Critical Appraisal of the Impact of the Systematic Adoption of Advanced Minimally Invasive Hepatobiliary and Pancreatic Surgery on the Surgical Management of Mirizzi Syndrome

Ye-Xin Koh[1] · Pallavi Basu[1] · Yi-Xin Liew[2] · Jin-Yao Teo[1] · Juinn-Huar Kam[1] ·
Ser-Yee Lee[1,3] · Peng-Chung Cheow[1,3] · Premaraj Jeyaraj[1,3] · Pierce K. H. Chow[1,3] ·
Alexander Y. F. Chung[1,3] · London L. P. J. Ooi[1,3] · Chung-Yip Chan[1,3] ·
Brian K. P. Goh[1,3]

Abstract

Background Minimally invasive surgery (MIS) for Mirizzi syndrome (MS) remains a technically challenging procedure with a high open conversion rate. We critically evaluated the impact of the systematic adoption of MI-HBP surgery on the surgical outcomes of MS.

Methods Ninety-five patients who underwent surgery for MS were retrospectively reviewed. Systematic adoption of advanced MI-HBP surgery started in 2012. The cohort was classified into a preadoption (2002–2012) (Era 1, $n = 58$) and post-adoption (2013–2017) (Era 2, $n = 37$). Furthermore, Era 2 was divided into a cohort operated by advanced minimally invasive surgeons (AMIS) (Era 2 AMIS, $n = 19$) and those by other surgeons (Era 2 others, $n = 19$).

Results Comparison between Era 2 and Era 1 demonstrated a significant increase in the frequency of MIS attempted (89% vs 33%, $p < 0.01$), increase in the use of choledochoplasty (24% vs 2%, $p < 0.01$), increase operation time (180 min vs 150 min, $p = 0.03$) and significantly lower open conversion rate (24% vs 58%, $p < 0.01$). Comparison between Era 2 AMIS and Era 2 others demonstrated a significantly greater adoption of MIS (100% vs 78%, $p = 0.046$) with lower open conversion rate (5% vs 50%, $p = 0.005$). Comparison between all attempted MIS cases with open procedures demonstrated a significantly higher proportion of subtotal cholecystectomies performed (40% vs 23%, $p = 0.04$), choledochoplasty (17% vs 2%, $p = 0.04$) and shorter hospital stay (4 days vs 9 days, $p < 0.01$).

Conclusions Systematic adoption of advanced MI-HBP surgery allowed surgeons to perform MIS for MS more frequently and with a significantly lower open conversion rate. Patients who underwent successful MIS had the shortest hospital stay compared to patients who underwent open surgery or required open conversion.

Introduction

Mirizzi syndrome (MS) is a relatively rare condition, and its surgical management remains challenging today [1, 2]. Ever since the introduction of laparoscopic cholecystectomy in the 1980s, laparoscopic cholecystectomy has become the approach of choice for the treatment of gallstones [3]. Over the past 2 decades, with the technological advancements in laparoscopic equipment such as high definition imaging systems and improvements in surgical techniques, this has allowed the progressive adoption of minimally invasive surgery (MIS) for straightforward conditions like biliary colic to more challenging conditions

✉ Brian K. P. Goh
bsgkp@hotmail.com

[1] Department of Hepatopancreatobiliary and Transplantation Surgery, Singapore General Hospital, 20 College Road, Academia, Singapore 169856, Singapore

[2] Department of Pharmacy, Singapore General Hospital, Singapore 169856, Singapore

[3] Duke-National University of Singapore (NUS) Medical School, Singapore 169856, Singapore

like acute cholecystitis, empyema and common bile duct stones [4–6].

However, despite the widespread adoption of MIS today, the application of MIS for MS remains a highly technically challenging procedure [7, 8]. Historically, open conversion and morbidity rates of MIS for MS have been reported to be over 40% and 20%, respectively [8]. Hence, when compared to laparoscopic cholecystectomies for conditions such as symptomatic cholelithiasis and acute cholecystitis, these conversion rates and complication rates were prohibitively high [1, 2, 8].

The initial adoption of MIS in the field of hepatobiliary and pancreatic (HBP) surgery has been relatively slow compared to other abdominal surgeries. However, over the past decade, there has been a rapid exponential adoption of laparoscopic surgery for complex liver and pancreatic resections worldwide [9–14]. Similarly at our institution, with the improved perioperative outcomes observed with MIS over its open counterpart, we have increasingly adopted laparoscopic liver and pancreatic resections over the past decade [9–12, 15, 16].

In this study, we critically reviewed our institutional experience with the surgical management of MS with the primary objective of evaluating the impact of the adoption of advanced minimally invasive (MI) HBP surgery on the surgical outcomes of MS.

Methods

From 2002 to 2017, 95 consecutive patients who underwent surgery for MS at the Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, were retrospectively reviewed. The study was granted approval by the Singhealth Institutional Review Board. During the same period, 13,882 cholecystectomies were performed at our institution. At our department, although laparoscopic liver and pancreatic resections were performed since 2006 [10–12, 15–20], it was not until 2012 whereby two surgeons (Chan and Goh) at our department decided to systematically embark on advanced minimally invasive HBP (MI-HBP) surgery such as complex hepatectomies and pancreatectomies resulting in an exponential increase in the number of MI hepatectomies and pancreatectomies performed at our institution [10–12, 15–20]. In the process, these two surgeons had acquired extensive experience in advanced MI-HBP techniques and skills such as hilar dissection and suturing. These two surgeons collectively performed 336 MI hepatectomies and pancreatectomies during the study period (2011–2017).

Hence, to determine the impact of the adoption of advanced MI-HBP surgery on the surgical outcomes of MS, we divided our patient cohort into 2 time periods, i.e.,

the Era 1 (before adoption) (2002–2012) and Era 2 (post-adoption) (2013–2017). Furthermore, we identified the cases in Era 2 performed by advanced minimally invasive surgeons (AMIS) (Era 2 AMIS) and those by other surgeons (Era 2 others). In this study, MIS included both conventional laparoscopic and robotic-assisted laparoscopic procedures. No cases of hand-assisted laparoscopic surgery were attempted at our institution. The decision to perform MIS or open surgery was based primarily on individual surgeon preference.

The electronic medical records for all patients diagnosed post-operatively with MS were retrospectively reviewed. The patient demographics, clinical presentation, diagnostic method, treatment procedure, complications and follow-up were recorded.

The patient characteristics were analyzed with regards to age, gender, comorbidities, American Society of Anesthesiologists (ASA) status, presenting symptoms, liver enzyme blood levels [total bilirubin, alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT) and gamma glutamyl transferase (GGT)] and total white (TW) cell count.

Ultrasound (US) or computed tomography (CT) was performed as the initial investigation in all patients. Magnetic resonance cholangiopancreatography (MRCP) was performed where additional information is required for delineation of the biliary tracts. Pre-operative biliary stenting and cholangiogram findings via endoscopic retrograde cholangiopancreatography (ERCP) were recorded. Pre-operative diagnosis of MS and identification of cholecysto-biliary or cholecysto-enteric fistula formation by imaging investigations (US, CT, MRCP) and ERCP were recorded.

Operative details regarding operative approach, intraoperative findings and complications and final pathology were extracted from operative and pathology reports. Postoperative classification of MS was based on Beltran's classification [21]. All postoperative complications were recorded up to 30 days or within the same hospital stay. Postoperative complications were graded according to the Clavien–Dindo classification [22]. Additionally, intraoperative/early ($\leq$ 30 days) and late ($>$ 30 days) surgical complications were recorded.

Data were expressed as whole numbers (%) or median values (interquartile range), p value for Fisher's exact test for categorical and for Mann–Whitney U for continuous data. A p value < 0.05 was considered statistically significant. When appropriate, a value of $p < 0.025$ was considered to be statistically significant after adjusting for multiple testing using Bonferroni correction. The database was processed with the statistical software SPSS 21 (IBM, Armonk, NY, USA).

Results

A total of 95 consecutive patients underwent surgery for MS during the study period. Fifty-eight patients underwent surgery during Era 1 and 37 during Era 2, of which 19 cases were performed by the Era 2 AMIS group and 18 were performed by the Era 2 Others group. Three MIS cases were performed with robotic assistance. The incidence of MS during the study period was 0.56%. Abdominal pain was the most common symptom, followed by obstructive jaundice and fever. All our patients had high total bilirubin and deranged liver enzymes (ALP, GGT, ALT, AST). The median follow-up period was 9 months (range 6–32 months).

Comparison of all surgeries done for MS according to Era 1 and 2 (Table 1)

Comparison between the baseline characteristics and surgical outcomes of patients between Era 1 and Era 2 is summarized in Table 1.

Comparison between Era 2 and Era 1 demonstrated a significant increase in the frequency of the laparoscopic approach attempted (89% vs 33%, $p < 0.01$), increase in the use of choledochoplasty (24% vs 2%, $p < 0.01$), decrease in the use of intraoperative cholangiogram (35% vs 59%, $p = 0.035$), decrease in the use of T-tube (22% vs 62% $p < 0.01$), increase in operation time (180 min vs 150 min $p = 0.03$), and more patients with planned postoperative stent removal (41% vs 17% $p = 0.008$). The open conversion rate was significantly lower in Era 2 vs Era 1 (24% vs 58%, $p < 0.01$).

Comparison of all surgeries done for MS according to Era 2 AMIS and Era 2 others (Table 2)

Comparison between Era 2 AMIS and Era 2 others demonstrated a significantly greater proportion of the adoption of the MIS approach (100% vs 78%, $p = 0.046$). Furthermore, the open conversion rate was significantly lower (5% vs 50%, $p = 0.005$). There were no significant differences in early or late complications nor the Clavien–Dindo severity of the complications.

Comparison of patients undergoing MIS for MS in Era 1 and 2 (Table 3)

A total of 52 patients underwent attempted MIS for MS in the entire cohort. Nineteen cases were performed in Era 1 and 33 were performed in Era 2 whereby Era 2 AMIS surgeons performed 19 cases and Era 2 Others surgeons performed 14 cases.

Comparison between MIS Era 2 ALL and MIS Era 1 ALL demonstrated a significantly lower open conversion rate (24% vs 58%, $p < 0.01$) at the expense of a significantly longer operation time (165 min vs 135 min $p = 0.013$). Comparison between Era 2 AMIS with Era 2 Others demonstrated a significantly lower open conversion rate (5% vs 50%, $p = 0.005$) when performed by the advanced MIS surgeons. Not surprisingly, Era 2 AMIS also had a significantly lower open conversion rate when compared to Era 1 ALL. (5% vs 58%, $p < 0.01$).

Comparison between Era 2 others and Era 1 ALL demonstrated no difference in all the postoperative outcomes including open conversion rate.

Comparison between all MIS and all open procedures (Table 4)

Table 3 summarizes comparisons between MIS attempted, MIS completed, MIS converted and open procedures.

Comparison between all attempted MIS cases with open procedures demonstrated a significantly higher proportion of subtotal cholecystectomies performed (40% vs 23%, $p = 0.04$), choledochoplasty (17% vs 2%, $p = 0.04$) and shorter hospital stay (4 days vs 9 days, $p < 0.01$).

Comparison between completed MIS cases and MIS cases which were converted to open demonstrated a significantly longer hospital stay associated with converted cases (6 days vs 2 days, $p < 0.01$).

Discussion

Over the past decade, with the rapid advancement of laparoscopic imaging systems, instrumentation and surgical technique, improvement has been seen in almost every field of laparoscopic surgery, including colorectal, upper gastrointestinal and HBP [23–25]. In the field of HBP surgery, the success of advanced laparoscopic procedures has made the relatively poor adoption of laparoscopic approach for Mirizzi syndrome (MS) even more conspicuous [13, 14, 26]. A systematic review published in 2010 on laparoscopic surgery for MS revealed a relatively high conversion rate of over 40% and concluded that laparoscopic surgery cannot be routinely recommended for MS [8]. The findings in this study were consistent with this systematic review [8], whereby our early laparoscopic experience in Era 1 was associated with a high open conversion rate of 58% [1].

Laparoscopic surgery for MS is well recognized to be a technically challenging procedure. This is due to the presence of an intense fibrotic process which is frequently associated with fistulation of the gallbladder into the common bile duct resulting in alteration to the normal

Table 1 Comparison of all surgeries (open and MIS) done for MS according to Era 1 and Era 2

	Total N = 95	Era 1 n = 58 (%)	Era 2 ALL n = 37 (%)	Era 2 AMIS n = 19 (%)	Era 2 others n = 18 (%)	P value1	P value2
Age in years (range)	60 (25)	55 (69)	62(55)	60 (12)	55 (24)	0.67	0.025
Male gender, n (%)	49 (48)	27 (47)	22 (60)	10 (53)	12 (67)	0.293	0.385
Comorbidities							
Diabetes mellitus, n (%)	26 (27)	16 (28)	10 (27)	6 (32)	4 (22)	1.00	0.522
Hyperlipidemia	18 (19)	8 (14)	10 (27)	6 (32)	4 (22)	0.11	0.522
Ischemic heart disease	12 (13)	8 (14)	4 (11)	3 (16)	1 (6)	0.760	0.316
Cerebrovascular disease	7 (7)	3 (5)	4 (11)	2 (11)	2 (11)	0.426	0.954
Malignancy	3 (3)	2 (3)	1 (3)	1 (5)	0 (0)	1.00	0.324
Hematological disorders/anticoagulation use	7 (7)	3 (5)	4 (11)	4 (21)	0 (0)	0.426	0.105
ASA score							
1	39 (41)	28 (48)	11(30)	6 (32)	5 (28)	0.089	1.00
2	45 (47)	23 (40)	22 (60)	11(58)	11 (61)	0.091	1.00
3	11 (12)	7 (12)	4 (11)	1 (5)	3 (17)	1.00	0.340
Symptoms							
Abdominal pain	64 (67)	37 (64)	27 (73)	17 (89)	10 (56)	0.379	0.02
Obstructive jaundice	51 (54)	32 (55)	19 (51)	10 (57)	9 (50)	0.833	0.873
Fever	24 (25)	17 (29)	7 (19)	4 (21)	3 (17)	0.335	0.734
Total bilirubin (mg/dL)	86 (102)	85 (102)	104 (120)	104 (110)	104 (92)	0.58	0.082
ALP (U/L)	238 (180)	235 (177)	283 (307)	329 (196)	282 (101)	0.44	0.301
GGT (U/L)	276 (265)	284 (263)	269 (418)	276 (678)	350 (259)	0.78	0.761
ALT (U/L)	175 (278)	161 (297)	233 (266)	242 (278)	299 (705)	0.92	1.000
AST (U/L)	134 (183)	134 (259)	141 (190)	146 (213)	118 (353)	0.53	0.519
TW (10^9/L)	10 (7)	10 (6)	10 (7)	10 (8)	8 (4)	0.53	0.832
Pre-op biliary stenting via ERCP	57 (58)	32 (57)	25 (65)	15 (79)	10 (56)	0.03	0.149
Pre-op diagnosis of MS	78 (82)	49 (85)	29 (78)	15 (79)	14 (78)	0.584	1.00
Pre-op diagnosis of cholecysto-biliary or cholecysto-enteric fistula	6 (6)	3 (5)	3 (8)	2 (11)	1 (6)	0.675	0.298
Postoperative Beltran classification							
I	61 (64)	40 (69)	21 (57)	10 (53)	11 (61)	0.275	0.743
II	29 (31)	15 (26)	14 (38)	7 (37)	7 (39)	0.257	1.00
III	5 (5)	3 (5)	2 (5)	2 (11)	0 (0)	1.00	0.487
Surgical approach						**<0.01**	**0.046**
Laparoscopic, n (%)	52 (55)	19 (33)	33 (89)	19 (100)	14 (78)		
Open	43 (45)	39 (64)	4 (11)	0	4 (22)		
Surgical procedure							
Total cholecystectomy	64 (67)	43 (74)	21 (57)	7 (37)	14 (77)	0.116	0.012
Subtotal cholecystectomy	31 (33)	15 (26)	16 (43)	12 (63)	4 (22)	0.116	0.012
Primary repair of enteric fistula	3 (3)	1 (2)	2 (5)	2 (11)	0 (0)	0.558	0.157
Primary repair of CBD	16 (17)	12 (21)	4 (11)	1 (5)	3 (17)	0.268	0.340
Choledochoplasty	10 (11)	1 (2)	9 (24)	7 (37)	2 (11)	**< 0.01**	**< 0.01**
Hepaticojejunostomy	8 (8)	6 (10)	2 (5)	0 (0)	2 (11)	0.447	0.207
Intraoperative cholangiogram	47 (50)	34 (59)	13 (35)	9 (47)	4 (22)	**0.035**	0.607
T tube insertion	44 (46)	36 (62)	8 (22)	7 (37)	1 (6)	**<0.01**	**0.021**
Open conversion, n (%)	19./52 (36.5)	11/19 (58)	8/33 (24)	1/19 (5)	7/14 (50)	**<0.01**	**0.005**
Operating time (minutes)	185 (90)	150 (92)	180 (70)	173 (73)	175 (95)	**0.03**	0.099
Postoperative hospital stay (days)	7 (7)	7 (6)	4 (7)	3.00 (4)	9 (26)	**0.07**	0.121

Table 1 continued

	Total N = 95	Era 1 n = 58 (%)	Era 2 ALL n = 37 (%)	Era 2 AMIS n = 19 (%)	Era 2 others n = 18 (%)	P value1	P value2
Postoperative ERCP							
Planned stent removal	25 (26)	10 (17)	15 (41)	11 (58)	7 (39)	**0.008**	0.172
Planned stone removal	3 (4)	0 (0)	3 (8)	3 (16)	0 (0)	0.2393	0.23
Postoperative morbidity, n (%)	17 (18)	11 (19)	6 (16)	1 (5)	5 (28)	0.791	0.090
Clavien–Dindo classification							
I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
II	10 (11)	6 (10)	4 (11)	1 (5)	3 (17)	1.00	0.340
III	5 (5)	3 (5)	2 (5)	0 (0)	2 (11)	1.00	0.230
IV	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
V	2 (2)	2 (3)	0 (0)	0 (0)	0 (0)	0.519	1.00
Early/intraoperative surgical complications	21 (22)	14 (38)	7 (19)	6 (32)	1 (6)	0.62	0.09
Common bile duct (CBD) injury, n (%)	1 (1)	1 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
Retained stones, n (%)	6 (6)	4 (7)	2 (5)	2 (19)	0 (0)	1.00	1.00
Bile leak	3 (3)	2 (3)	1(3)	0 (0)	1 (6)	1.00	0.298
Biliary stricture	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
Bowel injury	3 (3)	3 (5)	0 (0)	0 (0)	0 (0)	0.279	1.00
Liver or intra-abdominal abscess	6 (6)	4	2 (5)	2 (11)	0 (0)	1.00	0.157
Cholangitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
Perioperative bleeding	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
Recurrent CBD stones	2 (2)	0 (0)	2 (5)	2 (11)	0 (0)	0.296	0.580
Late surgical complications	15 (16)	10 (17)	4 (11)	2 (11)	2 (11)	0.55	1.00
Cholangitis	9 (9)	6 (10)	3 (8)	1 (5)	2 (11)	1.00	0.515
Recurrent stones	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
CBD stricture	3 (3)	2 (3)	0 (0)	0 (0)	0 (0)	1.00	1.00
Liver or intra-abdominal abscess	2 (2)	1 (2)	1 (3)	1 (5)	0 (0)	1.00	0.298
Ventral hernia	1 (1)	1 (2)	0 (0)	0 (0)	0 (0)	0.422	1.00

Data expressed as whole number (%) or median (interquartile range), *p* value for Fisher's exact test for categorical and for Mann–Whitney *U* for continuous data

P value[1]—Era 1 ALL vs Era 2 ALL

P value[2]—Era 2 AMIS vs Era 2 Others

anatomy of Calot's triangle which is crucial for the performance of a safe cholecystectomy [2, 7]. The commonest reason for open conversion reported in most studies was the dense adhesions preventing proper identification of Calot's triangle and the resultant abnormal anatomy of the extrahepatic biliary system [7, 8]. Hence, in order to successfully complete laparoscopic surgery for MS, the surgeon should be adept with navigating the altered anatomy in this context and also possess advanced laparoscopic skills to handle complex HBP anatomy such as dissection and suturing. Furthermore, the rarity of MS makes it extremely difficult for the individual surgeon to attain adequate experience, making the laparoscopic learning curve even more difficult to overcome [2].

Since 2012, our department had systematically adopted advanced MI-HBP procedures such as major liver and pancreatic resections which was mainly driven by two surgeons classified as AMIS in this study [9, 10, 15, 19]. In our post-adoption Era 2, there was both a significant increase in the proportion of patients with MS managed via MIS and a significantly lower rate of open conversion. This was even more evident among the procedures in the Era 2 AMIS group compared to the Era 2 Others group suggesting that these outcomes were mainly driven by the two surgeons who systematically embarked on advanced MI-HBP surgery (Tables 1, 2). Furthermore, there was also no significant difference in the outcomes of MIS including open conversion rates between Era 1 and Era 2 others suggesting that changes in perioperative management and outcomes over time did not have a major impact in the difference in outcomes observed. These results suggest that the experienced and skills gained from performing

Table 2 Comparison of all surgeries (open and MIS) done for MS according to Era 2 AMIS and Era 2 others

	Era 2 AMIS n = 19 (%)	Era 2 others n = 18 (%)	P value
Age in years (range)	60 (12)	55 (24)	0.025
Male gender, n (%)	10 (53)	12 (67)	0.385
Comorbidities			
Diabetes mellitus, n (%)	6 (32)	4 (22)	0.522
Hyperlipidemia	6 (32)	4 (22)	0.522
Ischemic heart disease	3 (16)	1 (6)	0.316
Cerebrovascular disease	2 (11)	2 (11)	0.954
Malignancy	1 (5)	0 (0)	0.324
Hematological disorders/anticoagulation use	4 (21)	0 (0)	0.105
ASA score			
1	6 (32)	5 (28)	1.00
2	11(58)	11 (61)	1.00
3	1 (5)	3 (17)	0.340
Symptoms			
Abdominal pain	17 (89)	10 (56)	0.02
Obstructive jaundice	10 (57)	9 (50)	0.873
Fever	4 (21)	3 (17)	0.734
Total bilirubin (mg/dL)	104 (110)	104 (92)	0.082
ALP (U/L)	329 (196)	282 (101)	0.301
GGT (U/L)	276 (678)	350 (259)	0.761
ALT (U/L)	242 (278)	299 (705)	1.000
AST (U/L)	146 (213)	118 (353)	0.519
TW (10^9/L)	10 (8)	8 (4)	0.832
Pre-op biliary stenting via ERCP	15 (79)	10 (56)	0.149
Pre-op diagnosis of MS	15 (79)	14 (78)	1.00
Pre-op diagnosis of cholecysto-biliary or cholecysto-enteric fistula	2 (11)	1 (6)	0.298
Postoperative Beltran classification			
I	10 (53)	11 (61)	0.743
II	7 (37)	7 (39)	1.00
III	2 (11)	0 (0)	0.487
Surgical approach			**0.046**
Laparoscopic, n (%)	19 (100)	14 (78)	
Open	0	4 (22)	
Surgical procedure			
Total cholecystectomy	7 (37)	14 (77)	0.012
Subtotal cholecystectomy	12 (63)	4 (22)	0.012
Primary repair of enteric fistula	2 (11)	0 (0)	0.157
Primary repair of CBD	1 (5)	3 (17)	0.340
Choledochoplasty	7 (37)	2 (11)	**< 0.01**
Hepaticojejunostomy	0 (0)	2 (11)	0.207
Intraoperative cholangiogram	9 (47)	4 (22)	0.607
T tube insertion	7 (37)	1 (6)	**0.021**
Open conversion, n (%)	1/19 (5)	7/14 (50)	**0.005**
Operating time (minutes)	173 (73)	175 (95)	0.099
Postoperative hospital stay (days)	3.00 (4)	9 (26)	0.121
Postoperative ERCP			
Planned stent removal	11 (58)	7 (39)	0.172

Table 2 continued

	Era 2 AMIS $n = 19$ (%)	Era 2 others $n = 18$ (%)	*P* value
Planned stone removal	3 (16)	0 (0)	0.23
Postoperative morbidity, n (%)	**1 (5)**	**5 (28)**	0.090
Clavien–Dindo Classification			
I	0 (0)	0 (0)	1.00
II	1 (5)	3 (17)	0.340
III	0 (0)	2 (11)	0.230
IV	0 (0)	0 (0)	1.00
Early/intraoperative surgical complications	6 (32)	1 (6)	0.09
Common bile duct (CBD) injury, *n* (%)	0 (0)	0 (0)	1.00
Retained stones, *n* (%)	2 (19)	0 (0)	1.00
Bile leak	0 (0)	1 (6)	0.298
Biliary stricture	0 (0)	0 (0)	1.00
Bowel injury	0 (0)	0 (0)	1.00
Liver or intra-abdominal abscess	2 (11)	0 (0)	0.157
Cholangitis	0 (0)	0 (0)	1.00
Perioperative bleeding	0 (0)	0 (0)	1.00
Recurrent CBD stones	2 (11)	0 (0)	0.580
Late surgical complications	2 (11)	2 (11)	1.00
Cholangitis	1 (5)	2 (11)	0.515
Recurrent stones	0 (0)	0 (0)	1.00
CBD stricture	0 (0)	0 (0)	1.00
Liver or intra-abdominal abscess	1 (5)	0 (0)	0.298
Ventral hernia	0 (0)	0 (0)	1.00

advanced MI-HBP procedures such as hepatectomies and pancreatectomies was the major reason allowing these two surgeons (Era 2 AMIS) to attempt MIS more frequently and to complete MIS for MS with a higher success rate.

In prior studies on advanced laparoscopic HBP procedures, an average of 50–60 cases were typically cited as the requisite to overcome the learning curve [27–29]. Even for minor laparoscopic liver resections, more recent studies have stated that a minimum of 20 cases was needed to achieve competency [30]. These findings are especially important with regards to MS due to its rarity, whereby it is especially difficult for an individual surgeon to accumulate sufficient case-specific experience to achieve competency [1, 2]. The results of the present study are important as it demonstrates the transferability of advanced laparoscopic skills acquired from other advanced HBP surgeries such as hepatectomies and pancreatectomies in achieving proficiency for a rare but challenging biliary condition.

Over the years, our experience with MS with severely contracted gallbladders or dense fibrotic Calot's triangle has led us to employ a endovesicular approach in situations where the Calot's cannot be safely navigated from the traditional "critical view of safety." This approach

likewise has been described by other institutions but not exclusively for MS [31]. In our context, this approach has been pivotal for success in laparoscopy for MS. As was shown in our study, it is necessary to complement this approach with adept laparoscopic suturing in situations requiring a choledochoplasty with a gallbladder flap, closure of a wide Hartmann's pouch for a subtotal cholecystectomy, or placement of a T tube and closure of the choledochotomy. There was a significantly higher proportion of patients who underwent subtotal cholecystectomy, cholecystoplasty and T tube insertion in the Era 2 AMIS group compared to Era 1 or Era 2 others.

Some authors have suggested a combined intraoperative ERCP and MIS approach for MS [32]. However, due to logistical considerations and operating theater usage constraints at our institution, our preferred approach was to employ a strategy of pre-operative ERCP and stenting. The ERCP-placed stent was commonly left in place after surgery and only removed 4 to 6 weeks after surgery. In the post-adoption era 2, there were more patients with planned postoperative ERCP stent removal and stone removal. Although some authors have suggested that pre-operative ERCP might worsen the inflammation of the Calot's

Table 3 Comparison of patients undergoing MIS for MS in Era 1 and Era 2

	Total n = 52(%)	Era 1 ALL n = 19(%)	Era 2 ALL n = 33(%)	Era 2 AMIS n = 19(%)	Era 2 others n = 14(%)	P value[1]	P value[2]	P value[3]	P value[4]
Age in years (range)	60(22)	55 (52)	60 (18)	60 (12)	55 (24)	1.00	0.24	0.665	0.90
Male gender, n (%)	25 (48)	7 (37)	18 (55)	10 (53)	8 (57)	0.259	1.00	0.515	0.30
Comorbidities									
Diabetes Mellitus, n (%)	13 (25)	6 (32)	7 (21)	6 (32)	1 (7)	0.51	0.195	1.00	0.20
Hyperlipidemia	12 (23)	4 (21)	8 (24)	6 (32)	2 (14)	1.00	0.416	0.714	1.00
Ischemic heart disease	7 (13)	4 (21)	3 (9)	3 (16)	0 (0)	0.40	0.244	1.00	0.12
Cerebrovascular disease	3 (6)	0 (0)	3 (9)	2 (11)	1 (7)	0.29	1.00	0.486	0.42
Malignancy	3 (6)	2 (11)	1 (3)	1 (5)	0 (0)	0.55	1.00	1.00	0.50
Hematological disorders/anticoagulation use	4 (8)	0 (0)	4 (12)	4 (21)	0 (0)	0.28	0.119	0.105	1.00
ASA score									
1	20 (39)	9 (47)	11 (33)	5 (26)	6 (43)	0.382	0.459	0.31	1.00
2	28 (54)	9 (47)	19 (58)	11 (58)	8 (57)	0.569	0.491	1.00	0.73
3	4 (7)	1 (5)	3 (9)	3 (16)	0 (0)	1.00	0.244	0.341	1.00
Symptoms									
Abdominal pain	42 (81)	15 (79)	27 (82)	17 (89)	10 (71)	1.00	0.363	0.660	0.70
Obstructive jaundice	25 (48)	8 (42)	17 (51)	10 (53)	7 (50)	0.77	1.00	0.746	0.73
Fever	8 (15)	3 (16)	5 (15)	4 (21)	1 (7)	1.00	0.366	1.00	0.62
Total bilirubin (mg/dL)	86 (96)	70 (79)	104 (93)	105 (110)	104 (92)	**0.04**	0.88	0.56	0.10
ALP (U/L)	238 (284)	184 (100)	287 (155)	329 (196)	282 (101)	0.23	0.739	0.81	**0.02**
GGT (U/L)	274 (236)	206 (152)	349 (372)	276 (678)	350 (259)	0.42	0.762	0.199	0.05
ALT (U/L)	242 (305)	175 (368)	255 (273)	242 (27)	299 (705)	0.52	0.449	0.403	0.57
AST (U/L)	165 (249)	189 (334)	144 (235)	146 (213)	118 (353)	0.60	0.483	0.552	0.82
TW (10^9/L)	9 (7)	8 (9)	9 (6)	10 (8)	8 (4)	0.48	0.271	0.583	0.55
Pre-op biliary stenting via ERCP	33 (64)	9 (27)	24 (73)	15 (79)	9 (64)	0.13	0.442	0.091	0.48
Pre-op diagnosis of MS	44 (85)	18 (95)	26(79)	15 (79)	11 (79)	0.32	0.442	0.340	0.29
Pre-op diagnosis of cholecysto-biliary or cholecysto-enteric fistula	2 (4)	0 (0)	2(6)	2 (11)	0 (0)	0.52	0.496	0.486	1.00
Postoperative Beltran classification									
I	36 (69)	16 (84)	20 (61)	10 (53)	10 (71)	0.12	0.310	0.079	0.08
II	13 (25)	2 (11)	11 (33)	7 (37)	4 (29)	0.099	0.719	0.125	0.12
III	3 (6)	1 (5)	2 (6)	2 (11)	0 (0)	1.00	1.00	1.00	1.00
Conversion to open (rate in %)	19 (37)	11 (58)	8 (24)	1 (5)	7 (50)	**<0.01**	**0.005**	**0.001**	0.73
Reason for conversion									
Common bile duct injury	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00
Adhesions	7 (14)	4 (7)	3 (9)	1(5)	2 (14)	0.40	0.561	0.34	1.00

Table 3 continued

	Total n = 52(%)	Era 1 ALL n = 19(%)	Era 2 ALL n = 33(%)	Era 2 AMIS n = 19(%)	Era 2 others n = 14(%)	P value[1]	P value[2]	P value[3]	P value[4]
Bowel injury	1 (2)	1 (5)	0 (0)	0 (0)	0 (0)	0.37	1.00	1.00	1.00
Uncertain anatomy	4 (8)	2 (11)	2 (6)	0 (0)	2 (14)	0.62	0.172	1.00	1.00
Difficult retraction of gallbladder	4 (8)	4 (21)	0 (0)	0 (0)	0 (0)	0.02	1.00	1.00	0.11
Prolonged surgery	3 (6)	0 (0)	0 (0)	3 (6)	0 (0)	0.06	0.23	**0.01**	1.00
Surgical procedure									
Total cholecystectomy	31 (60)	14 (74)	17 (52)	7 (37)	10 (71)	0.24	0.08	0.049	1.00
Subtotal cholecystectomy	21 (40)	5 (26)	16 (49)	12 (63)	4 (29)	0.24	0.08	0.049	1.00
Primary repair of enteric fistula	3 (6)	1 (5)	2 (6)	2 (11)	0 (0)	1.00	0.496	1.00	1.00
Primary repair of CBD	4 (8)	1 (5)	3 (9)	1 (5)	2 (14)	1.00	0.561	1.00	0.56
Choledochoplasty	9 (17)	1 (5)	8 (24)	7 (37)	1 (7)	0.23	0.098	**0.042**	1.00
Hepaticojejunostomy	1 (2)	0 (0)	1 (3)	0 (0)	1 (7)	1.00	0.424	1.00	0.42
Intraoperative cholangiogram	17 (33)	6 (32)	11 (33)	9 (47)	2 (14)	1.00	0.067	0.508	0.42
T tube insertion	14 (27)	7 (37)	7 (21)	7 (37)	0 (0)	0.19	**0.013**	1.00	**0.01**
Operating time (minutes)	155 (75)	135 (65)	165 (70)	173 (73)	120 (0)	**0.02**	0.118	**0.018**	0.70
Postoperative hospital stay (days)	4 (5)	4.5 (4.5)	4 (4)	3 (4)	4 (2.5)	0.384	0.495	0.461	0.83
Postoperative ERCP									
Planned stent removal	21 (40)	6 (32)	15 (46)	8 (42)	7 (50)	0.18	1.00	0.317	0.47
Planned stone removal	3 (6)	0 (0)	3 (9)	3 (16)	0 (0)	0.09	0.244	0.230	1.00
Postoperative morbidity, n (%)	5 (10)	1 (5)	4 (12)	1 (5)	3 (21)	0.641	0.288	1.00	0.288
Clavien–Dindo classification									
II	3 (6)	0 (0)	3 (9)	1 (5)	2 (14)	0.291	0.561	1.00	0.172
III	2 (4)	1 (5)	1 (3)	0 (0)	1 (7)	1.00	0.424	1.00	1.00
Early/intraoperative surgical complications	12 (23)	3 (16)	9 (27)	8 (42)	1 (7)	0.499	**0.05**	0.604	1.00
Common bile duct (CBD) injury, n (%)	1 (2)	1 (5)	0 (0)	0 (0)	0 (0)				
Retained stones, n (%)	4 (8)	2 (11)	2 (6)	1 (5)	1 (7)	1.00	1.00	1.00	0.567
Bile leak	1 (2)	0 (0)	1 (3)	1 (5)	0 (0)	1.00	0.424	1.00	1.00
Biliary stricture	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	0.42
Bowel injury	1 (2)	1 (5)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00
Liver or intra-abdominal abscess	2 (4)	0 (0)	2 (6)	2 (11)	0 (0)	0.46	0.496	0.486	1.00
Cholangitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00
Perioperative bleeding	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00
Recurrent CBD stones	2 (4)	0 (0)	2 (6)	2 (11)	0 (0)	0.52	0.496	0.486	1.00
Late complications	8 (15)	4 (21)	4 (12)	1 (5)	3 (21)	0.44	0.282	1.00	1.00
Cholangitis	3 (6)	1 (5)	2 (6)	1 (5)	1 (7)	1.00	1.00	1.00	1.00

Table 3 continued

	Total $n = 52(\%)$	Era 1 ALL $n = 19(\%)$	Era 2 ALL $n = 33(\%)$	Era 2 AMIS $n = 19(\%)$	Era 2 others $n = 14(\%)$	P value[1]	P value[2]	P value[3]	P value[4]
Recurrent stones	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00
CBD stricture	2 (4)	1 (5)	1 (3)	0 (0)	1 (7)	1.00	0.424	1.00	1.00
Liver or intra-abdominal abscess	2 (4)	1 (5)	1 (3)	0 (0)	1 (7)	1.00	0.424	1.00	1.00
Ventral hernia	1 (2)	1 (5)	0 (0)	0 (0)	0 (0)	1.00	1.00	1.00	1.00

Data expressed as whole number (%) or median (interquartile range), p value for Fisher exact test for categorical and for Mann–Whitney U for continuous data

P value[1]—Era 1 ALL vs Era 2 ALL

P value[2]—Era 2 AMIS vs Era 2 others

P value[3]—Era 2 AMIS vs Era 1 ALL

P value[4]—Era 2 others vs Era 1 ALL

A value of $p < 0.025$ was considered to be statistically significant after adjusting for multiple testing using Bonferroni correction when appropriate

triangle making the laparoscopic approach more difficult, this was not the case in our study where we showed improved laparoscopic completion rates [33]. In our opinion, this combined approach has additional benefits such as improving postoperative biliary drainage which protects the choledochotomy or cholecystoplasty repair site and allows postoperative clearance of any retained bile duct stones during stent removal [6]. This change in practice was also reflected in the decrease in the frequency of use of intraoperative cholangiogram between Era 1 and Era 2 whereby we did not find it necessary to routinely perform intraoperative cholangiograms especially after choledochoscopy in cases whereby pre- and postoperative ERCP was planned for.

Early studies have attributed the high conversion rates of laparoscopic surgery to the poor predictability of diagnostic studies for MS. When studies stratified the pre-operative diagnostic rate, higher rates of pre-operative diagnosis ($> 80\%$) lead to improved conversion rates, at as low as 25% compared to over 54% in studies with poorer ($< 80\%$) pre-operative diagnosis rates [8, 34, 35]. In our experience, we did not find significant improvement of the diagnostic accuracy of MS between Era 1 and Era 2 (Table 1). Rather, we kept a high index of suspicion when approaching difficult cholecystectomies bearing in mind the possibility of an undiagnosed MS even when pre-operative imaging did not suggest it.

From our study, it is evident that the intraoperative diagnostic accuracy of MS and its associated cholecysto-biliary and cholecysto-enteric fistula exceed that of any pre-operative imaging modality. As shown in our study, the improved completion rate of MIS for MS is not significantly affected by the accuracy of the imaging modalities. Rather, the adoption of advanced laparoscopic HPB surgery improved the overall technical expertise and was pivotal in the progressive adoption of MIS for MS. The impact of successfully completed laparoscopic surgery for MS translated into significantly shorter hospital stay compared to open procedures, with a median stay of 2 days compared to 9 days ($p < 0.01$), with no significant differences in complication rates (Table 3).

The main limitation of this study is that this is a single-center retrospective analysis and has inherent confounders and biases which can only be overcome by conducting a prospective randomized controlled trial. However, due to the rarity of MS, it would be extremely difficult to conduct a randomized controlled trial. A second limitation is that the results of this study were mainly based on the experience of two surgeons rather than the entire institution and may not be universally applicable. Nevertheless, the findings in this study are important as it is the first study to report the positive impact of the adoption of advanced MI-HBP surgery on the improved outcomes of MIS for MS.

Table 4 Comparison between all MIS vs all open procedures

	Total $n = 95(\%)$	MIS Attempted $N = 52 (\%)$	Open $N = 43(\%)$	MIS completed $N = 33 (\%)$	MIS converted $N = 19 (\%)$	P value[1]	P value[2]
Age in years (range)	60 (25)	60(22)	60 (69)	57 (19)	60 (24)	1.00	0.601
Male gender, n (%)	49 (48)	25 (48)	24 (56)	13 (39)	12 (63)	1.00	0.150
Female gender, n (%)	46 (52)	27 (52)	19 (44)	20 (61)	7 (37)		
Comorbidities							
Diabetes mellitus, n (%)	26 (27)	13 (25)	13 (33)	8 (24)	5 (26)	0.72	1.0
Hyperlipidemia	18 (19)	12 (23)	6 (14)	9 (27)	3 (16)	0.70	0.499
Ischemic heart disease	12 (13)	7(14)	5 (12)	4 (12)	3 (16)	0.35	0.697
Cerebrovascular disease	7 (7)	3 (6)	4 (9)	2 (6)	1 (5)	0.46	1.00
Malignancy	3 (3)	3 (6)	0 (0)	1 (3)	2 (11)	1.00	0.546
Hematological disorders/anticoagulation use	7 (7)	4 (8)	3 (7)	4 (12)	0 (0)	0.20	0.284
ASA score							
1	39 (41)	20 (39)	19 (44)	12 (36)	8 (42)	0.49	0.638
2	45 (47)	28 (54)	17 (40)	18 (55)	10 (53)	1.00	1.00
3	11 (12)	4 (7)	7 (16)	3 (9)	1 (5)	0.31	1.00
Symptoms							
Abdominal pain	64 (67)	42 (81)	22 (51)	27 (82)	15 (79)	0.35	1.00
Obstructive jaundice	51 (54)	25 (48)	26 (60)	15 (45)	10 (53)	0.74	0.774
Fever	24 (25)	8 (15)	16 (37)	5 (15)	3 (16)	0.68	0.709
Total bilirubin (mg/dL)	86 (102)	86 (96)	95 (114)	86 (81)	86 (113)	**0.04**	0.712
ALP (U/L)	238 (180)	184 (100)	287 (202)	238 (186)	237 (164)	0.23	0.639
GGT (U/L)	276 (265)	206 (152)	315 (328)	271 (434)	289 (204)	0.42	0.888
ALT (U/L)	175 (278)	175 (368)	143 (261)	315 (333)	132 (315)	0.52	0.302
AST (U/L)	134 (183)	189 (334)	115 (224)	180 (287)	105 (183)	0.60	0.166
TW (10^9/L)	10 (7)	8 (9)	10 (6)	9 (7)	9 (7)	0.48	0.535
Pre-op biliary stenting via ERCP	57 (58)	33 (64)	24 (56)	24 (73)	9 (47)	0.17	0.081
Pre-op diagnosis of MS	78 (82)	44 (85)	34 (79)	26 (79)	18 (95)	0.16	0.232
Pre-op diagnosis of cholecysto-biliary or cholecysto-enteric fistula	6 (6)	2 (4)	4 (12)	2 (6)	0 (0)	1.00	0.527
Postoperative Beltran classification							
I	61 (64)	36 (69)	25 (58)	21 (64)	15 (79)	0.29	0.35
II	29 (31)	13 (25)	16 (37)	10 (30)	3 (16)	0.26	0.33
III	5 (5)	3 (6)	2 (5)	2 (6)	1(5)	1.00	1.00
Open conversion, n (%)	NA	19 (36.5)	NA	NA	NA	NA	NA
Reason for conversion							
Common bile duct injury	1 (1)	0 (0)	1(2)	0 (0)	0 (0)	1.00	1.00

Table 4 continued

	Total n = 95(%)	MIS Attempted N = 52 (%)	Open N = 43(%)	MIS completed N = 33 (%)	MIS converted N = 19 (%)	P value[1]	P value[2]
Adhesions	5 (6)	NA	NA	NA	5 (6)	1.00	NA
Bowel injury	1 (1)	NA	NA	NA	1 (1)	0.46	NA
Uncertain anatomy	2 (3)	NA	NA	NA	2 (3)	1.00	NA
Difficult retraction of gallbladder	4 (5)	NA	NA	NA	4 (5)	0.57	NA
Prolonged surgery	3(6)	0 (0)	0 (0)	0 (0)	3(6)	0.06	NA
Surgical procedure							
Total cholecystectomy	64 (67)	31 (61)	33 (77)	17 (52)	14 (74)	**0.04**	0.149
Subtotal cholecystectomy	31 (33)	21 (40)	10 (23)	16 (48)	5 (26)	**0.04**	0.149
Primary repair of enteric fistula	3 (3)	3 (6)	0 (0)	2 (6)	1 (5)	1.00	1.00
Primary repair of CBD	16 (17)	4 (8)	12 (28)	2 (6)	2 (11)	1.00	0.617
Choledochoplasty	10 (11)	9 (17)	1 (2)	8 (24)	1 (5)	**0.04**	0.130
Hepaticojejunostomy	8 (8)	1 (2)	7 (16)	1 (3)	0 (0)	1.00	1.00
Intraoperative cholangiogram	47 (50)	17 (33)	30 (70)	11 (33)	6 (32)	0.50	1.00
T tube insertion	44 (46)	14 (27)	30 (70)	9 (27)	5 (26)	0.74	1.00
Operating time (minutes)	185 (90)	155 (75)	165 (109)	158 (59)	140 (111)	0.81	0.655
Postoperative hospital Stay (days)	7 (7)	4 (5)	9 (7)	2 (2)	6 (4)	**<0.01**	**<0.01**
Postoperative ERCP							
Planned stent removal	25 (26)	21 (40)	4 (9)	15 (45)	6 (32)	0.18	0.389
Planned stone removal	3 (4)	3 (6)	0 (0)	2 (6)	1 (5)	0.09	1.00
Postoperative morbidity, n (%)	17 (18)	5 (10)	12 (28)	4 (12)	1 (5)	0.030	0.641
Clavien–Dindo classification							
II	10 (11)	3 (6)	7 (16)	2 (6)	1 (5)	0.177	1.00
III	5 (5)	2 (4)	3 (7)	2 (6)	0 (0)	0.656	0.527
V	2 (2)	0 (0)	2 (5)	0 (0)	0 (0)	0.202	1.00
Common bile duct (CBD) injury, n (%)	1 (1)	0 (0)	1(2)	0 (0)	0 (0)	1.00	1.00
Retained stones, n (%)	6 (6)	4 (8)	2 (5)	4 (12)	0 (0)	1.00	1.00
Bile leak	3 (3)	1 (2)	2 (5)	1 (3)	0 (0)	1.00	1.00
Biliary stricture	2 (0)	0 (0)	2 (5)	0 (0)	0 (0)	1.00	1.00
Bowel injury	3 (3)	1 (2)	2 (5)	0 (0)	0 (0)	1.00	1.00
Liver or intra-abdominal abscess	6 (6)	2 (4)	4 (10)	2 (6)	0 (0)	0.46	1.00
Cholangitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.00	1.00
Perioperative bleeding	2 (2)	0 (0)	2 (5)	0 (0)	0 (0)	1.00	1.00
Recurrent CBD stones	2 (2)	2 (4)	0 (0)	2 (6)	0 (0)	0.46	1.00
Late complications	17	8	9	4	4	0.59	0.44
Cholangitis	9 (9)	3 (5)	6 (12)	1 (5)	2 (11)	1.00	0.29

Table 4 continued

	Total n = 95(%)	MIS Attempted N = 52 (%)	Open N = 43(%)	MIS completed N = 33 (%)	MIS converted N = 19 (%)	P value[1]	P value[2]
Recurrent stones	2 (2)	0 (0)	2 (5)	0 (0)	0 (0)	1.00	1.00
CBD stricture	3 (3)	2 (5)	1 (2)	1 (3)	1 (5)	1.00	1.00
Liver or intra-abdominal abscess	2 (2)	2 (5)	0 (0)	1 (3)	1 (5)	1.00	1.00
Ventral hernia	1 (1)	1 (5)	0 (0)	1 (3)	0 (0)	1.00	1.00

Data expressed as whole number (%) or median (interquartile range), p value for Fisher exact test for categorical and for Mann–Whitney U for continuous data

P value[1]—ALL MIS attempted vs ALL Open

P value[2]—ALL MIS completed vs MIS converted

A value of $p < 0.025$ was considered to be statistically significant after adjusting for multiple testing using Bonferroni correction when appropriate

This study could serve as a lead-point for more in-depth investigation and quantitative analysis on the skill transferability between laparoscopic procedures.

In conclusion, in our experience the systematic adoption of advanced MI-HBP surgery allowed surgeons in our institution to attempt MIS for MS more frequently with a significantly lower open conversion rate. Patients who underwent successful MIS had the shortest hospital stay compared to patients who underwent open surgery or required open conversion.

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ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. BKG: Conception or design of the work; interpretation of data for the work; revising critically for important intellectual content; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with ethical standards

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