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Factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital bile duct cyst : A multicenter study

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Factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital bile duct cyst : A multicenter study

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Competing interests

The authors declare that they have no competing interests.

Abstract

Objective

The aim of this study was to assess factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital bile duct cyst (CBD).

Design

This is a retrospective case-control study. A 3-year retrospective study was performed between January 2013 and December 2015 in four centers in China, to detected factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with CBD.

Setting

This is a retrospective chart review of pediatric patients with CBD in four large hospital in China.

Participants

65 pediatric patients with CBD was conducted in four centers, and included review of information on demographics, clinical characteristics, preoperative complications, and surgical methods, if available.

Interventions

Univariate and multivariate logistical regression were used, we measured factors significantly affecting the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases.

Results

Twenty-three of the 65 case surgeries were performed using laparoscopic technique, and 42 surgeries were performed by conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). The morphological subtype

and the presence of cholecystitis or cholangitis were the only factors found to affect the operative time (p<0.05). Logistic regression analysis confirmed cholangitis as an independent risk factor.

Conclusions

The morphological subtype and the presence of cholecystitis or cholangitis affect the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases, whereas cholangitis is an independent risk factor.

Keywords: Congenital choledochal cysts, hepaticojejunostomy, operative time, influencing factors,

Strengths and limitations of this study

A retrospective study was carried out in four centers over a 3-year period. A stepwise logistic regression analysis of 65 pediatric CBD cases in 4 centers in southeast China, in an attempt to identify factors affecting the operative time.

The morphological subtype and the presence of cholecystitis or cholangitis affect the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases, whereas cholangitis is an independent risk factor.

Our study has a number of limitations. Firstly, the sample size was relatively small, as CBD is a rare pediatric disease and thus selection bias may have been a factor. Secondly, this was a retrospective multicenter study of only 3-years duration. A prospective multicenter study over a longer period is necessary.

Introduction

Congenital bile duct cyst (CBD) is a rare congenital anomaly that presents as extra and/or intrahepatic bile duct dilatation, and its incidence is more frequent in Asia than in Western countries [1-3]. The majority of cases seen in the clinic are in infants and children. Most CBD cases present clinically with abdominal pain, jaundice, and a mass, sometimes accompanied by vomiting and fever. CBD leads to higher rates of cholestasis, stone formation, pancreatitis, hyperplasia, and epithelial atypical growth of the bile duct or gallbladder, as well as tumor formation thought to be caused by pancreaticobilliary maljunction (PBM) with two-way reflux of bile and pancreatic juice [4-7].

Early prevention of long-term complications such as recurrent cholangitis, gallstones, pancreatitis, and especially, malignant tumors in the bile duct and gallbladder is desirable. Complete excision of the cyst and Roux-en-Y hepaticojejunostomy is the main option for CBD treatment in children [8-10]. Cyst excision and hepaticojejunostomy by either open surgery or laparoscopy in pediatric CBD are feasible and popularly undertaken [11-12]. Jackson *et al*. and Jenkins *et al*. reported that the complexity and difficulty of a surgical procedure is reflected by the operative time [13, 14]. Qiao *et al*. reported on an extensive series of CBD cases in 7 centers and found that postoperative complications were associated with longer operative time [10].

Up to now, few studies have focused on factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases. We retrospectively studied the clinical presentation and surgical management of 65

pediatric CBD cases that had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy between January 2013 and December 2015 in 4 centers in southeast China, in an attempt to identify factors affecting the operative time. As the operative time reflects the difficulty of surgical procedures, the experience of surgeons, and medical technology, efforts were made to ensure that the pediatric surgeons involved in this clinical study across all four centers were similarly and suitably trained. Medical technologies were also similar among the four centers in the present study. Our findings highlight the importance not only in planning surgical intervention for pediatric CBD patients but also in the scheduling of cases as well as the effective use of operating room time to improve the quality of care.

Materials and Methods

Study subjects

Data was collected after study protocol approval from the institutional review boards of each participating institution and informed consent was signed by the guardians of the subjects. All methods were carried out in strict accordance with the relevant institution guidelines regarding the acquisition and use of human tissues. Sixty-five pediatric CBD cases were recruited into this clinical study. Twenty-nine subjects were from the Children's Hospital of Soochow University, 11 subjects from Xuzhou Children's hospitals, 12 subjects from the Affiliated Hospital of Guizhou Medical College, and 13 subjects from the Affiliated Hospital of Nantong Medical College. All patients were diagnosed by ultrasound, CT, MRCP, and IOC. All patients were operated on with cyst excision and hepaticojejunostomy using the same laparoscopic or conventional open surgical approach, performed by pediatric surgeons from the 4 hospital surgical teams. All procedures were performed by expert pediatric surgeons

who have advanced skills and are capable of independently completing surgical procedures in cases with huge choledochal cysts. With respect to the laparoscopic procedure, 23 cases in this group were operated with the same laparoscopic surgical approach performed by surgeons who had participated at laparoscopic surgery studying sessions. The operative times of each surgical team were analyzed among the 4 subject cohorts.

Factor analysis

The patients were assessed for gender, age, common bile duct shape, Todani type, and presence of a stone in the cyst. Ages were grouped as infant (<1 year of age) or pediatric (>1 year of age). Common bile duct shape, Todani type, and presence of cyst stones were assessed by ultrasound and MRCP combined with IOC. Common bile duct shape was classified as either cystiform or fusiform. Clinical symptoms at presentation, preoperative complications, operative methods (conventional open or laparoscopic cyst excision and hepaticojejunostomy), and operative time were analyzed. Cholangitis was defined as any symptom of the Charcot triad (abdominal pain, jaundice, or fever) with an increase in total bilirubin, AST, and ALT levels above the normal range. Cholecystitis was confirmed by ultrasound combined with pathological findings. The operative time was grouped as <300 minutes or ≥300 minutes (Figure 1)

Statistical analysis

Analyses were performed with SAS software, JMP 9.0 (SAS Institute, Cary, NC, USA). Data are presented as number (*n*), percentage, and median. Multi-group ordered variable data comparisons were performed using Kruskal–Wallis test.

Univariate comparisons were performed using nonparametric one-way Wilcoxon rank sum, χ^2, or T test, depending on the statistical distribution. To evaluate risk factors affecting the operative time, logistic regression analysis was performed. The ROC curve was used to assess the accuracy of the logistic regression model. $p<0.05$ was considered statistically significant.

Results

Clinical characteristics and general findings of pediatric CBD cases

The present clinical study comprised 65 pediatric CBD cases diagnosed by ultrasound, computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), and intraoperative cholangiography (IOC). Among the 65 pediatric CBD cases, there were 25 (38.5%) male and 40 (61.5%) female patients with CBD. The median age of the patients was 3 years (range 3 months to 13 years). Fifty-two cases were defined as PBM by MRCP with IOC. The morphological subtype of bile duct dilatation was cystic (Figure 2) in 40 cases (8 were large cysts descending into the introitus of the pelvis) and fusiform (Figure 3) in 25 cases. All 65 cases underwent complete cyst excision and Roux-en-Y hepaticojejunostomy. Twenty-three cases were performed using laparoscopic technique, whereas the other 42 cases were performed using conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). Figure 4 illustrates the distribution of operative time between the 4 centers, and there was no significant difference in the operative time across centers.

Related risk factors affecting the operative time in pediatric CBD cases

Table 1 depicts a comparison of the clinical characteristics, preoperative complications, and surgical methods for the <300 minutes and ≥300 minutes operative

time groups. Univariate analysis revealed that the morphological subtype and the presence of cholecystitis or cholangitis affected the operative time (p<0.05). No other factors were found to affect the operative time. Logistic regression analysis was performed to assess independent predictors that affect the operative time in 65 pediatric CBD cases. Again, the presence of cholangitis was the most important risk factor (Table 2). These data agreed with Hosmer and Lemeshow's goodness-of-fit test (p=0.4191). To further assess the accuracy of logistic regression model for the obtained results, analysis of the receiver operating characteristic (ROC) curve was performed with the area under the curve (AUC) at 0.8913 (Figure 5).

Discussion

General findings

Due to the obstruction of bile or pancreatic juice discharge, pediatric CBD cases often present with abdominal pain, jaundice, and a mass, and harbor a risk of malignancy as well as other serious complications. Prophylactic surgery is recommended, once the diagnosis is confirmed. The operative time has been used previously as a measure of operative difficulty and complexity [13-14]. Sorokin *et al*. reported that increased postoperative complications were associated with the prolonged operative time [15]. Qiao *et al*. reported on 956 pediatric cases with CBD, in which all the patients had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy [10]. The mean operation time in that study was 3.52 hours (range 2.21-5.75 hours). In addition, they found that postoperative complications were associated with the increased operative time. Their operative time was similar to that in our study. However, there has been less research focusing on the risk factors affecting operative time in CBD surgery. Our study on a multicenter cohort of pediatric patients who underwent

complete cyst excision and hepaticojejunostomy showed the operative time ranged from 120-430 minutes, similar to the previously reported [16]. Moreover, we also focused on factors that potentially affect the operative time.

Factors affecting the operative time in pediatric CBD cases

To investigate factors that potentially influence the operative time, we described the clinical characteristics, preoperative complications, and the surgical methods employed in our series of pediatric CBD cases. Univariate analysis indicated that the morphological subtype and the presence of cholecystitis or cholangitis affected the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy. Patients with cystic biliary dilatations had longer operative times than those with fusiform biliary dilatations, and this was especially true for those with larger cysts. Patients with cystic biliary dilatations often presented with displacement of vessels, severe biliary obstruction, and coagulopathy, consequently making surgery more difficult with a greater risk of injury to the surrounding tissues. This in turn increased the operative time, and these results were comparable to the previously reported [17]. In addition, we compared operative times for laparoscopy and conventional open surgery, but found no statistically significant difference between the two groups and this is consistent with the report by Diao *et al*. [18].

The presence of cholecystitis was another factor affecting the operative time. Forty of our cases presented with cholecystitis, of which 75.0% were defined as having CBD with PBM. Sugai *et al*. compared the preoperative ultrasound measurements of gallbladder wall thickness and the actual wall thickness measurements in resected gallbladder specimens; the results showed a concordance rate of 89%, with 25.9%

cases showing chronic inflammation [19]. Park *et al*. reported that CBD cases with PBM were often found to have clinical cholecystitis, and that this was strongly related to inflammatory changes in the duct and periductular structures [20]. It is possible that chronic cholecystitis leads to adhesion to the surrounding tissue, increasing the difficulty of procedures and dissection time.

Cholangitis is a common preoperative comorbidity that may increase the operative time in CBD. Morine *et al*. reported on 952 pediatric biliary dilatation cases and found 16.2% with cholangitis [21]. Ouaissi *et al*. and Visser *et al*. reported a series of CBD cases and found 26.3% and 21% with cholangitis, respectively [22, 23]. Lal *et al*. compared cases with and without infective complications, concluding that CBD with infective complications requires meticulous planning and a multimodal approach, with more time required for the operative procedure [24]. In our study, 20.0% of cases had infective complications. Multiple logistic regression confirmed that the presence of cholangitis was an independent factor affecting the operative time, suggesting that such cases need more operative time and meticulous planning to decrease the risk of postoperative complications. Qiao *et al*. reported that pediatric CBD with cholangitis led to increased operative time and postoperative complications, which was further supported by Diao *et al*. [10, 17]. It is conceivable that the prolonged operative time during complete cyst excision and Roux-en-Y hepaticojejunostomy contributes to the morbidity of postoperative complications. However, as the operative time also reflects the difficulty of surgical procedures and the experience of surgeons, efforts were made to ensure that the pediatric surgeons involved in this study across all four centers were similarly and suitably trained. While the operative time is not an adequate surrogate for predicting long-term

postoperative complications, our findings highlight the importance not only in planning surgical intervention for pediatric CBD patients but also in the scheduling of cases and the effective use of operating room time to improve the quality of care.

Limitations

Our study has a number of limitations. Firstly, the sample size was relatively small, as CBD is a rare pediatric disease and thus selection bias may have been a factor. Secondly, this was a retrospective multicenter study of only 3-years duration. A prospective multicenter study over a longer period is necessary.

Conclusions

In this series of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases, the median operative time was 215 minutes (range 120-430 minutes). The morphological CBD subtype and the presence of cholecystitis or cholangitis affected the operative time, with cholangitis as an independent risk factor. These findings are potentially important and will assist in planning surgical intervention for pediatric CBD patients to improve the quality of care.

Authors' Contributions

SH and JW designed the study, WG, SH, FF, ZY,YD, and JZ, collected data, YD, JZ ,FF and ZY analyzed data, WG, SH, and JW wrote the manuscript, and all authors read and approved the final version of manuscript.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases. The operative time in 80% (52/65) is less than 300 minute.

Figure 2. A one-year old female pediatric patient with CBD (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

Figure 3. A three-year old female pediatric patient with CBD (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

Figure 4. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases from four cohorts. There was no significant difference in the distribution of operative time among the four surgical teams (Chi-Square = 0.7189, $p = 0.9489$).

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

Table 1. Risk factors associate with operative time in pediatric CBD cases

Variables	Duration surgery< 300 minutes (52 cases)	Duration surgery≥ 300 minutes (13 cases)	*p* value
Gender (F)	35	5	0.0559
Infant	7	2	1.0000
Type IV	22	5	
Type I	30	8	0.7472
Fusiformis*	24	1	0.0114
Cyst stones	7	4	0.2092
Biliary tract infection***	3	10	<0.0001
Abdominal pain	41	9	0.4617
Jaundice	16	3	0.7385
Mass	15	3	1.0000
Vomit	33	10	0.2551
Fever	25	10	0.0620
Cholecystitis*	28	12	0.0114
Pancreatitis	2	0	1.0000
Laparoscopy	19	4	0.6972
Preoperative complications	10	-	0.0856
Gastrointestinal polyps	1	-	
Cyst rupture	1	-	
Appendicitis	2	-	
Ascites	1	-	
Pleural effusion	1	-	
Upper respiratory tract infection	4	-	

*p<0.05, ***p<0.001.

Table 2. Logistic regression model for factors affecting operative time in pediatric CBD cases

Variable	Chi-Square	OR	95%Wald Confidence Limits	P value
Biliary tract infection***	11.2195	30.609	4.134-226.607	0.0008
Cystiform	1.1194	3.377	0.354-32.191	0.2900
Cholecystitis	1.8755	5.892	0.465-74.573	0.1708

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.4191)
***p<0.001.

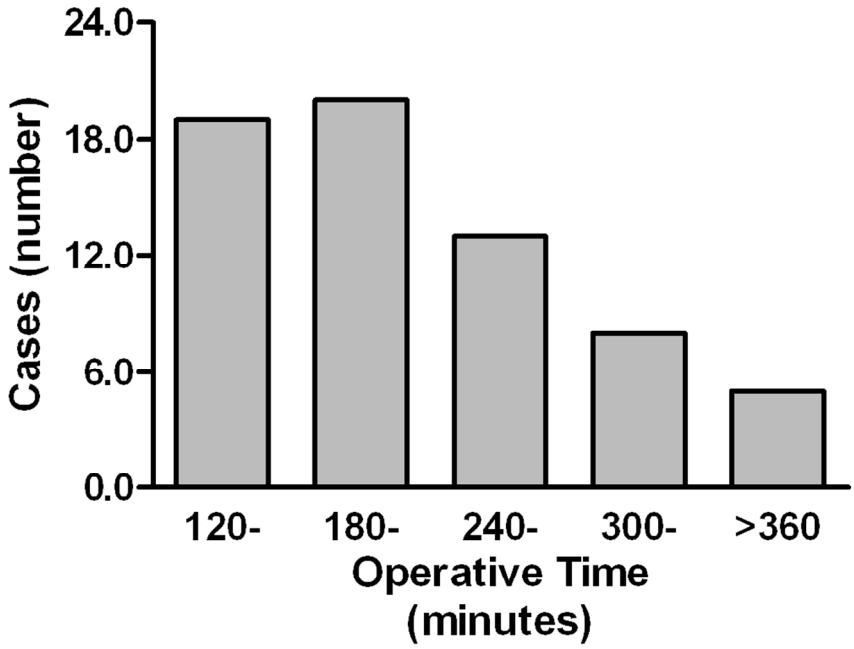

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases. The operative time in 80% (52/65) is less than 300 minute.

100x73mm (300 x 300 DPI)

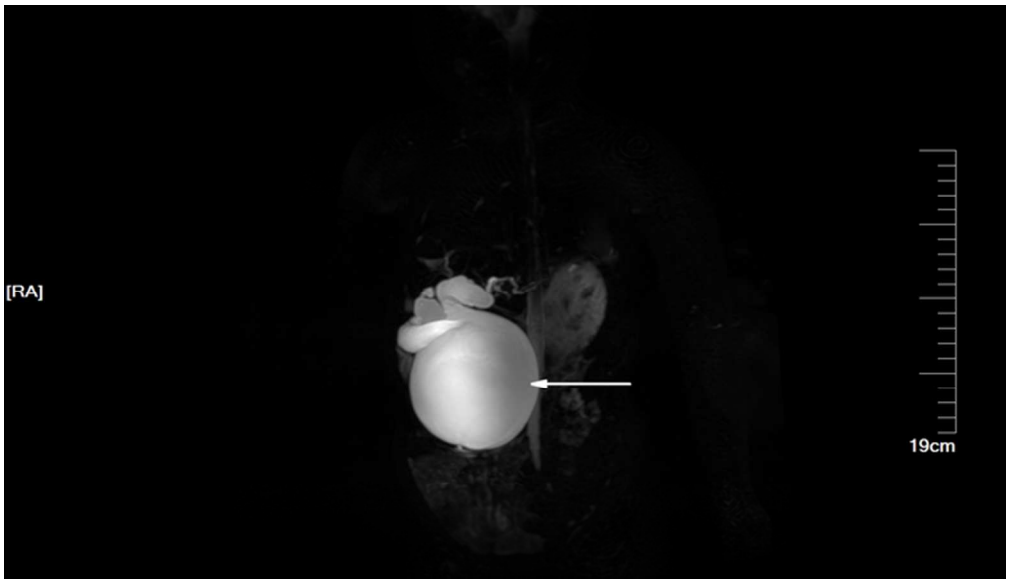

Figure 2. A one-year old female pediatric patient with CBD (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

31x18mm (600 x 600 DPI)

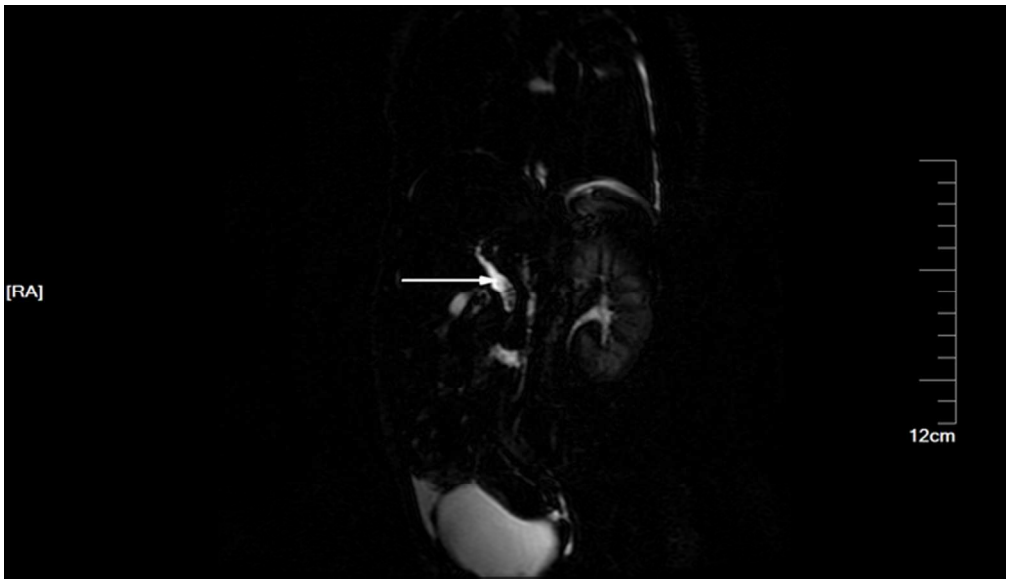

Figure 3. A three-year old female pediatric patient with CBD (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

31x18mm (600 x 600 DPI)

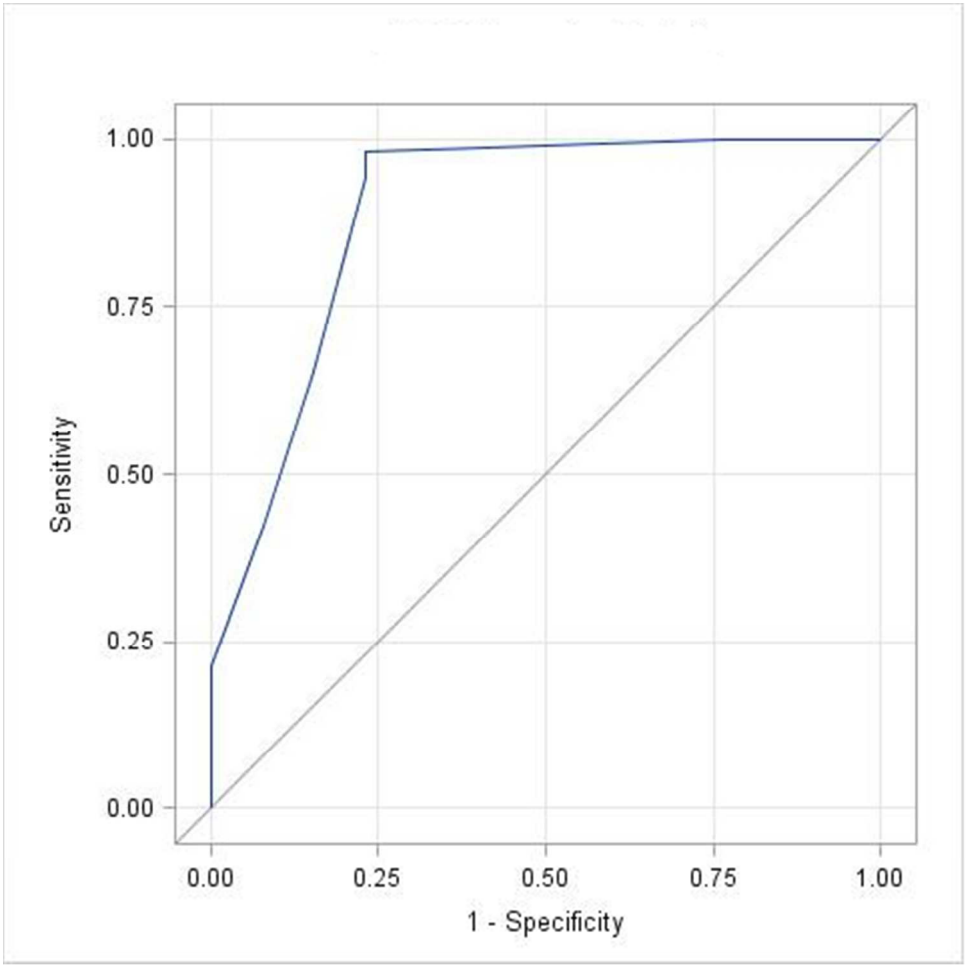

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

127x127mm (96 x 96 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6
Bias	9	Describe any efforts to address potential sources of bias	Page 11
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen	N/A

		and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6-7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 7
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Page 7-8
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	

Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	None

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital choledochal malformation: a retrospective case study in southeast China

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Competing interests

The authors declare that they have no competing interests.

Abstract

Objective

The aim of this study was to assess factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital choledochal malformation (CCM).

Design

This is a retrospective case-control study. A 3-year retrospective study was performed between January 2013 and December 2015 in four centers in China, to detected factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with CCM.

Setting

This is a retrospective chart review of pediatric patients with CCM in four large hospital in China.

Participants

65 pediatric patients with CCM was conducted in four centers, and included review of information on demographics, clinical characteristics, preoperative complications, and surgical methods, if available.

Interventions

Univariate and multivariate logistical regression were used, we measured factors significantly affecting the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases.

Results

Twenty-three of the 65 case surgeries were performed using laparoscopic technique, and 42 surgeries were performed by conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). The morphological subtype

and the presence of cholecystitis or cholangitis were the only factors found to affect the operative time (p<0.05). Logistic regression analysis confirmed cholangitis as an independent risk factor.

Conclusions

The morphological subtype and the presence of cholecystitis or cholangitis affect the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, whereas cholangitis is an independent risk factor.

Keywords: congenital choledochal malformation, hepaticojejunostomy, operative time, influencing factors,

Strengths and limitations of this study

A retrospective study was carried out in four centers over a 3-year period. A stepwise logistic regression analysis of 65 pediatric CCM cases in an attempt to identify factors affecting the operative time.

The morphological subtype and the presence of cholecystitis or cholangitis affect the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, whereas cholangitis is an independent risk factor.

The sample size was relatively small, as CCM is a rare pediatric disease and thus selection bias may have been a factor.

Introduction

Congenital choledochal malformation (CCM) is a rare congenital anomaly that presents as extra and/or intrahepatic bile duct dilatation, and its incidence is more frequent in Asia than in Western countries [1-4]. The majority of cases seen in the clinic are in infants and children. Most CCM cases present clinically with abdominal pain, jaundice, and a mass, sometimes accompanied by vomiting and fever. CCM leads to higher rates of cholestasis, stone formation, pancreatitis, hyperplasia, and epithelial atypical growth of the bile duct or gallbladder, as well as tumor formation thought to be caused by pancreaticobilliary maljunction (PBM) with two-way reflux of bile and pancreatic juice [5-8].

Early prevention of long-term complications such as recurrent cholangitis, gallstones, pancreatitis, and especially, malignant tumors in the bile duct and gallbladder is desirable. Complete excision of the cyst and Roux-en-Y hepaticojejunostomy is the main option for CCM treatment in children [9-11]. Cyst excision and hepaticojejunostomy by either open surgery or laparoscopy in pediatric CCM are feasible and popularly undertaken [12-13]. Jackson *et al*. and Jenkins *et al*. reported that the complexity and difficulty of a surgical procedure is reflected by the operative time [14-15]. Qiao *et al*. reported on an extensive series of CCM cases in 7 centers and found that postoperative complications were associated with longer operative time [11].

Up to now, few studies have focused on factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases. We retrospectively studied the clinical presentation and surgical management of 65

pediatric CCM cases that had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy between January 2013 and December 2015 in 4 centers in southeast China, in an attempt to identify factors affecting the operative time.

Materials and Methods

Study subjects

Data was collected after study protocol approval from the institutional review boards of each participating institution and informed consent was signed by the guardians of the subjects. All methods were carried out in strict accordance with the relevant institution guidelines regarding the acquisition and use of human tissues. Sixty-five pediatric CCM cases were recruited into this clinical study. Twenty-nine subjects were from the Children's Hospital of Soochow University, 11 subjects from Xuzhou Children's hospitals, 12 subjects from the Affiliated Hospital of Guizhou Medical College, and 13 subjects from the Affiliated Hospital of Nantong Medical College. All patients were diagnosed by ultrasound, CT, MRCP, and IOC. All patients were operated on with cyst excision and hepaticojejunostomy using the same laparoscopic or conventional open surgical approach, performed by pediatric surgeons from the 4 hospital surgical teams. All procedures were performed by expert pediatric surgeons who have advanced skills and are capable of independently completing surgical procedures in cases with huge choledochal cysts. With respect to the laparoscopic procedure, 23 cases in this group were operated with the same laparoscopic surgical approach performed by surgeons who had participated at laparoscopic surgery studying sessions. The operative times (from incision to skin closure) of each surgical team were analyzed among the 4 subject cohorts.

Factor analysis

The patients were assessed for gender, age, common bile duct shape, Todani type, and presence of a stone in the cyst. Ages were grouped as infant (<1 year of age) or pediatric (>1 year of age). Common bile duct shape, Todani type, and presence of cyst stones were assessed by ultrasound and MRCP combined with IOC. Common bile duct shape was classified as either cystiform or fusiform. Clinical symptoms at presentation, preoperative complications, operative methods (conventional open or laparoscopic cyst excision and hepaticojejunostomy), and operative time were analyzed. Cholangitis was defined as any symptom of the Charcot triad (abdominal pain, jaundice, or fever) with an increase in total bilirubin, AST, and ALT levels above the normal range. Cholecystitis was confirmed by ultrasound combined with pathological findings. Eighty percent (52/65) of cases the operative time is less than 300 minutes. The operative time was grouped as <300 minutes or ≥300 minutes (Figure 1).

Patient and Public involvement

Patient and Public were not involvement.

Statistical analysis

Analyses were performed with SAS software, JMP 9.0 (SAS Institute, Cary, NC, USA). Data are presented as number (*n*), percentage, and median. Multi-group ordered variable data comparisons were performed using Kruskal–Wallis test. Univariate comparisons were performed using nonparametric one-way Wilcoxon rank sum, χ^2, or T test, depending on the statistical distribution. To evaluate risk factors affecting the operative time, logistic regression analysis was performed. The ROC curve was used to assess the accuracy of the logistic regression model. $p<0.05$ was

considered statistically significant.

Results

Clinical characteristics and general findings of pediatric CCM cases

The present clinical study comprised 65 pediatric CCM cases diagnosed by ultrasound, computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), and intraoperative cholangiography (IOC). Among the 65 pediatric CCM cases, there were 25 (38.5%) male and 40 (61.5%) female patients with CCM. The median age of the patients was 3 years (range 3 months to 13 years). Fifty-two cases were defined as PBM by MRCP with IOC. The morphological subtype of bile duct dilatation was cystic (Figure 2) in 40 cases (8 were large cysts descending into the introitus of the pelvis) and fusiform (Figure 3) in 25 cases. All 65 cases underwent complete cyst excision and Roux-en-Y hepaticojejunostomy. Twenty-three cases were performed using laparoscopic technique, whereas the other 42 cases were performed using conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). Figure 4 and supplemental table 1 illustrates the distribution of operative time between the 4 centers, and there was no significant difference in the operative time across centers.

Related risk factors affecting the operative time in pediatric CCM cases

Table 1 depicts a comparison of the clinical characteristics, preoperative complications, and surgical methods for the <300 minutes and ≥300 minutes operative time groups. Supplemental table 2 depicts a comparison of the operative time of surgical methods between laparoscopic surgery and open surgery. Univariate analysis revealed that the morphological subtype and the presence of cholecystitis or

cholangitis affected the operative time (p<0.05). No other factors were found to affect the operative time. Logistic regression analysis was performed to assess independent predictors that affect the operative time in 65 pediatric CCM cases. Again, the presence of cholangitis was the most important risk factor (Table 2). These data agreed with Hosmer and Lemeshow's goodness-of-fit test (p=0.4191). To further assess the accuracy of logistic regression model for the obtained results, analysis of the receiver operating characteristic (ROC) curve was performed with the area under the curve (AUC) at 0.8913 (Figure 5).

Discussion

General findings

Due to the obstruction of bile or pancreatic juice discharge, pediatric CCM cases often present with abdominal pain, jaundice, and a mass, and harbor a risk of malignancy as well as other serious complications. Prophylactic surgery is recommended, once the diagnosis is confirmed. The operative time has been used previously as a measure of operative difficulty and complexity [14-15]. Sorokin *et al*. reported that increased postoperative complications were associated with the prolonged operative time [16]. Qiao *et al*. reported on 956 pediatric cases with CCM, in which all the patients had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy [11]. The mean operation time in that study was 3.52 hours (range 2.21-5.75 hours). In addition, they found that postoperative complications were associated with the increased operative time. Their operative time was similar to that in our study. However, there has been less research focusing on the risk factors affecting operative time in CCM surgery. Our study on a multicenter cohort of pediatric patients who underwent complete cyst excision and hepaticojejunostomy showed the operative time ranged

from 120-430 minutes, similar to the previously reported [17]. Moreover, we also focused on factors that potentially affect the operative time.

Factors affecting the operative time in pediatric CCM cases

To investigate factors that potentially influence the operative time, we described the clinical characteristics, preoperative complications, and the surgical methods employed in our series of pediatric CCM cases. Univariate analysis indicated that the morphological subtype and the presence of cholecystitis or cholangitis affected the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy. Patients with cystic biliary dilatations had longer operative times than those with fusiform biliary dilatations, and this was especially true for those with larger cysts. Patients with cystic biliary dilatations often presented with displacement of vessels, severe biliary obstruction, and coagulopathy, consequently making surgery more difficult with a greater risk of injury to the surrounding tissues. This in turn increased the operative time, and these results were comparable to the previously reported [18]. In addition, we compared operative times for laparoscopy and conventional open surgery. We found that laparoscopy surgery took longer time than conventional open surgery, however, we found no statistically significant difference between the two groups and this is consistent with the report by Diao et al. [19].

The presence of cholecystitis was another factor affecting the operative time. Forty of our cases presented with cholecystitis, of which 75.0% were defined as having CCM with PBM. Sugai *et al*. compared the preoperative ultrasound measurements of gallbladder wall thickness and the actual wall thickness measurements in resected gallbladder specimens; the results showed a concordance rate of 89%, with 25.9%

cases showing chronic inflammation [20]. Park *et al*. reported that CCM cases with PBM were often found to have clinical cholecystitis, and that this was strongly related to inflammatory changes in the duct and periductular structures [21]. It is possible that chronic cholecystitis leads to adhesion to the surrounding tissue, increasing the difficulty of procedures and dissection time.

Cholangitis is a common preoperative comorbidity that may increase the operative time in CCM. Morine *et al*. reported on 952 pediatric biliary dilatation cases and found 16.2% with cholangitis [22]. Ouaissi *et al*. and Visser *et al*. reported a series of CCM cases and found 26.3% and 21% with cholangitis, respectively [23,24]. Lal *et al*. compared cases with and without infective complications, concluding that CCM with infective complications requires meticulous planning and a multimodal approach, with more time required for the operative procedure [25]. In our study, 20.0% of cases had infective complications. Multiple logistic regression confirmed that the presence of cholangitis was an independent factor affecting the operative time, suggesting that such cases need more operative time and meticulous planning to decrease the risk of postoperative complications. Qiao *et al*. reported that pediatric CCM with cholangitis led to increased operative time and postoperative complications, which was further supported by Diao *et al*. [11,18]. It is conceivable that the prolonged operative time during complete cyst excision and Roux-en-Y hepaticojejunostomy contributes to the morbidity of postoperative complications. However, as the operative time also reflects the difficulty of surgical procedures and the experience of surgeons, efforts were made to ensure that the pediatric surgeons involved in this study across all four centers were similarly and suitably trained. While the operative time is not an adequate surrogate for predicting long-term

postoperative complications, our findings highlight the importance not only in planning surgical intervention for pediatric CCM patients but also in the scheduling of cases and the effective use of operating room time to improve the quality of care.

Limitations

Our study has a number of limitations. Firstly, the sample size was relatively small, as CCM is a rare pediatric disease and thus selection bias such as surgical methods may have been a factor. Secondly, this was a retrospective multicenter study of only 3-years duration. A prospective multicenter study over a longer period is necessary.

Conclusions

In this series of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, the median operative time was 215 minutes (range 120-430 minutes). The morphological CCM subtype and the presence of cholecystitis or cholangitis affected the operative time, with cholangitis as an independent risk factor. These findings are potentially important and will assist in planning surgical intervention for pediatric CCM patients to improve the quality of care.

Authors' Contributions

SH and JW designed the study, WG, SH, FF, ZY, YD, and JZ, collected data, YD, JZ ,FF and ZY analyzed data, WG, SH, and JW wrote the manuscript, and all authors read and approved the final version of manuscript.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases. The operative time in 80% (52/65) is less than 300 minutes.

Figure 2. A one-year old female pediatric patient with CCM (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

Figure 3. A three-year old female pediatric patient with CCM (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

Figure 4. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases from four cohorts. There was no significant difference in the distribution of operative time among the four surgical teams (Chi-Square = 0.7189, $p = 0.9489$).

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

Table 1. Risk factors associate with operative time in pediatric CCM cases

Variables	Duration surgery< 300 minutes (52 cases)	Duration surgery≥ 300 minutes (13 cases)	*p* value
Gender (F)	35	5	0.0559
Infant	7	2	1.0000
Type IV	22	5	
Type I	30	8	0.7472
Fusiformis*	24	1	0.0114
Cyst stones	7	4	0.2092
Biliary tract infection***	3	10	<0.0001
Abdominal pain	41	9	0.4617
Jaundice	16	3	0.7385
Mass	15	3	1.0000
Vomit	33	10	0.2551
Fever	25	10	0.0620
Cholecystitis*	28	12	0.0114
Pancreatitis	2	0	1.0000
Laparoscopy	19	4	0.6972
Preoperative complications	10	-	0.0856
Gastrointestinal polyps	1	-	
Cyst rupture	1	-	
Appendicitis	2	-	
Ascites	1	-	
Pleural effusion	1	-	
Upper respiratory tract infection	4	-	

*p<0.05, ***p<0.001.

Table 2. Logistic regression model for factors affecting operative time in pediatric CCM cases

Variable	Chi-Square	OR	95%Wald Confidence Limits	P value
Biliary tract infection***	11.2195	30.609	4.134-226.607	0.0008
Cystiform	1.1194	3.377	0.354-32.191	0.2900
Cholecystitis	1.8755	5.892	0.465-74.573	0.1708

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.4191)
***p<0.001.

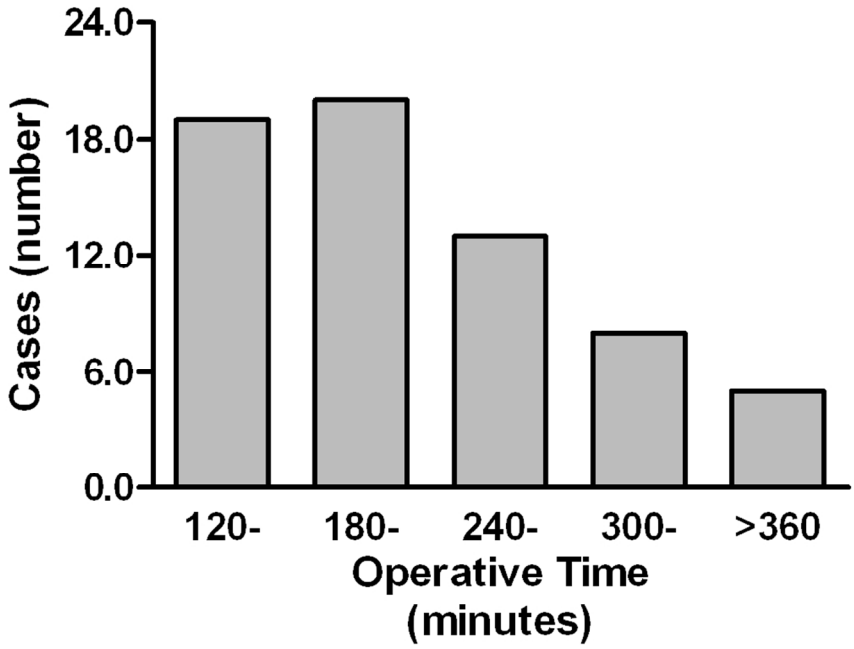

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases. The operative time in 80% (52/65) is less than 300 minute.

100x73mm (300 x 300 DPI)

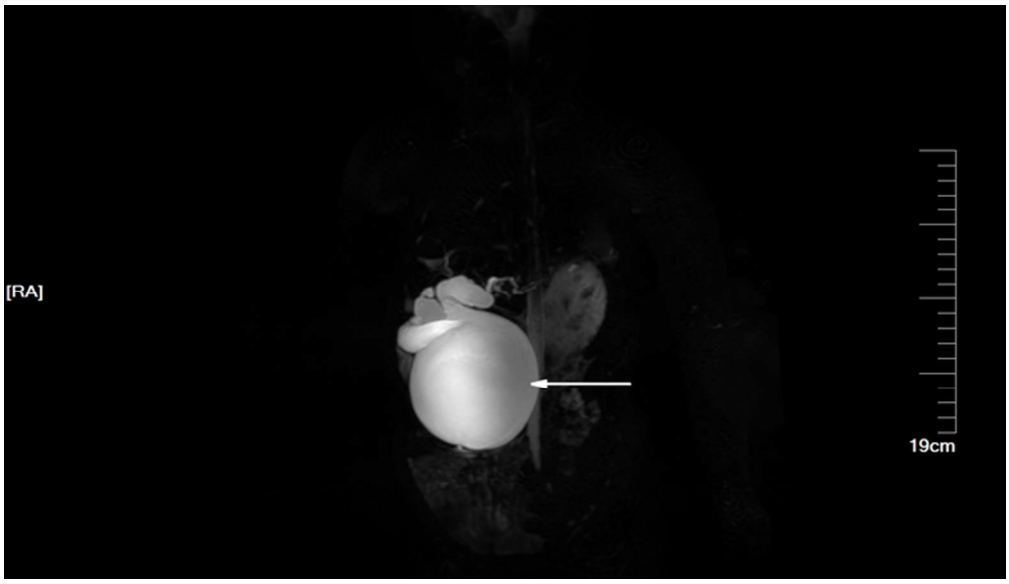

Figure 2. A one-year old female pediatric patient with CBD (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

31x18mm (600 x 600 DPI)

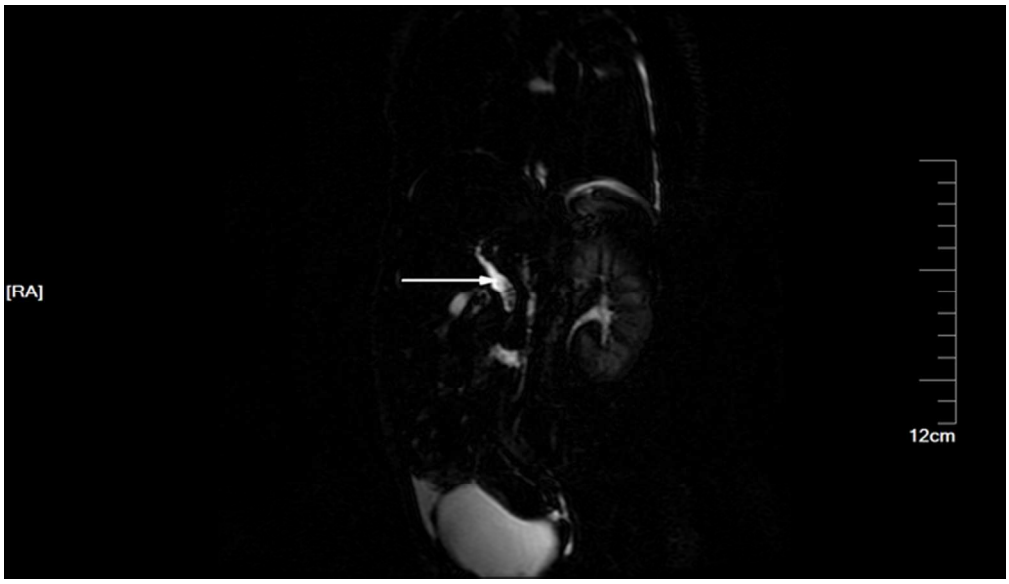

Figure 3. A three-year old female pediatric patient with CBD (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

31x18mm (600 x 600 DPI)

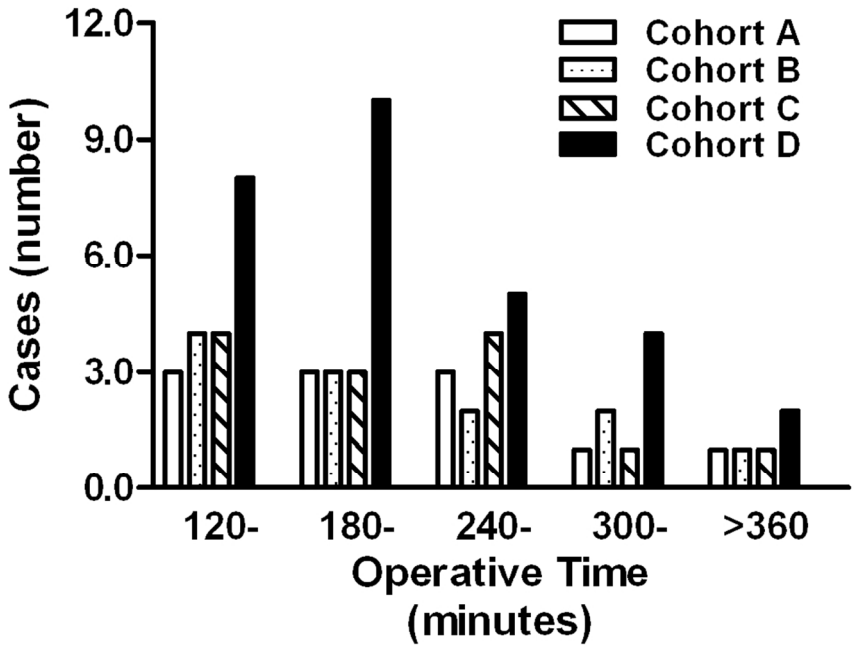

Figure 4. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases from four cohorts. There was no significant difference in the distribution of operative time among the four surgical teams (Chi-Square = 0.7189, p = 0.9489).

100x73mm (300 x 300 DPI)

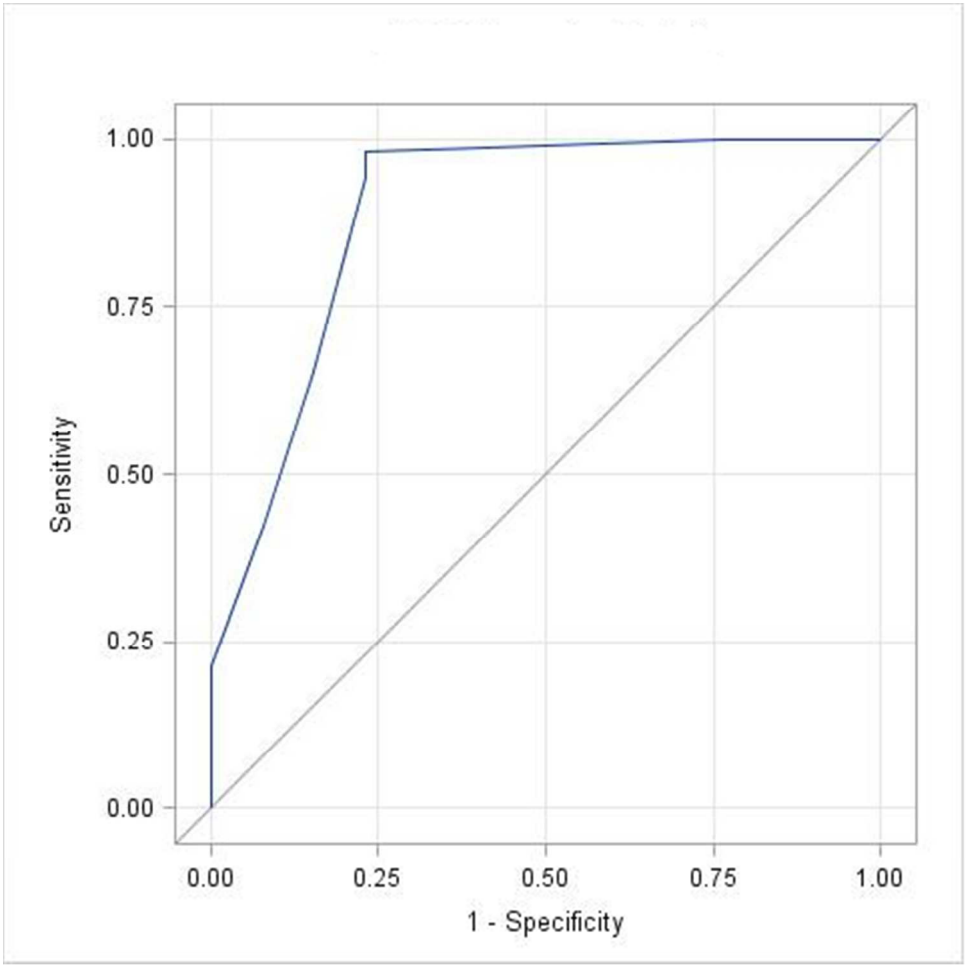

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

127x127mm (96 x 96 DPI)

Supplemental table 1. Analysis operative time undergone cyst excision and Roux-en-Y hepaticojejunostomy for children in four cohorts

varable	Cohort A(11)	Cohort B(12)	Cohort C(13)	Cohort D(29)
Mean±SD	236.27±79.233	235.42±84.972	233.08±70.045	227.24±80.073

Pair-wise comparison showed there is no significant difference between every two groups, Cohort A Vs Cohort B(p=1.0000) , Cohort A Vs Cohort C(p=0.8860) , Cohort A Vs Cohort D(p=0.5748) , Cohort B Vs Cohort C(p=0.9356), Cohort B Vs Cohort D(p=0.8973) and Cohort C Vs Cohort D(p=0.6435).

Supplemental table 2. Analysis operative time between laparoscopic surgery and open surgery undergone cyst excision and Roux-en-Y hepaticojejunostomy

group	N	mean± SD	P value
Laparoscopy	23	251.65±73.58	0.0825
open surgery	42	220.38±77.76	

Wilcoxon two-sample test

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6
Bias	9	Describe any efforts to address potential sources of bias	Page 11
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen	N/A

		and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6-7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 7
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Page 7-8
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	

Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	None

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital choledochal malformation: a retrospective case study in southeast China

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Factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital choledochal malformation: a retrospective case study in southeast China

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Competing interests

The authors declare that they have no competing interests.

Abstract

Objective

The aim of this study was to assess factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with congenital choledochal malformation (CCM).

Design

This is a retrospective case study. A 3-year retrospective study was performed between January 2013 and December 2015 in four centers in China, to detected factors affecting operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases with CCM.

Setting

This is a retrospective chart review of pediatric patients with CCM in four large hospital in southeast China.

Participants

65 pediatric patients with CCM was conducted in four centers, and included review of information on demographics, clinical characteristics, preoperative complications, and surgical methods, if available.

Interventions

Univariate and multivariate logistical regression were used, we measured factors significantly affecting the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases.

Results

Twenty-three of the 65 case surgeries were performed using laparoscopic technique, and 42 surgeries were performed by conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). The morphological subtype

and the presence of cholecystitis or cholangitis were the only factors found to affect the operative time (p<0.05). Logistic regression analysis confirmed cholangitis as an independent risk factor.

Conclusions

The morphological subtype and the presence of cholecystitis or cholangitis affect the operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, whereas cholangitis is an independent risk factor.

Keywords: congenital choledochal malformation, hepaticojejunostomy, operative time, influencing factors,

Strengths and limitations of this study

A multicenter retrospective study was carried out in southeast China over a 3-year period.

A stepwise logistic regression analysis of 65 pediatric CCM cases in an attempt to identify factors affecting the operative time. And the accuracy of logistic regression model for the obtained results was further assessed by the receiver operating characteristic curve(ROC).

The sample size was relatively small, as CCM is a rare pediatric disease and thus selection bias may have been a factor.

Introduction

Congenital choledochal malformation (CCM) is a rare congenital anomaly that presents as extra and/or intrahepatic bile duct dilatation, and its incidence is more frequent in Asia than in Western countries [1-4]. The majority of cases seen in the clinic are in infants and children. Most CCM cases present clinically with abdominal pain, jaundice, and a mass, sometimes accompanied by vomiting and fever. CCM leads to higher rates of cholestasis, stone formation, pancreatitis, hyperplasia, and epithelial atypical growth of the bile duct or gallbladder, as well as tumor formation thought to be caused by pancreaticobilliary maljunction (PBM) with two-way reflux of bile and pancreatic juice [5-8].

Early prevention of long-term complications such as recurrent cholangitis, gallstones, pancreatitis, and especially, malignant tumors in the bile duct and gallbladder is desirable. Complete excision of the cyst and Roux-en-Y hepaticojejunostomy is the main option for CCM treatment in children [9-11]. Cyst excision and hepaticojejunostomy by either open surgery or laparoscopy in pediatric CCM are feasible and popularly undertaken [12-13]. Jackson *et al*. and Jenkins *et al*. reported that the complexity and difficulty of a surgical procedure is reflected by the operative time [14-15]. Qiao *et al*. reported on an extensive series of CCM cases in 7 centers and found that postoperative complications were associated with longer operative time [11].

Up to now, few studies have focused on factors affecting operative time of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases. We retrospectively studied the clinical presentation and surgical management of 65

pediatric CCM cases that had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy between January 2013 and December 2015 in 4 centers in southeast China, in an attempt to identify factors affecting the operative time.

Materials and Methods

Study subjects

Data was collected after study protocol approval from the institutional review boards of each participating institution and informed consent was signed by the guardians of the subjects. All methods were carried out in strict accordance with the relevant institution guidelines regarding the acquisition and use of human tissues. Sixty-five pediatric CCM cases were recruited into this clinical study. Twenty-nine subjects were from the Children's Hospital of Soochow University, 11 subjects from Xuzhou Children's hospitals, 12 subjects from the Affiliated Hospital of Guizhou Medical College, and 13 subjects from the Affiliated Hospital of Nantong Medical College. All patients were diagnosed by ultrasound, CT, MRCP, and IOC. All patients were operated on with cyst excision and hepaticojejunostomy using the same laparoscopic or conventional open surgical approach, performed by pediatric surgeons from the 4 hospital surgical teams. All procedures were performed by expert pediatric surgeons who have advanced skills and are capable of independently completing surgical procedures in cases with huge choledochal cysts. With respect to the laparoscopic procedure, 23 cases in this group were operated with the same laparoscopic surgical approach performed by surgeons who had participated at laparoscopic surgery studying sessions. The operative times (from incision to skin closure) of each surgical team were analyzed among the 4 subject cohorts.

Factor analysis

The patients were assessed for gender, age, common bile duct shape, Todani type, and presence of a stone in the cyst. Ages were grouped as infant (<1 year of age) or pediatric (>1 year of age). Common bile duct shape, Todani type, and presence of cyst stones were assessed by ultrasound and MRCP combined with IOC. Common bile duct shape was classified as either cystiform or fusiform. Clinical symptoms at presentation, preoperative complications, operative methods (conventional open or laparoscopic cyst excision and hepaticojejunostomy), and operative time were analyzed. Cholangitis was defined as any symptom of the Charcot triad (abdominal pain, jaundice, or fever) with an increase in total bilirubin, AST, and ALT levels above the normal range. Cholecystitis was confirmed by ultrasound combined with pathological findings. Eighty percent (52/65) of cases the operative time is less than 300 minutes. The operative time was grouped as <300 minutes or ≥300 minutes (Figure 1).

Patient and Public involvement

Patient and Public were not involvement.

Statistical analysis

Analyses were performed with SAS software, JMP 9.0 (SAS Institute, Cary, NC, USA). Data are presented as number (*n*), percentage, and median. Multi-group ordered variable data comparisons were performed using Kruskal–Wallis test. Univariate comparisons were performed using nonparametric one-way Wilcoxon rank sum, χ^2, or T test, depending on the statistical distribution. To evaluate risk factors affecting the operative time, logistic regression analysis was performed. The ROC curve was used to assess the accuracy of the logistic regression model. $p<0.05$ was

considered statistically significant.

Results

Clinical characteristics and general findings of pediatric CCM cases

The present clinical study comprised 65 pediatric CCM cases diagnosed by ultrasound, computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), and intraoperative cholangiography (IOC). Among the 65 pediatric CCM cases, there were 25 (38.5%) male and 40 (61.5%) female patients with CCM. The median age of the patients was 3 years (range 3 months to 13 years). Fifty-two cases were defined as PBM by MRCP with IOC. The morphological subtype of bile duct dilatation was cystic (Figure 2) in 40 cases (8 were large cysts descending into the introitus of the pelvis) and fusiform (Figure 3) in 25 cases. All 65 cases underwent complete cyst excision and Roux-en-Y hepaticojejunostomy. Twenty-three cases were performed using laparoscopic technique, whereas the other 42 cases were performed using conventional open surgery. The median operative time was 215 minutes (range 120-430 minutes). Figure 4 and supplemental table 1 illustrates the distribution of operative time between the 4 centers, and there was no significant difference in the operative time across centers.

Related risk factors affecting the operative time in pediatric CCM cases

Table 1 depicts a comparison of the clinical characteristics, preoperative complications, and surgical methods for the <300 minutes and ≥300 minutes operative time groups. Supplemental table 2 depicts a comparison of the operative time of surgical methods between laparoscopic surgery and open surgery. Univariate analysis revealed that the morphological subtype and the presence of cholecystitis or

cholangitis affected the operative time (p<0.05). No other factors were found to affect the operative time. Logistic regression analysis was performed to assess independent predictors that affect the operative time in 65 pediatric CCM cases. Again, the presence of cholangitis was the most important risk factor (Table 2). These data agreed with Hosmer and Lemeshow's goodness-of-fit test (p=0.4191). To further assess the accuracy of logistic regression model for the obtained results, analysis of the receiver operating characteristic (ROC) curve was performed with the area under the curve (AUC) at 0.8913 (Figure 5).

Discussion

General findings

Due to the obstruction of bile or pancreatic juice discharge, pediatric CCM cases often present with abdominal pain, jaundice, and a mass, and harbor a risk of malignancy as well as other serious complications. Prophylactic surgery is recommended once the diagnosis is confirmed. The operative time has been used previously as a measure of operative difficulty and complexity [14-15]. Sorokin *et al*. reported that increased postoperative complications were associated with the prolonged operative time [16]. Qiao *et al*. reported on 956 pediatric cases with CCM, in which all the patients had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy [11]. The mean operation time in that study was 3.52 hours (range 2.21-5.75 hours). In addition, they found that postoperative complications were associated with the increased operative time. Their operative time was similar to that in our study. However, there has been less research focusing on the risk factors affecting operative time in CCM surgery. Our study on a multicenter cohort of pediatric patients who underwent complete cyst excision and hepaticojejunostomy showed the operative time ranged

from 120-430 minutes, similar to the previously reported [17]. Moreover, we also focused on factors that potentially affect the operative time.

Factors affecting the operative time in pediatric CCM cases

To investigate factors that potentially influence the operative time, we described the clinical characteristics, preoperative complications, and the surgical methods employed in our series of pediatric CCM cases. Univariate analysis indicated that the morphological subtype and the presence of cholecystitis or cholangitis affected the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy. Patients with cystic biliary dilatations had longer operative times than those with fusiform biliary dilatations, and this was especially true for those with larger cysts. Patients with cystic biliary dilatations often presented with displacement of vessels, severe biliary obstruction, and coagulopathy, consequently making surgery more difficult with a greater risk of injury to the surrounding tissues. This in turn increased the operative time, and these results were comparable to the previously reported [18]. In indicates that the operative difficulty and complexity of patients with cystic biliary dilatations is more difficult than those with fusiform biliary dilatations. In addition, we compared operative times for laparoscopy and conventional open surgery. We found that laparoscopy surgery took longer time than conventional open surgery, however, we found no statistically significant difference between the two groups and this is consistent with the report by Diao et al. [19].

The presence of cholecystitis was another factor affecting the operative time. Forty of our cases presented with cholecystitis, of which 75.0% were defined as having CCM with PBM. Sugai *et al*. compared the preoperative ultrasound measurements of

gallbladder wall thickness and the actual wall thickness measurements in resected gallbladder specimens; the results showed a concordance rate of 89%, with 25.9% cases showing chronic inflammation [20]. Park *et al*. reported that CCM cases with PBM were often found to have clinical cholecystitis, and that this was strongly related to inflammatory changes in the duct and periductular structures [21]. It is possible that chronic cholecystitis leads to adhesion to the surrounding tissue, increasing the difficulty of procedures and dissection time. In PBM with cholecystitis, meticulous planning is needed to decrease the risk of operative complications.

Cholangitis is a common preoperative comorbidity that may increase the operative time in CCM. Morine *et al*. reported on 952 pediatric biliary dilatation cases and found 16.2% with cholangitis [22]. Ouaissi *et al*. and Visser *et al*. reported a series of CCM cases and found 26.3% and 21% with cholangitis, respectively [23,24]. Lal *et al*. compared cases with and without infective complications, concluding that CCM with infective complications requires meticulous planning and a multimodal approach, with more time required for the operative procedure [25]. In our study, 20.0% of cases had infective complications. Multiple logistic regression confirmed that the presence of cholangitis was an independent factor affecting the operative time, suggesting that such cases need more operative time and meticulous planning to decrease the risk of postoperative complications. Qiao *et al*. reported that pediatric CCM with cholangitis led to increased operative time and postoperative complications, which was further supported by Diao *et al*. [11,18]. It is conceivable that the prolonged operative time during complete cyst excision and Roux-en-Y hepaticojejunostomy contributes to the morbidity of postoperative complications. However, as the operative time also reflects the difficulty of surgical procedures and

the experience of surgeons, efforts were made to ensure that the pediatric surgeons involved in this study across all four centers were similarly and suitably trained. While the operative time is not an adequate surrogate for predicting long-term postoperative complications, our findings highlight the importance not only in planning surgical intervention for pediatric CCM patients but also in the scheduling of cases and the effective use of operating room time to improve the quality of care.

Limitations

Our study has a number of limitations. Firstly, the sample size was relatively small, as CCM is a rare pediatric disease and thus selection bias such as surgical methods may have been a factor. Secondly, this was a retrospective multicenter study of only 3-years duration. A prospective multicenter study over a longer period is necessary.

Conclusions

In this series of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, the median operative time was 215 minutes (range 120-430 minutes). The morphological CCM subtype and the presence of cholecystitis or cholangitis affected the operative time, with cholangitis as an independent risk factor. These findings are potentially important and will assist in planning surgical intervention for pediatric CCM patients to improve the quality of care.

Authors' Contributions

SH and JW designed the study, WG, SH, FF, ZY, YD, and JZ, collected data, YD, JZ ,FF and ZY analyzed data, WG, SH, and JW wrote the manuscript, and all authors read and approved the final version of manuscript.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases. The operative time in 80% (52/65) is less than 300 minutes.

Figure 2. A one-year old female pediatric patient with CCM (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

Figure 3. A three-year old female pediatric patient with CCM (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

Figure 4. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases from four cohorts. There was no significant difference in the distribution of operative time among the four surgical teams (Chi-Square = 0.7189, $p = 0.9489$).

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

Table 1. Risk factors associate with operative time in pediatric CCM cases

Variables	Duration surgery< 300 minutes (52 cases)	Duration surgery≥ 300 minutes (13 cases)	*p* value
Gender (F)	35	5	0.0559
Infant	7	2	1.0000
Type IV	22	5	
Type I	30	8	0.7472
Fusiformis*	24	1	0.0114
Cyst stones	7	4	0.2092
Biliary tract infection***	3	10	<0.0001
Abdominal pain	41	9	0.4617
Jaundice	16	3	0.7385
Mass	15	3	1.0000
Vomit	33	10	0.2551
Fever	25	10	0.0620
Cholecystitis*	28	12	0.0114
Pancreatitis	2	0	1.0000
Laparoscopy	19	4	0.6972
Preoperative complications	10	-	0.0856
Gastrointestinal polyps	1	-	
Cyst rupture	1	-	
Appendicitis	2	-	
Ascites	1	-	
Pleural effusion	1	-	
Upper respiratory tract infection	4	-	

*p<0.05, ***p<0.001.

Table 2. Logistic regression model for factors affecting operative time in pediatric CCM cases

Variable	Chi-Square	OR	95%Wald Confidence Limits	P value
Biliary tract infection***	11.2195	30.609	4.134-226.607	0.0008
Cystiform	1.1194	3.377	0.354-32.191	0.2900
Cholecystitis	1.8755	5.892	0.465-74.573	0.1708

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.4191)
***p<0.001.

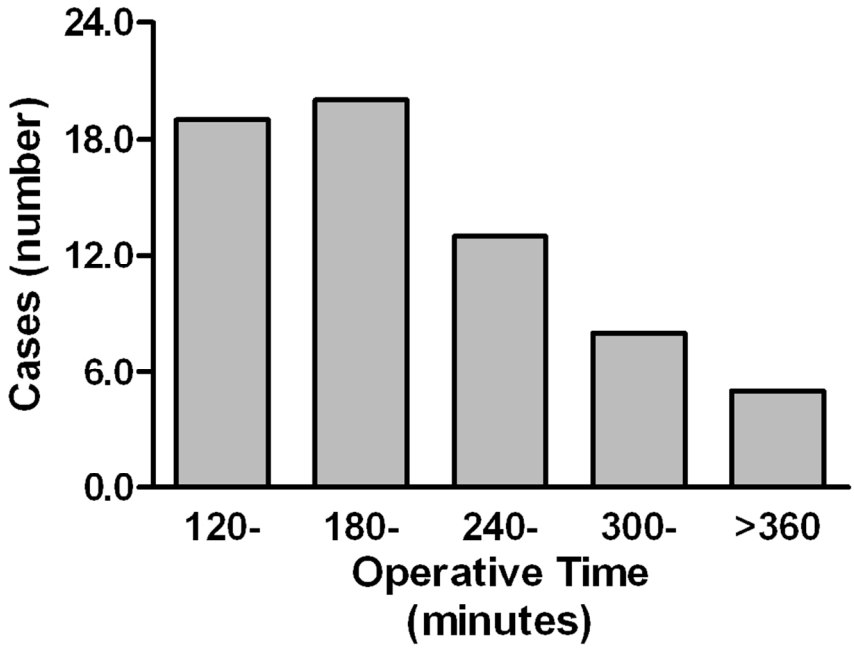

Figure 1. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases. The operative time in 80% (52/65) is less than 300 minute.

100x73mm (300 x 300 DPI)

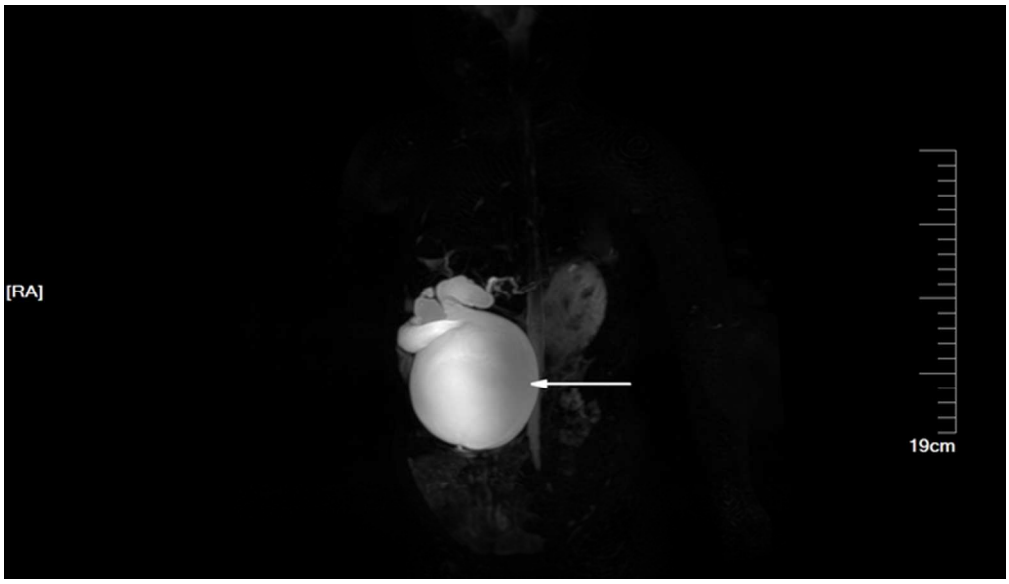

Figure 2. A one-year old female pediatric patient with CBD (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

31x18mm (600 x 600 DPI)

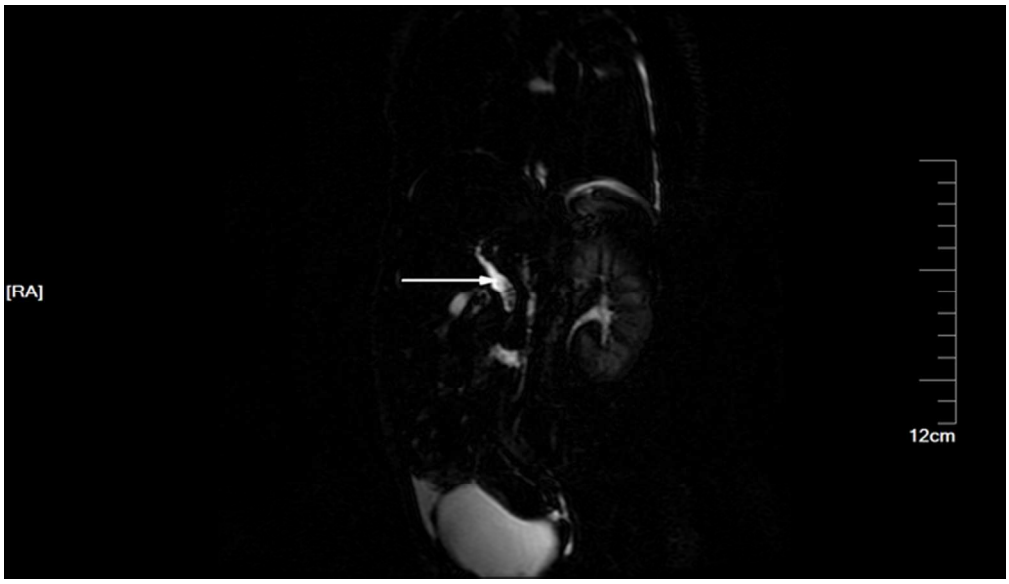

Figure 3. A three-year old female pediatric patient with CBD (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

31x18mm (600 x 600 DPI)

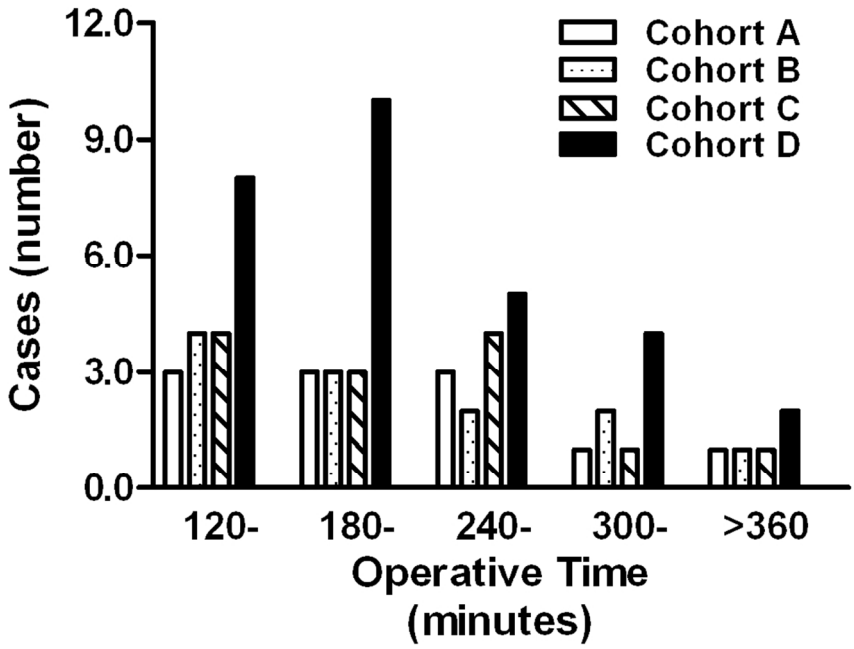

Figure 4. Distribution of the operative time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CBD cases from four cohorts. There was no significant difference in the distribution of operative time among the four surgical teams (Chi-Square = 0.7189, p = 0.9489).

100x73mm (300 x 300 DPI)

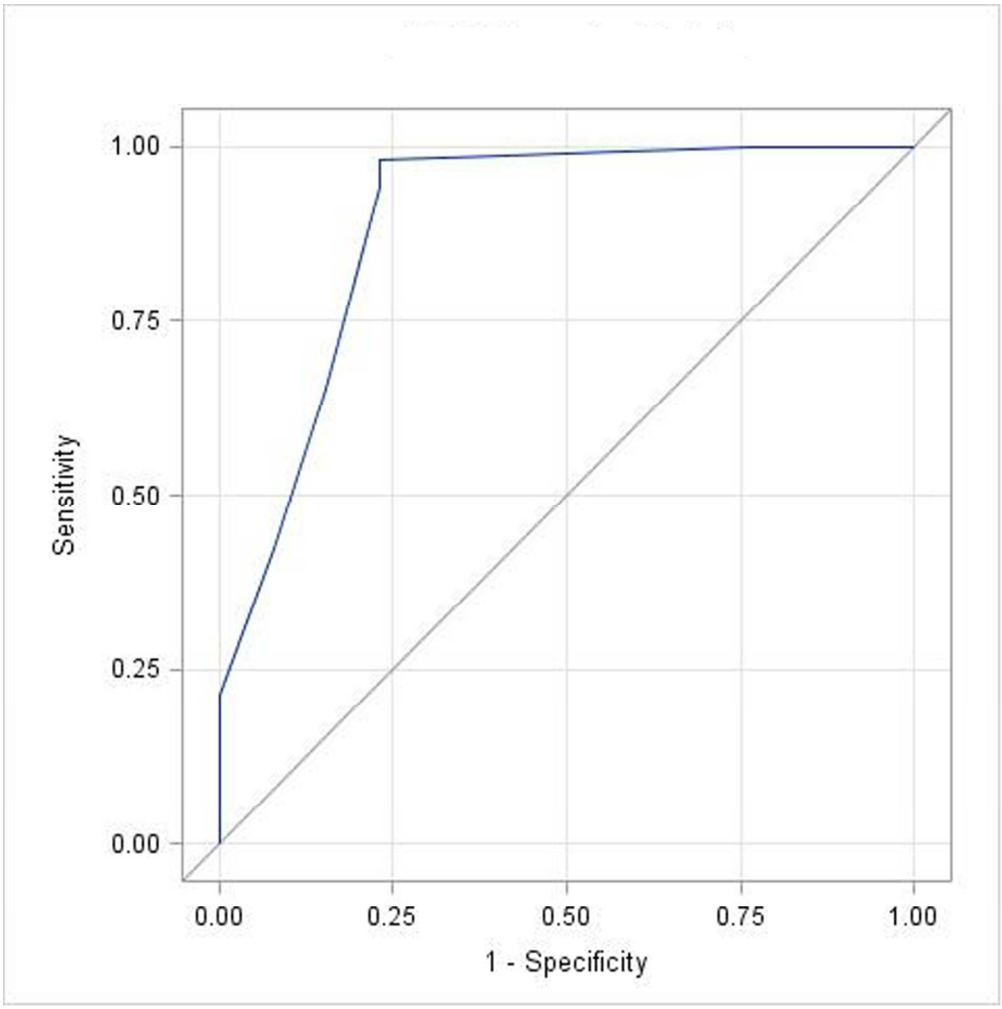

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

90x90mm (300 x 300 DPI)

Supplemental table 1. Analysis operative time undergone cyst excision and Roux-en-Y hepaticojejunostomy for children in four cohorts

varable	Cohort A(11)	Cohort B(12)	Cohort C(13)	Cohort D(29)
Mean±SD	236.27±79.233	235.42±84.972	233.08±70.045	227.24±80.073

Pair-wise comparison showed there is no significant difference between every two groups, Cohort A Vs Cohort B(p=1.0000) , Cohort A Vs Cohort C(p=0.8860) , Cohort A Vs Cohort D(p=0.5748) , Cohort B Vs Cohort C(p=0.9356), Cohort B Vs Cohort D(p=0.8973) and Cohort C Vs Cohort D(p=0.6435).

Supplemental table 2. Analysis operative time between laparoscopic surgery and open surgery undergone cyst excision and Roux-en-Y hepaticojejunostomy

group	N	mean± SD	P value
Laparoscopy	23	251.65±73.58	0.0825
open surgery	42	220.38±77.76	

Wilcoxon two-sample test

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6
Bias	9	Describe any efforts to address potential sources of bias	Page 11
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen	N/A

		and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6-7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 7
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Page 7-8
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	

Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	None

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Factors affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of congenital choledochal malformation: a retrospective case study in southeast China

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Factors affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of congenital choledochal malformation: a retrospective case study in southeast China

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Competing interests

The authors declare that they have no competing interests.

Abstract

Objective The aim of this study was to evaluate factors affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of congenital choledochal malformation (CCM).

Design A 3-year retrospective study was undertaken between January 2013 and December 2015 in four centers in China.

Setting This involved a retrospective chart review of pediatric patients with CCM in four large hospitals in southeast China.

Participants Sixty-five pediatric patients with CCM were included in this study. We derived all available information on patient demographics, clinical characteristics, preoperative complications, and surgical methods from the charts of all these patients.

Interventions Univariate and multivariate logistic regression analyses were used to evaluate factors significantly affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of CCM.

Results Twenty-three of the 65 case surgeries were performed using laparoscopic technique, and 42 surgeries were performed by conventional open surgery. The median operating time was 215 minutes (range 120-430 minutes). The morphological subtype of CCM and the presence of cholecystitis or cholangitis were the only factors found to affect the operating time ($p<0.05$). Logistic regression analysis confirmed cholangitis as an independent risk factor.

Conclusions The morphological subtype of CMM and the presence of cholecystitis or cholangitis are factors affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of CCM, whereas cholangitis is an independent risk factor.

Keywords: congenital choledochal malformation, hepaticojejunostomy, operating time, influencing factors

Strengths and limitations of this study

This was a multicenter retrospective study undertaken over a 3-year period in southeast China.

A stepwise logistic regression analysis of 65 pediatric CCM cases was performed in an attempt to identify factors affecting the operating time, and the accuracy of the logistic regression model for the obtained results was further assessed by the receiver operating characteristic curve (ROC).

The sample size was relatively small; however, CCM is a rare pediatric disease. Selection bias may have been a factor.

Introduction

Congenital choledochal malformation (CCM) is a rare congenital anomaly that presents as extra and/or intrahepatic bile duct dilatation, and its incidence is much higher in Asia than in Western countries [1-4]. The majority of cases seen in the clinic are in infants and children. Most CCM cases present clinically with abdominal pain, jaundice, and a mass, sometimes accompanied by vomiting and fever. CCM leads to higher rates of cholestasis, stone formation, pancreatitis, biliary hyperplasia, atypical epithelial growth of the bile duct or gallbladder, and tumor formation; the latter is thought to be caused by pancreaticobilliary maljunction (PBM) with a two-way reflux of bile and pancreatic juice [5-8].

Early prevention of long-term complications such as recurrent cholangitis, gallstones, pancreatitis, and especially, malignant tumors in the bile duct and gallbladder is of the essence. Complete excision of the cyst and Roux-en-Y hepaticojejunostomy is the main stay of treatment for children with CCM [9-11]. Cyst excision and hepaticojejunostomy by either open surgery or laparoscopic surgery in pediatric CCM are feasible and popularly undertaken [12-13]. Jackson *et al*. and Jenkins *et al*. reported that the complexity and difficulty of a surgical procedure is reflected by the operating time [14-15]. Qiao et al. reported on an extensive series of CCM cases in 7 centers and found that postoperative complications were associated with longer operating times [11].

Up to now, only few studies have focused on factors affecting the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric cases of CCM. We retrospectively studied the clinical presentation and surgical management of 65 pediatric cases of CCM that had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy between January 2013 and December 2015 in 4

centers in southeast China, in an attempt to identify factors affecting the operating time.

Materials and Methods

Study subjects

Data was collected after study protocol approval from the institutional review boards of each participating institution and informed consent was signed by the guardians of the subjects. All methods were carried out in strict accordance with the relevant institution guidelines regarding the acquisition and use of human tissues. Sixty-five pediatric cases of CCM were recruited into this clinical study. Twenty-nine subjects were from the Children's Hospital of Soochow University, 11 subjects were from Xuzhou Children's hospitals, 12 subjects were from the Affiliated Hospital of Guizhou Medical College, and 13 subjects were from the Affiliated Hospital of Nantong Medical College. All patients were diagnosed by ultrasound, computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), and intraoperative cholangiography (IOC). All patients underwent surgical excision of their choledochal cyst and hepaticojejunostomy by the way of similar laparoscopic or conventional open surgical approaches, performed by pediatric surgeons of the 4 participating hospitals. All procedures were undertaken by expert pediatric surgeons who have advanced skills and are capable of independently completing surgical procedures in cases with huge choledochal cysts. A total of 23 patients underwent their surgical procedure by way of the laparoscopic technique. In all of these patients, a similar laparoscopic surgical approach was used by the operating surgeons in the participating hospitals. The operating times (from incision to skin closure) of each surgical team were analyzed among the 4 subject cohorts.

Factor analysis

The patients were assessed for gender, age, common bile duct shape, Todani type, and presence of a stone in the choledocal cyst. Ages were grouped as infant (<1 year of age) or pediatric (>1 year of age). Common bile duct shape, Todani type, and presence of cyst stones were assessed by ultrasound and MRCP combined with IOC. Common bile duct shape was classified as either cystiform or fusiform. Clinical symptoms at presentation, preoperative complications, operative methods (conventional open or laparoscopic cyst excision and hepaticojejunostomy), and operating time were analyzed. Cholangitis was defined as any symptom of the Charcot triad (abdominal pain, jaundice, or fever) with an increase in total bilirubin, AST, and ALT levels above the normal range. Cholecystitis was confirmed by ultrasound combined with pathological findings. In 80% (52/65) of cases, the operating time was less than 300 minutes. The operating time was then dichotomized as <300 minutes or ≥300 minutes (**Figure 1**).

Patient and public involvement

There was no patient or public involvement in this study.

Statistical analysis

Analyses were performed with SAS software, JMP 9.0 (SAS Institute, Cary, NC, USA). Data are presented as number (*n*), percentage, and median. Multi-group ordered variable data comparisons were performed using Kruskal–Wallis test. Univariate comparisons were performed using nonparametric one-way Wilcoxon rank sum, χ^2, or T test, depending on the statistical distribution. To evaluate risk factors

affecting the operating time, logistic regression analysis was performed. The ROC curve was used to assess the accuracy of the logistic regression model. $p<0.05$ was considered statistically significant.

Results

Clinical characteristics and general findings of pediatric CCM cases

The present clinical study comprised 65 pediatric CCM cases diagnosed by ultrasound, CT, MRCP, and IOC. Among these 65 patients, there were 25 (38.5%) males and 40 (61.5%) females with CCM. The median age of the patients was 3 years (range 3 months to 13 years). Fifty-two cases were defined as PBM by MRCP with IOC. The morphological subtype of bile duct dilatation was cystic (**Figure 2**) in 40 cases (8 were large cysts descending into the introitus of the pelvis) and fusiform (**Figure 3**) in 25 cases. All 65 cases underwent complete cyst excision and Roux-en-Y hepaticojejunostomy. Twenty-three of these cases were performed using laparoscopic technique, whereas the other 42 cases were performed using conventional open surgery. The median operating time was 215 minutes (range 120-430 minutes). **Figure 4** and **supplemental table 1** illustrates the distribution of operating time between the 4 centers, and there was no significant difference in the operating time across centers.

Related risk factors affecting the operating time in pediatric CCM cases

Table 1 depicts a comparison of the clinical characteristics, preoperative complications, and surgical methods for the <300 minutes and ≥300 minutes operating time groups. Supplemental table 2 depicts a comparison of the operating time of surgical methods between laparoscopic surgery and open surgery. Univariate

analysis revealed that the morphological subtype and the presence of cholecystitis or cholangitis affected the operating time ($p<0.05$). No other factors were found to affect the operating time. Logistic regression analysis was performed to assess independent predictors that affect the operating time in 65 pediatric CCM cases. Again, the presence of cholangitis was the most important risk factor (**Table 2**). These data agreed with Hosmer and Lemeshow's goodness-of-fit test ($p=0.4191$). To further assess the accuracy of logistic regression model for the obtained results, analysis of the receiver operating characteristic (ROC) curve was performed with the area under the curve (AUC) at 0.8913 (**Figure 5**).

Discussion

General findings

Due to the obstruction of flow of bile or pancreatic juice, pediatric cases of CCM often present with abdominal pain, jaundice, and an abdominal mass. They also harbor a risk of malignancy as well as other serious complications. Pre-emptive surgery is recommended once diagnosis of CMM is confirmed. The operating time has been used previously as a measure of operative difficulty and complexity [14-15]. Sorokin et al. reported that increased postoperative complications were associated with the prolonged operating time [16]. Qiao et al. reported similar findings on assessing 956 pediatric cases with CCM, in which all the patients had undergone complete cyst excision and Roux-en-Y hepaticojejunostomy [11]. The mean operating time in the said study was 3.52 hours (range 2.21-5.75 hours). This operating time is similar to that in our study. However, there has been only little research focusing on the risk factors affecting operating time in CCM surgery. Our study on a multicenter cohort of pediatric patients who underwent complete cyst

excision and hepaticojejunostomy yielded operating times (ranged from 120-430 minutes), similar to those previously reported [17]. Thus, we are persuaded that the variable of operating time can be used as a measure of operative difficulty and complexity. Moreover, we also focused on factors that potentially affect the operating time.

Factors affecting the operating time in pediatric CCM cases

To investigate factors that potentially influence the operating time, we described the clinical characteristics, preoperative complications, and the surgical methods employed in our series of pediatric CCM cases. Univariate analysis indicated that the morphological subtype and the presence of cholecystitis or cholangitis affected the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy. Patients with cystic biliary dilatations had longer operating times compared to those with fusiform biliary dilatations, and this was especially true for those with larger cysts. Patients with cystic biliary dilatations often presented with displacement of vessels, severe biliary obstruction, and coagulopathy, consequently making surgery difficult and with a greater risk of injury to the surrounding tissues. This in turn increased the operating time. These results are comparable to those previously reported [18]. This indicates that the operative difficulty and complexity in patients with cystic biliary dilatations is greater than those with fusiform biliary dilatations. In addition, we compared operating times for laparoscopic and conventional open surgery. We found that the operating time for laparoscopic surgery was longer compared to conventional open surgery, albeit the difference in operating times between the two groups was not statistically significant. This finding is consistent with the report by Diao et al. [19].

The presence of cholecystitis was another factor affecting the operating time. Forty of our cases presented with cholecystitis, of which 75.0% were defined as having CCM with PBM. Sugai et al. previously compared the preoperative ultrasound measurements of gallbladder wall thickness and the actual wall thickness measurements in resected gallbladder specimens; the results showed a concordance rate of 89%, with 25.9% cases showing chronic inflammation [20]. Park *et al*. reported that CCM cases with PBM were often found to have clinical cholecystitis, and that this was strongly related to inflammatory changes in the duct and periductal structures [21]. It is likely that chronic cholecystitis resulting in the formation of adhesions is a factor, contributing to the increase in the difficulty of procedures and dissection time. As such, in CCM cases with PBM having cholecystitis, meticulous planning is needed to decrease the risk of operative complications.

Cholangitis is a common preoperative comorbidity that may increase the operating time in CCM. Morine et al., on assessing 952 pediatric biliary dilatation cases, reported that 16.2% of these patients also had cholangitis [22]. Ouaissi et al. and Visser et al., in their studies assessing several CCM cases, respectively reported 26.3% and 21% of patients having cholangitis [23,24]. Lal et al. compared cases with and without infective complications and concluded that CCM with infective complications requires meticulous planning and a multimodal approach, with more time required for the operative procedure [25]. In our study, 20.0% of cases had infective complications. Multiple logistic regression analysis confirmed that the presence of cholangitis was an independent factor affecting the operating time, suggesting that such cases need more operating time and meticulous planning to decrease the risk of operative complications. Qiao et al. reported that pediatric CCM with cholangitis led to increased operating time and postoperative complications.

This finding is further supported by Diao et al. [11,18]. It is conceivable that the increased operating time during complete cyst excision and Roux-en-Y hepaticojejunostomy contributes to the operative complications and postoperative morbidity in these cases. However, giver that the operating time reflects the difficulty of surgical procedures, and also the relative experience of the surgeon, efforts were made to ensure that the pediatric surgeons involved in this study across all four centers were similarly and suitably trained. While the operating time is seemingly not an adequate surrogate for predicting long-term postoperative complications, our findings highlight the importance not only of meticulously planning surgical intervention for pediatric CCM patients but also of the necessity to schedule these cases so as to allow for the effective use of operating room time in order to improve the quality of patient care.

Limitations

Our study has a number of limitations. Firstly, the sample size was relatively small; however, CCM is a rare pediatric disease. Selection bias such as surgical methods may have been a factor. Secondly, this was a retrospective multicenter study of only 3-years duration. A prospective multicenter study over a longer period is a necessary future endeavor.

Conclusions

In this series of complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases, the median operating time was 215 minutes (range 120-430 minutes). The morphological CCM subtype and the presence of cholecystitis or cholangitis affected the operating time, with cholangitis as an independent risk factor.

These findings are potentially important and will be useful in planning surgical interventions for pediatric patients with CCM in China. This has the potential to improve the quality of patient care in CCM in China.

Authors' Contributions

SH and JW designed the study, WG, SH, FF, ZY, YD, and JZ, collected data, YD, JZ ,FF and ZY analyzed data, WG, SH, and JW wrote the manuscript, and all authors read and approved the final version of manuscript.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1. Distribution of the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases. The operating time in 80% (52/65) of cases was less than 300 minutes.

Figure 2. A pediatric patient with CCM (Todani type, Type IV). MRCP shows the cystic dilatation of the common bile duct (Arrow).

Figure 3. A pediatric patient with CCM (Todani type, Type I). MRCP showed the fusiformis dilatation of the common bile duct with stones (Arrow).

Figure 4. Distribution of the operating time for complete cyst excision and Roux-en-Y hepaticojejunostomy in pediatric CCM cases from four cohorts. There was no significant difference in the distribution of operating time among the four surgical teams (Chi-Square = 0.7189, $p = 0.9489$).

Figure 5. Use of the receiver operating characteristic (ROC) curve to assess the accuracy of the logistic regression model. The area under the curve (AUC) is at 0.8913 for the obtained results.

Table 1. Risk factors associate with operating time in pediatric CCM cases

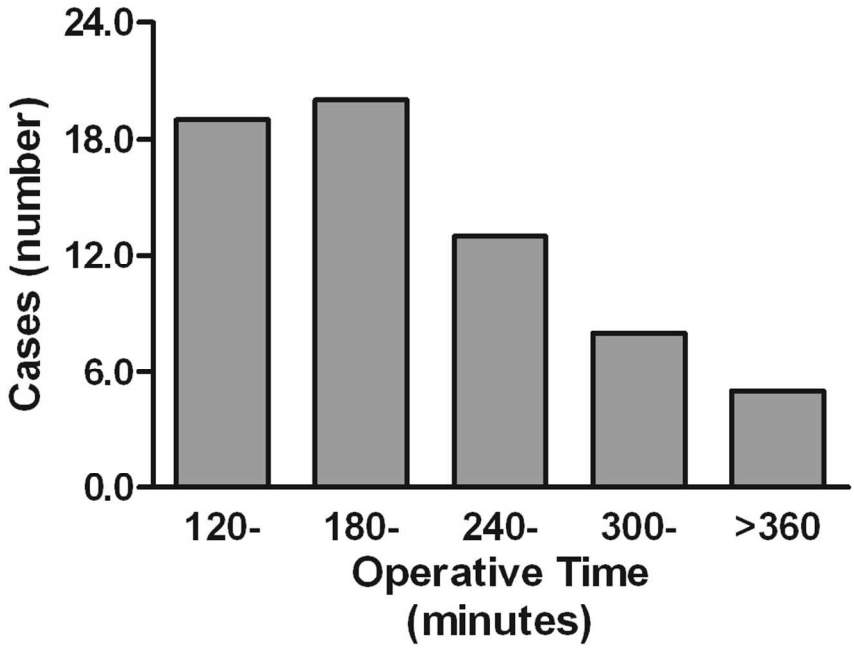
Variables	Duration surgery< 300 minutes (52 cases)	Duration surgery≥ 300 minutes (13 cases)	*p* value
Gender (F)	35	5	0.0559
Infant	7	2	1.0000
Type IV	22	5	
Type I	30	8	0.7472
Fusiformis*	24	1	0.0114
Cyst stones	7	4	0.2092
Biliary tract infection***	3	10	<0.0001
Abdominal pain	41	9	0.4617
Jaundice	16	3	0.7385
Mass	15	3	1.0000
Vomit	33	10	0.2551
Fever	25	10	0.0620
Cholecystitis*	28	12	0.0114
Pancreatitis	2	0	1.0000
Laparoscopy	19	4	0.6972
Preoperative complications	10	-	0.0856
Gastrointestinal polyps	1	-	
Cyst rupture	1	-	
Appendicitis	2	-	
Ascites	1	-	
Pleural effusion	1	-	
Upper respiratory tract infection	4	-	

*p<0.05, ***p<0.001.

Table 2. Logistic regression model for factors affecting the operating time in pediatric CCM cases

Variable	Chi-Square	OR	95%Wald Confidence Limits	P value
Biliary tract infection***	11.2195	30.609	4.134-226.607	0.0008
Cystiform	1.1194	3.377	0.354-32.191	0.2900
Cholecystitis	1.8755	5.892	0.465-74.573	0.1708

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.4191)
***p<0.001.



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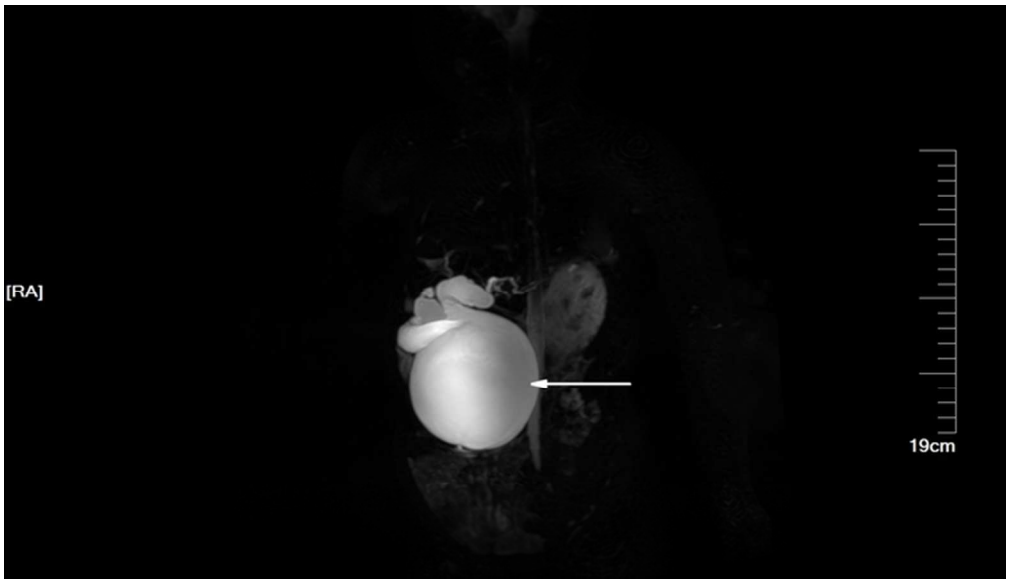

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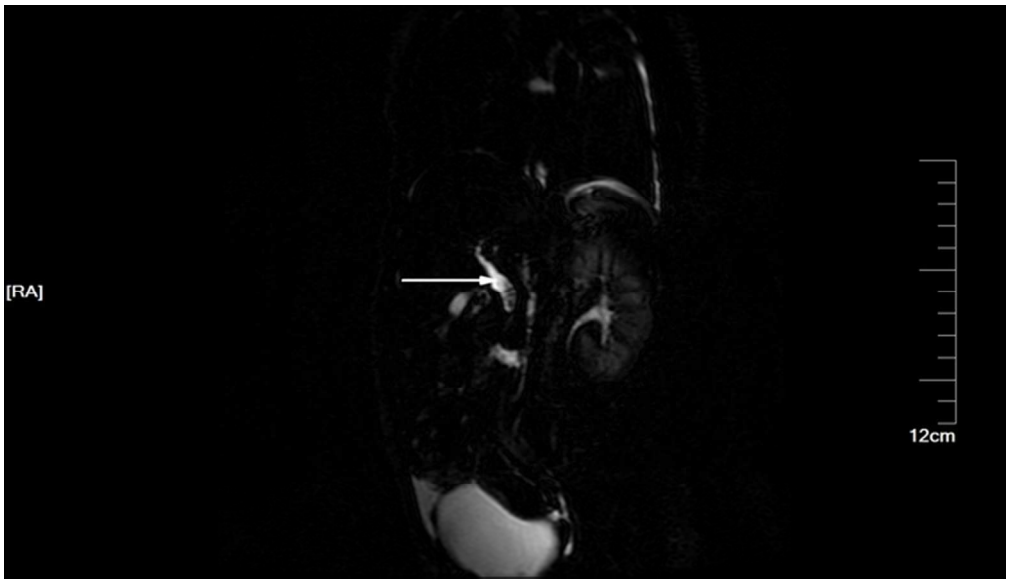

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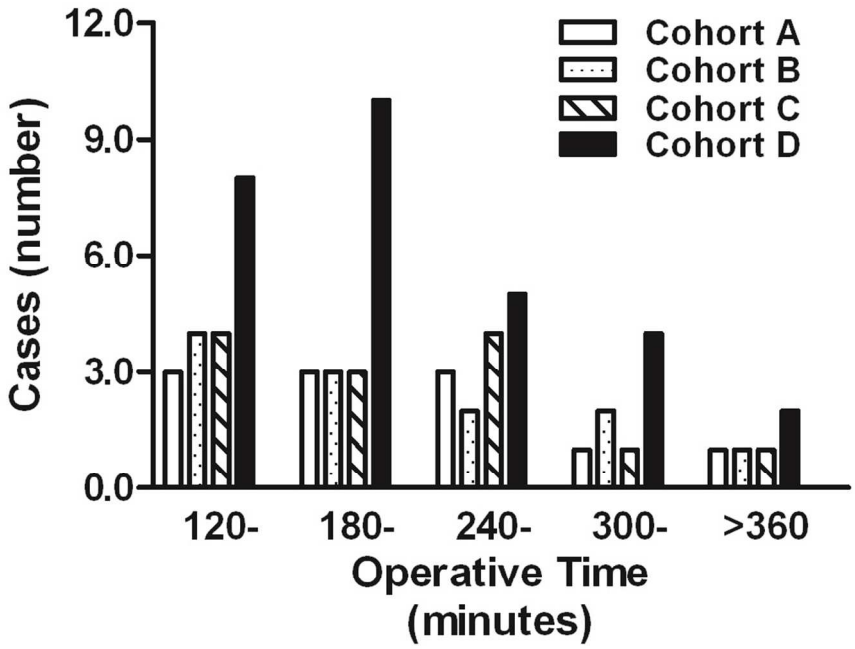

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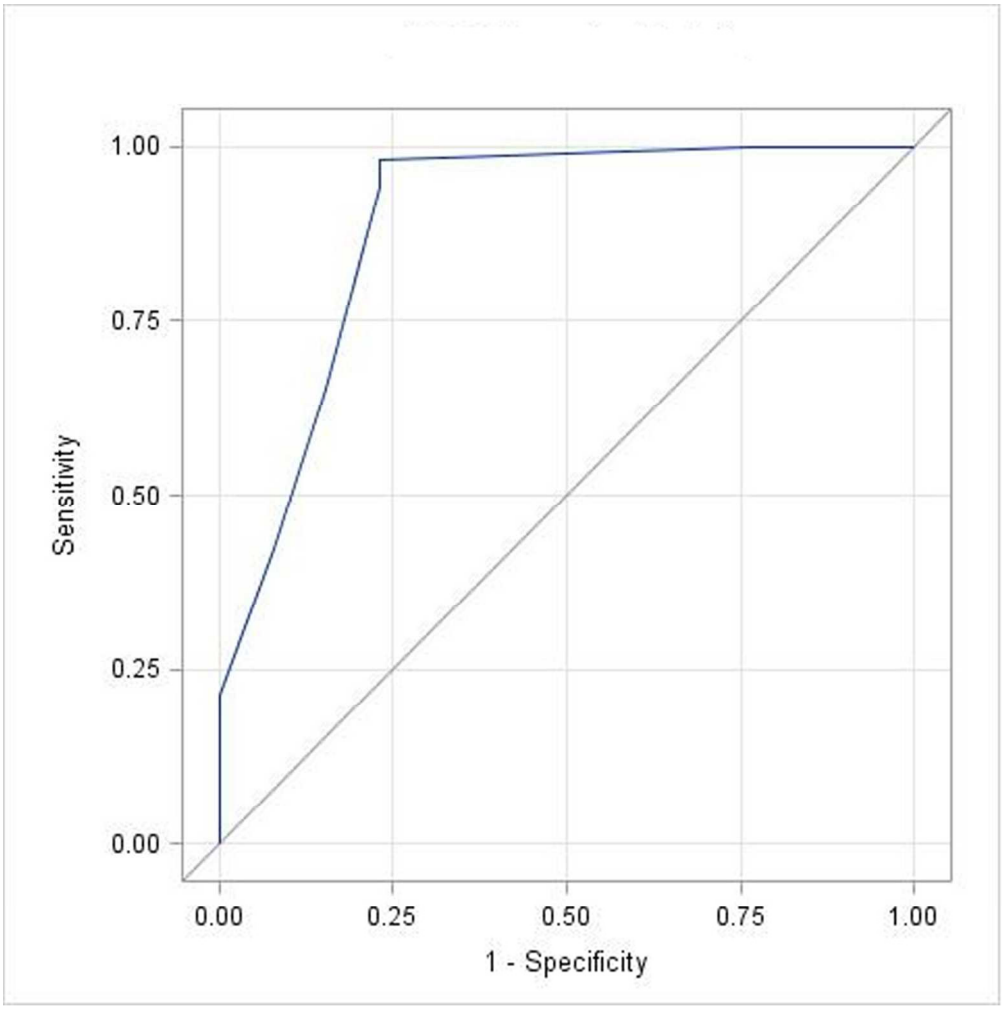

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Supplemental table 1. Analysis the operativing time undergone cyst excision and Roux-en-Y hepaticojejunostomy for children in four cohorts

varable	Cohort A(11)	Cohort B(12)	Cohort C(13)	Cohort D(29)
Mean±SD	236.27±79.233	235.42±84.972	233.08±70.045	227.24±80.073

Pair-wise comparison showed there is no significant difference between every two groups, Cohort A Vs Cohort B(p=1.0000) , Cohort A Vs Cohort C(p=0.8860) , Cohort A Vs Cohort D(p=0.5748) , Cohort B Vs Cohort C(p=0.9356), Cohort B Vs Cohort D(p=0.8973) and Cohort C Vs Cohort D(p=0.6435).

Supplemental table 2. Analysis the operativing time between laparoscopic surgery and open surgery undergone cyst excision and Roux-en-Y hepaticojejunostomy

group	N	mean± SD	P value
Laparoscopy	23	251.65±73.58	0.0825
open surgery	42	220.38±77.76	

Wilcoxon two-sample test

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6
Bias	9	Describe any efforts to address potential sources of bias	Page 11
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen	N/A

		and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6-7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 7
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Page 7-8
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	

Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 8-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	None

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.