contracted gallbladders with gallstones. The primary endpoints included conversion rate, complication rate, bile duct injury rate, operation time, and postoperative hospital stay.

## Patients and methods

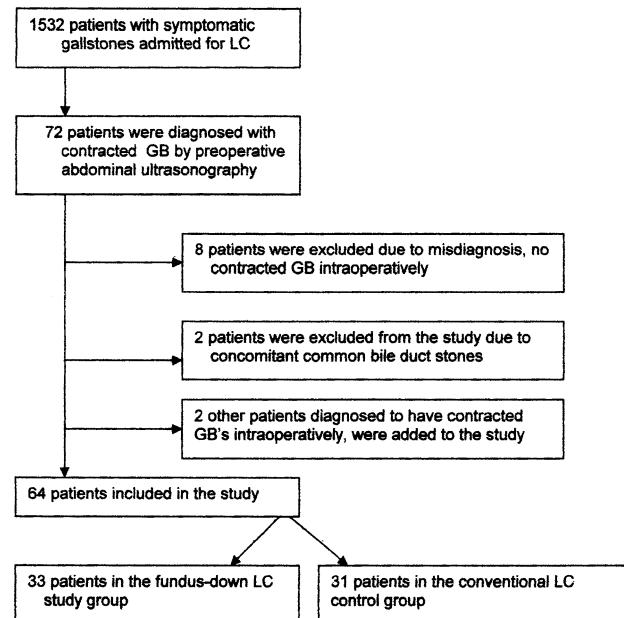
### Patients

Between January 1, 1999 and May 31, 2008, 1,532 consecutive patients with symptomatic gallstone disease

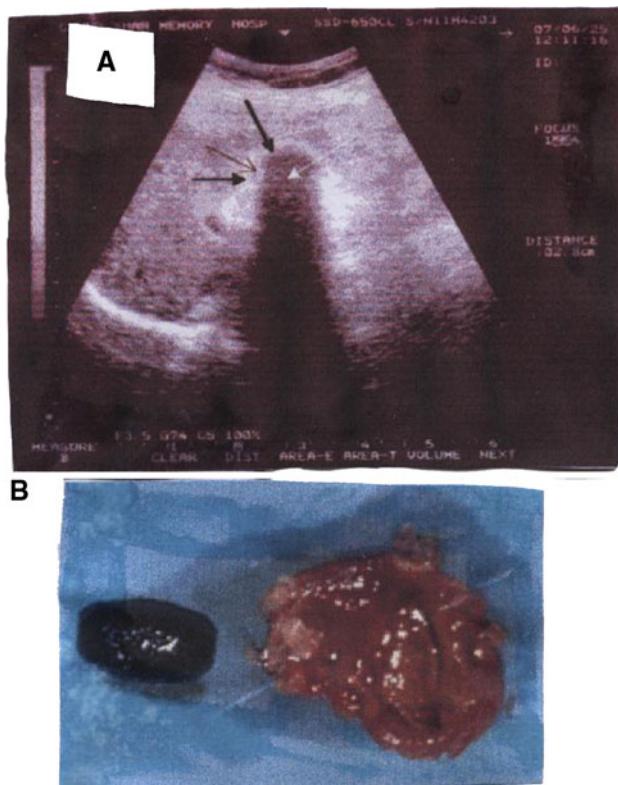
underwent laparoscopic cholecystectomy under the authors' service. Among them, 72 patients were diagnosed to have contracted gallbladder (GB) by preoperative abdominal ultrasonography and initially enrolled in the study. They were assigned consecutive numbers. Patients with odd numbers underwent conventional laparoscopic cholecystectomy (LC), while patients with even numbers underwent fundus-down laparoscopic cholecystectomy. Eight patients were excluded from the study due to misdiagnosis, i.e., no contracted GB was found intraoperatively. Two patients were excluded from the study due to concomitant stones in the common bile duct. Two other patients who were diagnosed to have contracted GB intraoperatively, although missed in the preoperative ultrasonography, were added to the study. Ultimately, 64 patients (4.2%, 64/1,532) were found to have contracted gallbladders and entered this study. The study group consisted of 33 patients undergoing fundus-down laparoscopic cholecystectomy, while the control group consisted of 31 patients undergoing conventional laparoscopic cholecystectomy. These are illustrated in a flow chart in Fig. 1.

The initial diagnostic method for contracted gallbladders was preoperative real-time ultrasonography with a 3.5-MHz probe according to Raptopoulos et al.'s criteria [17] or McDonald's wall-echogenicity-shadow (WES) triad [18] (Fig. 2A) confirmed by intraoperative findings (Fig. 2B) and postoperative pathology.

Demographic data including age, gender, body mass index, white blood cell count, serum alanine transaminase,



**Fig. 1** Flowchart of 1,532 patients diagnosed preoperatively with symptomatic gallstones. Patients were admitted for laparoscopic cholecystectomy between January 1, 1999 and May 31, 2008. *LC* laparoscopic cholecystectomy, *GB* gallbladder



**Fig. 2** Cholecystosonographic and pathologic characteristics of contracted gallbladders: **A** cholecystosonographic pathognomonic double-arcuate–shadow sign: two parallel arcuate echogenic lines (two large black arrows) separated by a thin anechoic space (a small black arrow) with distal acoustic shadowing (a white arrow), and **B** pathologic characteristics: severe fibrosis, thickening with loss of elasticity of wall of the gallbladder

aspartate transaminase, alkaline phosphatase, total bilirubin levels, preoperative cholecystosonographic findings, intraoperative and pathologic findings, intraoperative complications, conversions, postoperative complications, postoperative hospital stay, and pathologic findings were recorded.

#### Equipment

A 30° oblique-viewing telescope was used for better visualization of the lateral and superior borders of gallbladder–liver junctions. An endosheath was used for a better angle in the dissections of the gallbladder–liver junctions.

#### Techniques

The techniques used in conventional laparoscopic cholecystectomy were as described in the literature [1–5]. In brief, four trocars were used in fundus-down laparoscopic cholecystectomy, just as in conventional laparoscopic cholecystectomy. The fundus-down LC technique

starts with dissections of the lateral attachments of the gallbladder–liver junctions (Fig. 3A). These are followed by dissections of the superior border of the gallbladder–liver junctions (Fig. 3B). Then the medial border is dissected (Fig. 3C). Dissections of the triangle of Calot, wherein lie the cystic artery, cystic duct, and occasionally the right hepatic artery and accessory bile duct, come last. Structures in the triangle of Calot are the important anatomic structures of which to be aware. We then apply endoloops/endoclips to the last ductal structures, i.e., the cystic artery and the cystic duct, separately (Fig. 3D). We transect the cystic duct and artery between the endoloops/endoclips. Finally, we remove the gallbladder from the peritoneal cavity by putting it into an endobag. A Jackson–Pratt vacuum drain is left in the Morrison pouch occasionally, only if large drainage amount is expected.

#### Statistics

We used Student's unpaired *t* test for numerical data including age, biochemical values, operation time, and postoperative hospital stay. We adopted chi-square test for categorical data such as gender. We adopted Fisher's exact test for categorical data such as bile duct injury rate, complication rate, and conversion rate. *P* value < 0.05 was considered statistically significant. We calculated rate ratios with 95% confidence interval to demonstrate association and precision.

#### Ethics

The operative procedures were well explained to all patients. Informed consent was signed by every patient for both laparoscopic and open cholecystectomies. There was no formal ethics review committee (institutional or regional) existing at the start of patient enrollment. However, the principles outlined in the Declaration of Helsinki of 1975 (revised in 1983) were followed throughout the study period.

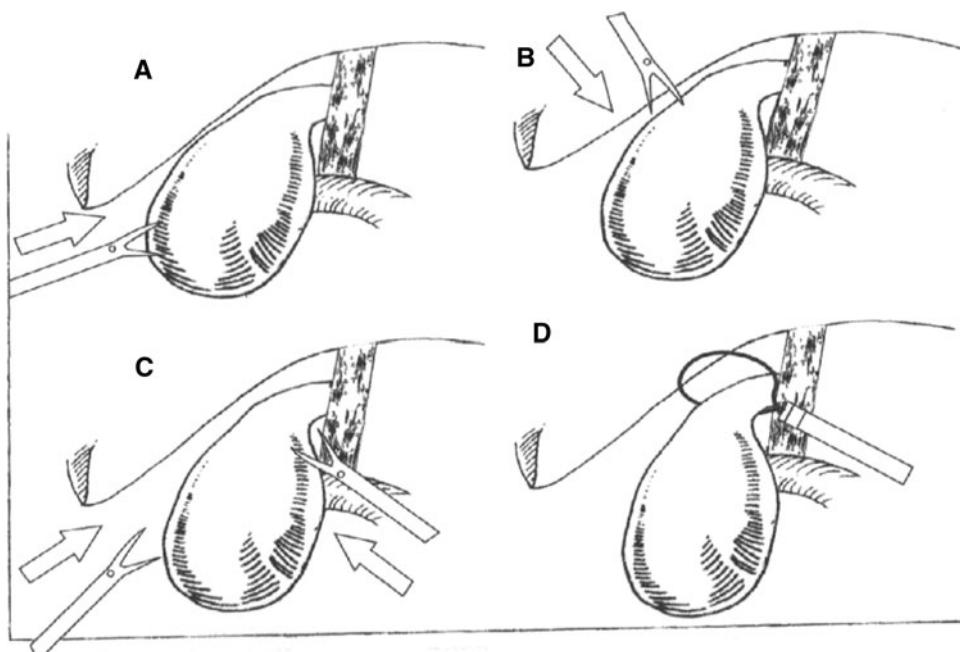
#### Results

There was no difference between the two groups in terms of age, gender, body mass index, white blood cell count, serum alanine transaminase, aspartate transaminase, alkaline phosphatase or total bilirubin levels (data not shown).

The accuracy rate of preoperative ultrasonography for contracted gallbladders in this study was 99.3% (64 + 1,460/1,534), i.e., 64 true-positive and 1,460 true-negative among 1,534 preoperative abdominal ultrasonographies.

Male preponderance in both groups of patients with contracted gallbladders was noted (male/female ratio 19/14 vs. 18/13, *P* = 1.00).

**Fig. 3** Diagrammatic illustrations of techniques of fundus-down LC for contracted gallbladders: **A** The fundus-down LC starts with dissections of the lateral attachments of the gallbladder to the liver junction. **B** The dissections of the superior border. **C** The dissections of the medial border. **D** The dissections of the triangle of Calot, i.e., the cystic artery and the cystic duct. LC, laparoscopic cholecystectomy



In gallstone patients with contracted gallbladders undergoing laparoscopic cholecystectomy ( $N = 64$ ), the operation time was longer than that in the average gallstone patients undergoing laparoscopic cholecystectomy ( $N = 1,468$ ) by an average of 54.6 min ( $150.9 \pm 40.6$  vs.  $95.9 \pm 26.7$  min;  $P < 0.0001$ ). Postoperative stay was longer by 3 days ( $6 \pm 3$  vs.  $3 \pm 3$  days;  $P < 0.0001$ ). The conversion rate was higher by 13.3 percentage points (15.6% vs. 2.3%;  $P < 0.0001$ ). The relative risk was 6.75. The complication rate was higher by 11.1 percentage points [12.5% (8/64) vs. 1.4% (21/1,468);  $P < 0.0001$ ]. The relative risk was 8.74. The bile duct injury rate was higher by 2.7 percentage points [3.1% (2/64) vs. 0.4% (6/1,468);  $P = 0.04$ ]. The relative risk was 7.65 (Table 1).

The reasons for the 34 conversion were bile duct injury (4), cystic artery bleeding (1), previous upper abdominal

surgery (8), obscure triangle of Calot anatomy (13), common bile duct clipping (1), and acute cholecystitis (7). The conversion rate was 2.3% (34/1,468).

When comparing the fundus-down group patients with the conventional group patients, the former had shorter postoperative hospital stays by an average of 2 days ( $5 \pm 3$  days vs.  $7 \pm 3$  days;  $P = 0.003$ ). The complication rate was also lower in the fundus-down group patients by 19.6 percentage points [3.0% (1/33) vs. 22.6% (7/31);  $P = 0.02$ ]. Complications included bile duct injuries (two), urinary tract infection (one), and wound infection (four) in the conventional LC group patients, and wound infection (one) in the fundus-down LC group patients. The conversion rate was markedly lower in the fundus-down group patients by 32.3 percentage points [0.0% (0/33) vs. 32.3% (10/31);  $P = 0.0009$ ]. The reasons for conversions included

**Table 1** Comparison of operation time, postoperative hospital stay, complication and conversion rates between contracted gallbladder stones patients and average gallbladder stones patients undergoing LC

Variables	Contracted gallbladder patients ( $N = 64$ )	Average gallbladder patients ( $N = 1,468$ )	P value	Relative risk (difference)	95% CI
Operation time <sup>#</sup> (min)	$150.5 \pm 40.6$	$95.9 \pm 26.7$	<0.0001**	(54.6)	47.7–61.5
Postoperative stay <sup>#</sup> (days)	$6 \pm 3$	$3 \pm 3$	<0.0001**	(3)	2.25–3.75
Complications (%)	8 (12.5)	21 (1.4)	<0.0001**	8.74	4.03–18.96
Bile duct injury (%)	2 (3.1)	6 (0.4)	0.04*	7.65	1.57–37.14
Conversions (%)	10 (15.6)	34 (2.3)	<0.0001**	6.75	3.49–13.04

LC laparoscopic cholecystectomy, CI confidence interval

\*  $P < 0.05$ , statistically significant

\*\* Extremely statistically significant

<sup>#</sup> Arithmetic mean  $\pm$  standard deviation (SD)

**Table 2** Operation time, complication rate, conversion rate, and postoperative hospital stay of fundus-down LC versus conventional LC in 64 patients with contracted GB

Variables	Fundus-down LC (N = 33)	Conventional LC (N = 31)	P value	Relative risk (difference)	95% CI
Operation time <sup>#</sup> (min.+)	146.3 ± 37.4	155.4 ± 43.4	0.37	(−9.1)	−29.1 to 11.1
Postoperative stay <sup>#</sup> (days)	5 ± 3	7 ± 3	0.003*	(−2)	−4 to −1
Complications (%)	1 (3.0)	7 (22.6)	0.02*	0.13	—
Urinary tract infections (%)	0 (0)	2 (6.5)	0.49	0	— <sup>a</sup>
Wound infection	1 (3.0)	3 (9.7)	0.11	0.31	—
Conversions (%)	0 (0)	10 (32.3)	0.0009*	0	— <sup>a</sup>
Obscured anatomy (%)	0 (0)	5 (16.1)	0.02*	0	— <sup>a</sup>
Hemorrhage (%)	0 (0)	3 (9.7)	0.11	0	— <sup>a</sup>
Bile duct injury (%)	0 (0)	2 (6.5)	0.23	0	— <sup>a</sup>

LC laparoscopic cholecystectomy, CI confidence interval, GB gallbladder, min minutes

\* P < 0.05, statistically significant

<sup>#</sup> Arithmetic mean ± standard deviation (SD)

<sup>a</sup> 95% confidence interval could not be calculated due to the denominator of the sampling variance being zero

bile duct injuries (two), intraoperative hemorrhage (three), and obscured anatomy (five) (Table 2).

When comparing bile duct injury rates between the fundus-down and conventional LC groups, the difference was not statistically significant [0% (0/33) vs. 6.5% (2/31); P = 0.23, Table 3]. However, in subgroup analysis comparing both groups separately with the average LC patients, fundus-down LC seemed to have lower bile duct injury rate [2/31 (6.5%) to 0/33 (0%) compared with 6/1,468 (0.4%); P = 0.01 between 6.5% and 0.4% vs. P = 1.00 between 0% and 0.4%].

Among the 1,468 patients with normal gallbladders by preoperative imaging, 6 had bile duct injuries and 34 required conversion to open surgery. In the first patient with bile duct injury, the triangle of Calot anatomy seemed clear. Axial traction of infundibulum put common bile duct par-

allel to the cystic duct, for which it was mistaken. Cut of the common bile duct was recognized immediately. Primary repair was performed on conversion to an open procedure. The patient presented with bile duct stricture and bilateral intrahepatic duct stones 18 months later. She underwent open choledochojejunostomy and was well during follow-up [19]. The second patient was a victim of right hepatic duct injury, and following open conversion a 12-Fr silicon T-tube was inserted. Postoperative course was uneventful. The third patient was an obese female. Her posterior branch cystic artery was accidentally injured during laparoscopic cholecystectomy, causing brisk bleeding. An endoclip was applied to successfully control the bleeder. Jaundice gradually appeared after the procedure, and endoscopic retrograde cholangiopancreatography revealed obstructed common bile duct. Exploratory laparotomy on the fifth postoperative day revealed an endoclip in the vicinity of the common bile duct causing severe adhesions and acute inflammation. The proximal duct was distended with thinning wall burst rupture with gentle dissection. Choledochojejunostomy was performed. Wound infection developed and she was hospitalized for 1 month. The other three patients suffered from delayed bile leakage due to electrocautery injury of the common bile duct near cystic-common duct junction. They underwent open conversion and T-tube placement without further sequelae [19].

Two patients from the conventional group sustained bile duct injuries of minor severity. No patients from the fundus-down group sustained any bile duct injury. In one patient, severe fibrosis in the triangle of Calot distorted the biliary anatomy with elevation of the common bile duct toward the cystic duct area. An accidental small cut on the common duct was inflicted and found immediately

**Table 3** Comparison of number of bile duct injuries between different groups

Groups	Contracted GB		Non-contracted GB <sup>c</sup>	P value <sup>#</sup>
	Fundus-down LC <sup>a</sup>	Conventional LC <sup>b</sup>		
Bile duct injury				
Yes	0	2	6	0.23*
No	33	29	1,462	0.01**
Total	33	31	1,468	1.00***

GB gallbladder, LC laparoscopic cholecystectomy

<sup>#</sup> Fisher's exact test

<sup>\*</sup> P value of a vs. b

<sup>\*\*</sup> P value of b vs. c

<sup>\*\*\*</sup> P value of a vs. c

intraoperatively. The operation was converted to open surgery with a T-tube inserted into the common bile duct. Postoperative course was uneventful. In the second patient, the biliary anatomy in the triangle of Calot was also distorted. Intraoperative cholangiography was performed only to find that the cholangiography catheter was inserted via a choledochotomy instead of via the cystic duct. The operation was converted to open surgery, and a T-tube was inserted in the common bile duct. Postoperative course was also uneventful.

The operation time was similar in the fundus-down and conventional LC groups ( $146.3 \pm 37.4$  vs.  $155.4 \pm 43.4$  min;  $P = 0.37$ , Table 2).

There was no mortality in patients of the fundus-down or the conventional LC groups.

## Discussion

The results of this study show that fundus-down laparoscopic cholecystectomy is feasible in gallstone patients with contracted gallbladders. We find that fundus-down laparoscopic cholecystectomy had no conversion, no bile duct injury, less complications (3%), and shorter hospital stay, whereas conventional laparoscopic cholecystectomy had a 32.3% conversion rate, a 6.5% bile duct injury rate, a 22.6% complication rate, and longer hospital stay.

In contracted gallbladders, rigid fibrosis of areolar tissue makes cystic duct and cystic artery structures relatively more fragile and vulnerable to injury during triangle of Calot dissections. It might be the fibrotic rigidity nature of pericholecystic areolar tissue in patients with contracted gallbladders that contributes to the high incidence of obscure anatomy in triangle of Calot (16.1%, 5/31), intraoperative hemorrhage (9.5%, 3/31), and bile duct injury (6.5%, 2/31) encountered during conventional LC.

Among the 1,468 patients with normal gallbladders, 10 laparoscopic cholecystectomies were performed with fundus-down approach, whereas the other 1,458 laparoscopic cholecystectomies were performed in the traditional manner. The 10 patients undergoing the fundus-down technique demonstrated high efficacy and safety before application to patients with contracted gallbladders.

Common bile duct injury rate for open cholecystectomy remains at 0.1–0.4% [20], whereas the rate in laparoscopic cholecystectomy ranges from 0.5% to 0.9% [21–25], twice as high. Causes of injury to common bile duct include anatomic variation, technical difficulty in identifying/exposing the structures, and thermal injury [26]. The overall bile duct injury rate in our series was 0.52% (8/1,532). The bile duct injury rate in contracted gallbladder undergoing laparoscopic cholecystectomy was 3.1% (2/64), much higher than that of noncontracted gallbladders

undergoing laparoscopic cholecystectomy [0.4% (6/1,468);  $P = 0.04$ ].

Raj et al. [15] and Ichihara et al. [16] adopted fundus-down laparoscopic cholecystectomy to treat patients of gallstone disease with noncontracted gallbladders. They assumed that fundus-down laparoscopic cholecystectomy could decrease incidence of bile duct injury. However, in their case series reports, they applied the fundus-down laparoscopic cholecystectomy technique in gallstone patients with normal or chronic cholecytic (noncontracted) gallbladders. Furthermore, there were no control groups to compare with. It was not known whether the fundus-down technique was applicable in patients with contracted gallbladders. Besides, most laparoscopic surgeons are more comfortable with the conventional approach and less familiar with the fundus-down approach.

Theoretically, the fundus-down technique mandates performing the dissection of the gallbladder–liver junction first without prior ligation of the cystic artery, which could cause increased bleeding. However, this did not happen in clinical practice. The reasons may be twofold. First, the authors found that the cystic artery in patients with contracted gallbladders was almost always partially obliterated by perivascular scar contracture, causing decreased blood flow. Second, the gallbladder–liver junction in patients with contracted gallbladders comprises a hard, fibrosed gallbladder on the one side and soft liver parenchyma on the other. Therefore, it was relatively easy to dissect out the plane without much bleeding. Instead, the most frequent bleeding problem encountered came from oozing when dissecting the omentum covering the contracted gallbladders. However, the amount of blood loss was small.

In this prospective randomized controlled trial, we found that fundus-down laparoscopic cholecystectomy technique was feasible in patients with contracted gallbladders, being associated with lower conversion rate, lower complication rate, and shorter postoperative hospital stay than conventional laparoscopic cholecystectomy.

Cholecystoduodenal fistulas occur in 3–5% of patients with cholelithiasis, as reported in the literature [27]. We encountered one patient with cholecystoduodenal fistula in our series (0.07%, 1/1,532). No patients with contracted gallbladders and gallstone disease developed cholecystoduodenal fistula in this series. Mirizzi's syndrome accounts for less than 1% of patients with cholelithiasis, as reported in the literature [28]. No patients with Mirizzi's syndrome were encountered in our series of gallstone disease.

Male preponderance in male/female ratio may be due to the predominantly male veterans patient populations at Veterans General Hospital, Taipei.

The average postoperative hospital stay of our patients undergoing LC was  $3 \pm 3$  days, apparently longer than

that reported in most series. The reasons for the apparent prolongation may be twofold. First, in the early days, our countrymen mostly lived in a developing society and harbored the notion that “patients should stay in hospital when going through major surgery until they get well.” So they habitually asked the attending surgeon to postpone their discharge for a day or two. Second, the average postoperative hospital stay was further elevated by those patients with complications. Nowadays, the average postoperative hospital stay of our patients undergoing an LC is around 1–2 days. Some patients are even discharged on the day of the operation.

Compared with patients with gallstones and normal gallbladder, patients with gallstones and contracted gallbladders were associated with apparently longer postoperative stay, i.e., 5–7 days. The reasons may be twofold. First, most of the contracted gallbladders were covered with omentum, and severe adhesions were present. Dissections in these patients leave large area of rough surfaces and oozing. Therefore, Jackson–Pratt vacuum drains were left in a considerable portion of these patients to evacuate postoperative fluid or blood adequately. This resulted in longer average postoperative stay (i.e., 5 days). Second, the average postoperative hospital stay was further elevated by complications, especially in those patients undergoing conventional LC (i.e., 7 days).

There are limitations to this study. The number of available contracted gallbladder patients is small. The sample size is too small to demonstrate statistically significant difference of bile duct injury rate by fundus-down laparoscopic cholecystectomy in treating this subgroup of complicated gallstone patients (Table 3). However, with subgroup analysis, we were able to demonstrate the capability of the fundus-down laparoscopic techniques to bring the bile duct injury rate of the conventional laparoscopic techniques down to the level of that for average gallstone patients.

Gallstone patients with contracted gallbladders have not received as much attention in the literature as they deserve, just because they have difficult, complicated gallbladders and are in a minority subgroup. However, from our limited data, the fundus-down techniques appear to be a promising alternative approach to this difficult gallbladder problem. Future studies with larger sample sizes are warranted to find a better treatment strategy for this subgroup of patients so that they might benefit from minimally invasive surgery.

After reviewing our limited data, however, the authors would like to recommend the following algorithm regarding laparoscopic management of gallstone patients with contracted gallbladders. Firstly, the laparoscopic surgeon should try conventional LC, as the techniques are most familiar and comfortable to most surgeons. Secondly, if during the procedure, obscure anatomy should occur

without proceeding to irreparable hemorrhage or bile duct injury, the laparoscopic surgeon should resort to fundus-down approach on site. Usually, this will solve the problem. Thirdly, if hemorrhage or bile duct injury do occur, conversion to open surgery is always a viable choice and should not be deemed a failure.

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**Author contributions** Study concept and design: Huang SM, Wu CW, Lui WY, Pan H, and Yao CC. Acquisition of data: Huang SM, Yao CC, Wu CW, and Lui WY. Analysis and interpretation of data: Huang SM, Wu CW, Hsiao KM, and Pan HC. Drafting of the manuscript: Huang SM, Yao CC, Wu CW, Chen LY, Hsiao KM, Pan HC, and Lui WY. Critical revision of the manuscript for important intellectual content: Huang SM, Wu CW, Pan H, and Hsiao KM. Statistical analysis: Huang SM, Wu CW, Hsiao KM, and Pan HC. Obtaining funding: Huang SM, Chen LY and Hsiao KM. Administrative, technical, and material support: Huang SM, Chen LY, Hsiao KM, Wu CW, Yao CC, Lai TJ, and Lui WY. Study supervision: Lai TJ and Lui WY.

**Disclosures** Authors Shing-Moo Huang, Chung-Chin Yao, Te-Jen Lai, Ling-Yun Chen, Huichin Pan, Kuang-Ming Hsiao, Chew-Wun Wu, and Wing-Yiu Lui have no conflicts of interest or financial ties to disclose.

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