

Minimally Invasive Resection of Choledochal Cyst: a Feasible and Safe Surgical Option

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Abstract

Background The use of minimally invasive surgery (MIS) for choledochal cyst (CC) has not been well documented. We sought to define the overall utilization and outcomes associated with the use of the open versus MIS approach for CC. We examined the factors associated with receipt of MIS for CC, as well as characterized perioperative and long-term outcomes following open versus MIS for CC.

Methods Between 1972 and 2014, a total of 368 patients who underwent resection for CC were identified from an international, multicenter database. A 2:1 propensity score matching was used to create comparable cohorts of patients to assess the effect of MIS on short-term outcomes.

Results Three hundred thirty-two patients had an open procedure, whereas 36 patients underwent an MIS approach. Children were more likely to be treated with a MIS approach (children, 24.0 % vs. adults, 2.1 %; $P < 0.001$). Conversely, patients who had any medical comorbidity were less likely to undergo MIS surgery (open, 26.2 % vs. MIS, 2.8 %; $P = 0.002$). In the propensity-matched cohort, MIS resection was associated with decreased length of stay (open, 7 days vs. MIS, 5 days), lower estimated blood loss (open, 50 mL vs. MIS, 17.5 mL), and longer operative time (open, 237 min vs. MIS, 301 min) compared with open surgery (all $P < 0.05$). The overall and degree of complication did not differ between the open (grades I–II, $n = 13$; grades III–IV, $n = 15$) versus MIS (grades I–II, $n = 5$; grades III–IV, $n = 5$) cohorts ($P = 0.85$). Five-year overall survival was 98.6 % (open, 98.0 % vs. MIS, 100.0 %; $P = 0.45$); no patient who underwent MIS developed a subsequent cholangiocarcinoma.

Conclusions MIS resection of CC was demonstrated to be a feasible and safe approach with acceptable short-term outcomes in the pediatric population. MIS for benign CC disease was associated with similar perioperative morbidity but a shorter length of stay and a lower blood loss when compared with open resection.

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Introduction

Choledochal cysts (CCs) are rare congenital cystic dilations of the biliary tract that are more common in East Asian populations, with a four times higher incidence in female patients.^{1–3} Because CCs are predominantly (80 %) diagnosed in pediatric patients within the first decade of life,^{4,5} data on adult patients are rare.^{6,7} While the exact etiology of CC remains elusive, several theories have been proposed.^{8–10} Among various CC classifications, the Todani classification is the most widely accepted and incorporates cyst location, cyst number, and the presence of an abnormal pancreaticobiliary junction (PBM).¹¹ According to the Japanese Study Group, PBM is defined as a union of the pancreatic and biliary ducts outside the duodenal wall allowing for the reflux of pancreatic fluid into the biliary tree.⁸ Complications of CC include an increased risk of cholangitis, as well as malignant transformation.^{12–14} As such, total cyst excision, commonly in association with resection of the extrahepatic biliary tree and bilioenteric reconstruction, is recommended for most patients with CC.^{3,15–18}

Minimally invasive surgery (MIS) has gained increased acceptance and applicability in general surgery.^{19–25} The MIS approach has been suggested to decrease the incidence of wound complications, as well as lead to shorter hospital stay, fewer intra-abdominal adhesions, better cosmesis, and more rapid return to baseline functional status.^{26–28} While the MIS approach has been utilized for a number of hepatopancreatico-biliary indications,^{29–33} the use of MIS for CC has not been well documented. In 1995, Farrello et al. reported the first minimally invasive resection of CC with bilioenteric reconstruction.³⁴ Since then, a few scattered reports have been published on the use of MIS for the surgical management of CC.^{17,35–37} Most reports, however, were small, single institution case reports/series that were mostly confined to pediatric populations.^{35,36} Moreover, data on the MIS approach for CC surgery have largely been derived from specialized, high-volume hepatobiliary centers in Asia.^{38,39} Considering differences in patient characteristics between the USA and East Asia (e.g., body habitus), MIS data derived exclusively from East Asian cohorts may not be generalizable to Western patients. Moreover, previous studies that compared the open versus MIS approach failed to match patients on various perioperative variables and, therefore, may be particularly biased with regard to patient selection. In the current study, we sought to define the overall utilization and outcomes associated with the use of open versus MIS approach for CC using a large, multi-institutional database. We examined the

factors associated with receipt of MIS for CC, as well as characterized perioperative and long-term outcomes following open versus MIS approach for CC.

Specifically, we utilized propensity score matching to more fully control for potential baseline differences between the open and MIS cohorts and thereby minimize confounding by indication.

Methods

Patient selection

Patients who underwent surgery for CC between 1972 and 2014 in one of the eight major academic institutions participating in the study (Johns Hopkins Hospital, Baltimore, MD; Emory University, Atlanta, GA; Stanford University, Stanford, CA; University of Virginia, Charlottesville, VA; University of Wisconsin, Madison, WI; Universite Catholique de Louvain, Brussels, Belgium; Scientific Institute San Raffaele, Milan, Italy; Curry Cabral Hospital, Lisbon, Portugal) were identified. The institutional review boards of each institution approved this study. Patients who underwent conversion to an open procedure were classified in the open group. In total, 36 patients underwent MIS (including laparoscopic, laparoscopic hand assist, and robotic procedures); 73 matched-pair control patients were selected from 332 patients who underwent open resection.

Data on demographic and clinicopathological characteristics, including age, sex, ethnicity, body mass index (BMI), presenting symptoms, previous biliary surgery, and overall comorbidities, were collected. The following CC characteristics were obtained: type of cyst (Todani's classification), histological type, cyst diameter, and concomitant abnormal PBM. Data regarding treatment details were also collected including type of resection, type of biliary reconstruction (i.e., Roux-en-Y hepaticojejunostomy, hepaticoduodenostomy, no reconstruction), concurrent Whipple, concurrent liver resection (partial hepatectomy), operative time, and estimated blood loss (EBL).

Data on postoperative outcome metrics included length of stay (LOS), complications within 30 days of the operation, system-specific complications, Clavien-Dindo stage of complication,⁴⁰ incidence of readmission, repeat biliary procedures, and reoperation. Date of last follow-up and recurrence were also obtained for all patients.

Statistical Analysis

Demographic and clinicopathologic characteristics of the study population, as well as the type of surgical procedure, were stratified according to open versus MIS approach. Continuous variables were described as medians with interquartile range (IQR). Categorical variables were described as totals

and frequencies. The differences between groups were assessed by the chi-square, Fisher's exact, and Mann-Whitney tests, as appropriate. Univariable and multivariable logistic regression models were constructed to explore the association of preoperative covariates with MIS resection. Propensity score methods were used to account for clinicopathologic differences in patients undergoing open versus MIS. Propensity score matching (nearest neighbor algorithm) was used to create comparable cohorts of patients to assess the effect of MIS on short-term outcomes. Age, sex, ethnicity, type of choledochal cyst, and cyst pathology (benign vs. malignant), as well as year of surgery, were used in the propensity score logistic regression model. The propensity-matched cohorts were compared to assess the effect of MIS versus open surgery on perioperative outcomes. All analyses were carried out with STATA version 12.0 (StataCorp, College Station, TX), and a *P* value of <0.05 (two-tailed) was considered statistically significant.

Results

Demographic and Clinicopathologic Characteristics of Overall Cohort

Between 1972 and 2014, a total of 368 patients who underwent resection for CC were identified from an international, multicenter database. Among these patients, 332 patients had an open procedure, whereas 36 patients underwent an MIS approach. As expected, the baseline characteristics of the open versus MIS cohort differed. Specifically, MIS patients were younger (open, 35 years vs. MIS, 6 years), more likely to have a lower BMI (open, 23.8 kg/m² vs. MIS, 15.9 kg/m²), fewer overall medical comorbidities (open, 26.2 % vs. MIS, 2.8 %), a higher level of preoperative AST (open, 34 U/L vs. MIS, 71.5 U/L), and a higher incidence of PBM (open, 13.9 % vs. MIS, 40.0 %) (all *P*<0.05). Specifically, children (<18 years old) were more likely to be treated with an MIS rather than an open approach compared to adults (MIS, children, 24.0 % vs. adults, 2.1 %; *P*<0.001). Conversely, patients who had any medical comorbidities were less likely to undergo MIS surgery (open, 26.2 % vs. MIS, 2.8 %; *P*=0.002). At the time of surgery, an open versus MIS operative approach was also associated with a difference in the type of biliary reconstruction. Specifically, hepaticoduodenostomy was more common among patients who underwent an MIS resection (open, 3.5 % vs. MIS, 19.4 %), whereas Roux-en-Y hepaticojejunostomy was more common among patients who underwent an open resection (open, 88.2 % vs. MIS, 75.0 %) (*P*=0.001).

Propensity-Matched Open and MIS Cohorts: Perioperative Details and Outcome

Propensity score matching was then utilized to create more comparable cohorts of patients in the open versus MIS groups to minimize confounding by indication. The clinicopathologic characteristics for the propensity-matched open versus MIS cohorts (open, *n*=73 vs. MIS, *n*=36) are shown in Table 1. After propensity matching for age, sex, ethnicity, cyst pathology (benign vs. malignant), and type of choledochal cyst based on Todani's classification, the demographic and clinicopathologic characteristics of the cohorts were much more comparable. Among the entire matched cohort, the median age was 7 years, and 81.7 % of patients were female. The overwhelming majority of patients presented with symptomatic disease (87.2 %) with the most common symptom being abdominal pain (*n*=59, 54.1 %). The majority of patients (*n*=75, 68.8 %) had a type I CC according to Todani's classification, and the incidence of PBM was 19.5 % (*n*=15). Median preoperative AST and bilirubin values were 52.5 U/L and 0.8 mg/dL, respectively.

The median year of surgery in the open group was 2008 (range 1996–2014), while the median year of surgery in the MIS group was 2009 (range 1997–2013). At the time of surgery, most patients underwent excision of the cyst with extrahepatic biliary resection and hepaticocenterostomy (*n*=92, 84.4 %); a smaller number had only cyst excision with no biliary reconstruction (*n*=8, 7.3 %) (Table 2). Among patients who underwent an open procedure, the overwhelming majority was reconstructed with a Roux-en-Y hepaticojejunostomy (*n*=66, 90.4 %). A hepaticoduodenostomy was performed more frequently in the MIS group (*n*=7, 19.4 %) compared to the open group (*n*=1, 1.4 %). A small subset of patients underwent a concurrent liver resection (9.2 %) (open, *n*=8 vs. MIS, *n*=2) or a concurrent Whipple procedure (2.8 %) (open, *n*=3 vs. MIS, *n*=0). Among the propensity-matched cohort, median operative time was 257 min (IQR 205–325 min) (open, 237 min vs. MIS, 301 min) and median EBL was 30 mL (IQR 15–150 mL) (open, 50 mL vs. MIS, 17.5 mL) (both *P*<0.05) (Table 3) (Fig. 1). On final pathology, histopathology demonstrated a median cyst size of 2.5 cm (IQR 1.4–4 cm) (open, 2.5 cm vs. MIS, 2.5 cm). While the overwhelming majority of CC lesions was benign in nature (*n*=104, 95.4 %) (open, *n*=70 vs. MIS, *n*=34), a small subset of patients did harbor an underlying cholangiocarcinoma (open, *n*=3 vs. MIS, *n*=0).

Within 30 days of surgery, 38 patients experienced a postoperative complication for an overall morbidity of 34.9 %. While roughly half the complications (*n*=18) were minor (grade I or II), 20 patients did experience a Clavien-Dindo grades III–IV complication. The overall and degree of complication did not differ between the open (grades I–II, *n*=13; grades III–IV, *n*=15) versus MIS (grades I–II, *n*=5; grades III–IV, *n*=5) cohorts (*P*=0.85). There were no perioperative

Table 1 Clinical and pathological features stratified by operative approach

Variable	Propensity-matched sample			P value
	All (n=109)	Open (n=73)	MIS (n=36)	
Age, year	7.0 (2.0–24.0)	14.0 (2.0–26.0)	6.0 (3.0–12.0)	0.26
Male sex	20 (18.3)	13 (17.8)	7 (19.4)	0.84
Ethnicity				0.84
Caucasian	56 (51.4)	37 (50.7)	19 (52.8)	
Other	53 (48.6)	36 (49.3)	17 (47.2)	
BMI, kg/m ²	16.9 (15.0–21.1)	19.4 (15.2–23.0)	15.9 (14.5–19.0)	0.06
Comorbidity, overall	6 (5.5)	5 (6.8)	1 (2.8)	0.38
Symptoms				
Abdominal pain	59 (54.1)	39 (53.4)	20 (55.6)	0.83
Abdominal mass	1 (0.9)	1 (1.4)	0	0.48
Early satiety	11 (10.1)	11 (15.1)	0	0.01
Nausea/vomiting	6 (5.5)	4 (5.5)	2 (5.6)	0.99
Jaundice	24 (22.0)	19 (26.0)	5 (13.9)	0.15
Pancreatitis	31 (28.4)	20 (27.4)	11 (30.6)	0.73
Cholangitis	6 (5.5)	4 (5.5)	2 (5.6)	0.99
Weight loss	6 (5.5)	4 (5.5)	2 (5.6)	0.99
Others	3 (2.8)	2 (2.7)	1 (2.8)	0.99
None	14 (12.8)	11 (15.1)	3 (8.3)	0.32
Previous biliary surgery	12 (11.1)	8 (11.0)	4 (11.4)	0.61
Pre-op bilirubin	0.8 (0.5–2.1)	0.8 (0.5–2.7)	1.0 (0.5–1.8)	0.99
Pre-op AST	52.5 (27.0–166.0)	45.5 (25.0–157.0)	71.5 (34.0–295.0)	0.14
Todani's type				0.93
I	75 (68.8)	50 (68.5)	25 (69.4)	
II	7 (6.4)	4 (5.5)	3 (8.3)	
III	3 (2.8)	2 (2.7)	1 (2.8)	
IV	24 (22.0)	17 (23.3)	7 (19.4)	
V	0	0	0	
Cyst diameter, cm	2.5 (1.4–4.0)	2.5 (1.2–3.5)	2.5 (1.7–4.0)	0.57
Benign	104 (95.4)	70 (95.9)	34 (94.4)	0.73
Malignant	3 (2.8)	3 (4.1)	0	0.22
PBM rate (n=77)	15 (19.5)	5 (9.6)	10 (40.0)	<0.001

deaths in either the open or MIS group. The overall median LOS was 7 days (IQR 5–10 days) for the entire matched cohort. Of note, LOS was longer among patients undergoing an open (7 days) versus an MIS (5 days) approach ($P<0.001$). Following discharge, 29 patients were readmitted for an overall 30-day readmission of 26.6 % (open, $n=19$ vs. MIS, $n=10$; $P=0.85$). In addition, a subset of patients required either a reoperation (open, $n=7$ vs. MIS, $n=5$) or repeat biliary procedure (open, $n=14$ vs. MIS, $n=3$) (both $P>0.05$) (Table 3).

At a median follow-up of 25.9 months, 5-year overall survival was 98.6 % (open, 98.0 % vs. MIS, 100.0 %; $P=0.45$). No patient who initially had benign CC ($n=104$) developed a subsequent cholangiocarcinoma. In addition, all

three patients who had a cholangiocarcinoma noted on surgical pathology remained disease-free at last follow-up.

Discussion

Over the last 2 decades, the MIS approach has increasingly been used for a wide range of surgical procedures.^{19–25} The MIS approach has been adopted for both benign and malignant indications, with good oncological results reported in patients with lung, colorectal, and pancreatic cancer.^{20–25} Similarly, the MIS approach has been employed for a number of different benign diseases such as biliary colic, obesity, and

Table 2 Procedure type stratified by operative approach

Variable	Propensity-matched sample			P value
	All (n=109)	Open (n=73)	MIS (n=36)	
Type of resection				0.38
Internal drainage	1 (0.9)	0	1 (2.8)	
Excision of cyst with extrahepatic biliary resection and bile duct closure	4 (3.7)	3 (4.1)	1 (2.8)	
Excision of cyst with extrahepatic biliary resection and hepaticoenterostomy	92 (84.4)	60 (82.2)	32 (88.9)	
Excision of cyst with extrahepatic biliary resection, hepaticoenterostomy, and liver resection	9 (8.3)	7 (9.6)	2 (5.6)	
Whipple	3 (2.8)	3 (4.1)	0	
Type of hepaticoenterostomy				0.003
None	8 (7.3)	6 (8.2)	2 (5.6)	
Roux-en-Y hepaticojejunostomy	93 (85.4)	66 (90.4)	27 (75.0)	
Hepaticoduodenostomy	8 (7.3)	1 (1.4)	7 (19.4)	
Concurrent liver resection				0.59
None	99 (90.8)	65 (89.0)	34 (94.4)	
Partial hepatectomy	10 (9.2)	8 (11.0)	2 (5.6)	

The median year of surgery in the open group was 2008 (range 1996–2014), while the median year of surgery in the MIS group was 2009 (range 1997–2013)

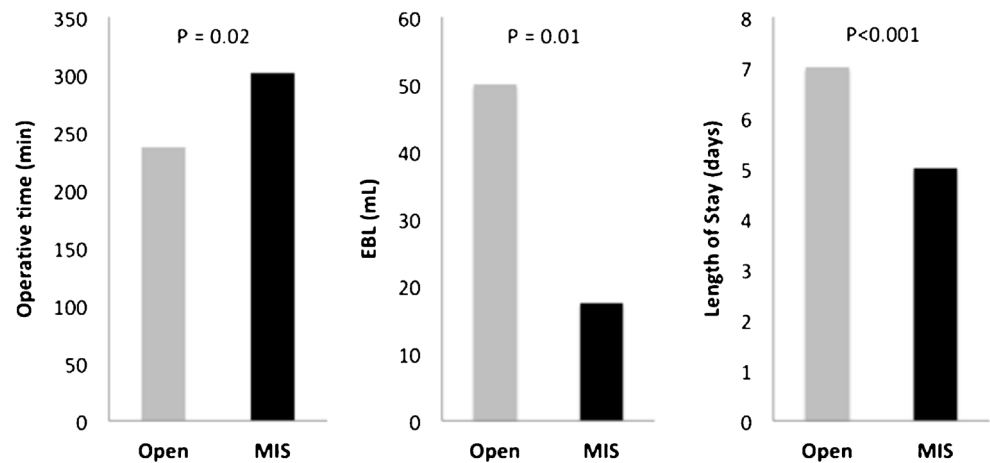
gastroesophageal reflux with good clinical outcomes.^{20,41,42} Specifically, the MIS approach has been associated with a lower incidence of wound complications, shorter hospital stay,

and quicker return to baseline functional status.^{26–28} While the MIS approach has been widely reported for hepatic and pancreatic procedures, its use to treat CC has been

Table 3 Operative details and postoperative outcomes stratified by operative approach

Variable	Propensity-matched sample			P value
	All (n=109)	Open (n=73)	MIS (n=36)	
Operative time	257 (205–325)	237 (205–270)	301.5 (241–400)	0.02
EBL	30.0 (15.0–150.0)	50.0 (20.0–250.0)	17.5 (5.0–50.0)	0.01
Length of stay	7.0 (5.0–10.0)	7.0 (6.0–12.0)	5.0 (5.0–8.0)	<0.001
Grade of comp				0.85
I/II	18 (47.4)	13 (46.4)	5 (50.0)	
III/IV	20 (52.6)	15 (53.6)	5 (50.0)	
Complications within 30 days	38 (34.9)	28 (38.4)	10 (27.8)	0.28
Hepatic/biliary complication	17 (15.6)	9 (12.3)	8 (22.2)	0.18
Cholangitis	5 (4.6)	3 (4.1)	2 (5.6)	0.73
Bile leak	7 (6.4)	5 (6.8)	2 (5.6)	0.80
Perihepatic abscess	3 (2.8)	3 (4.1)	0	0.22
GI complication	12 (11.0)	10 (13.7)	2 (5.6)	0.20
Renal/urologic complication	2 (1.9)	0	2 (5.7)	0.10
Cardiovascular complication	1 (0.9)	1 (1.4)	0	0.49
Pulmonary complication	2 (1.9)	1 (1.4)	1 (2.9)	0.59
Wound complication	7 (6.4)	4 (5.5)	3 (8.3)	0.57
Hemorrhagic complication	3 (2.8)	2 (2.7)	1 (2.9)	0.97
Readmission	29 (26.6)	19 (26.0)	10 (27.8)	0.85
Repeat biliary procedure	17 (15.6)	14 (19.2)	3 (8.3)	0.14
Reoperation	12 (11.5)	7 (10.3)	5 (13.9)	0.59
Recurrence	4 (3.9)	3 (4.5)	1 (2.8)	0.66

Fig. 1 Operative time, estimated blood loss, and length of hospital stay for patients who underwent MIS vs. open resection for choledochal cyst



underreported.^{29,30–33,35,43,44} In particular, due to the relative increased complexity and steeper learning curve of MIS biliary reconstruction, the MIS approach has not been as widely utilized for biliary indications.^{45–48} Due in part to this, as well as the overall low incidence of CC in the West, there have been no reports on the MIS approach for CC among Western patients. In fact, the only data on MIS for CC have been derived from data based on single institution East Asia cohorts of pediatric populations.^{17,35–37,49} As such, the current study is important as it is, to the best of our knowledge, the only multi-institutional study to compare open versus MIS approach for CC in a Western cohort of patients. We report both short- and long-term outcomes of MIS, analyzing the data using propensity score matching. We note that MIS for CC is feasible and safe among a pediatric population with comparable short- and long-term outcomes as patients who undergo an open procedure.

Selection of patients for open versus MIS surgical procedures is important to ensuring good outcomes. In most clinical settings, both patient- and disease-specific factors impact the choice regarding the operative approach. For example, Ejaz et al. reported a comparison of open and minimally invasive surgery for hepatic and pancreatic resections using the Nationwide Inpatient Sample.²⁹ In this study, the authors noted that, compared with patients undergoing an open procedure, MIS patients were older and had a greater incidence of multiple comorbidities. In a separate study examining open versus MIS approach for gastric cancer, Spolverato et al. found no differences in patient characteristics such as age or ASA score between the open versus MIS cohorts but did note that MIS patients were more likely to have less advanced disease (i.e., smaller tumors, no obstruction, etc.).⁵⁰ In the current study, we noted that children were more likely to undergo MIS. This is consistent with previous reports, which have almost exclusively reported the MIS approach in pediatric populations.^{44,51} It is important to note that the 13.9 % of patients who underwent an MIS approach in our study were adult,

demonstrating that an MIS approach for CC in adult populations is indeed feasible. Of note, most patients who had an MIS approach had a type I CC (69.4 %) suggesting that the MIS approach is probably most applicable for that subset of patients.

A main objective of the current study was to establish the feasibility and safety of MIS for CC compared with open surgery. In examining several perioperative metrics, MIS compared favorably to open surgery for CC. While the median operative time in the MIS group was slightly longer (64 min), EBL was lower in the MIS group (Fig. 1). Of note, in a study of 35 patients in China who underwent an MIS approach, Liu et al. also noted that the operative time associated with the MIS was about 100 min longer.⁵² In this study, however, the authors showed that operative time of MIS for CC decreased significantly with accumulating surgical experience.⁵² More recently, other authors have similarly reported on the learning curve for more complex hepatic and pancreatic surgery and have found operative time dramatically decreasing with increasing experience.^{53,54} Thus, the potential time disadvantage of the MIS approach for CC may be mitigated over time in the hands of an experienced MIS HPB surgeon.

While some groups have noted a lower risk of postoperative complications following an MIS versus open surgery,^{26–28} other groups have reported comparable short-term outcomes.^{55,56} In the current study, we did not note any differences in either the overall incidence of postoperative complications or the grade of complication between the two groups. We did find that the median LOS following MIS was 2 days fewer than the open group, which was comparable to the difference in LOS seen after MIS versus surgery reported for other types of surgical procedures such as gastrectomy.⁵⁰ Interestingly, the LOS of 5 days for the MIS group reported herein was comparable to the LOS of 6 days reported for adult patients undergoing MIS CC resection in at least one previous report.⁵² Collectively, this data suggest that MIS surgery for CC is not only feasible but also associated with comparable

short-term outcomes and potentially a shorter LOS compared with the open approach. In addition, while the assessment of long-term outcomes was not a primary focus of the current study, we similarly noted that no patient who initially had benign CC resected using an MIS approach developed a subsequent cholangiocarcinoma.

There are several limitations that need to be considered when interpreting our data. The utilization of the MIS approach was relatively low ($\approx 10\%$), and therefore, despite having the one of the largest series of CC patients in the West, the relatively low number of MIS CC patients limited our statistical analyses. In addition, while selection bias is unavoidable in any retrospective study, we did attempt to mitigate this through propensity matching. Despite propensity matching, there remained some differences in the two cohorts. For example, while patients in both the open and MIS groups were children, the age of patients in the open group was slightly—but not statistically significant—older. Finally, while a subset of adult patients did undergo an MIS approach, the majority of MIS procedures were performed in a pediatric population. As such, further data are needed on the MIS approach among adult patients.

In conclusion, we report the first data on a multi-institutional Western series of patients managed with an MIS approach for CC. MIS resection of CC was demonstrated to be a feasible and safe approach with acceptable short-term outcomes, especially among a pediatric population. The MIS approach for benign CC disease was associated with a shorter length of stay and a lower blood loss when compared with open resection. In addition, overall morbidity and 30-day readmission were similar in both cohorts. As such, MIS is an appropriate surgical option to manage patients with CC. As with other MIS applications, MIS for CC treatment will certainly continue to expand over time.

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