Pediatric Surgery International (2023) 39:30
https://doi.org/10.1007/s00383-022-05293-x

ORIGINAL ARTICLE

Postoperative anastomotic stricture following excision of choledochal cyst: a systematic review and meta-analysis

Rina Tanaka[1] · Hiroki Nakamura[1] · Sakiko Yoshimoto[1] · Tokiko Okunobo[1] · Ryosuke Satake[1] · Takashi Doi[1]

Accepted: 14 November 2022 / Published online: 1 December 2022

Abstract

Purpose Postoperative anastomotic stricture (PAS) is a well-known complication after correcting choledochal cyst (CC). Although the exact cause of PAS is unknown, various risk factors, such as Todani classification type IV-A, hepaticoduodenostomy, and narrow anastomosis have been reported to be associated with PAS. As far as we know, there is no report with a cumulative analysis of such risk factors of PAS. This systematic review and meta-analysis aimed to investigate the risk factors of PAS following surgical correction of CC in children.

Methods A systematic literature search for relevant articles was performed in four databases using the combinations of the following terms "Congenital biliary dilatation", "Congenital choledochal cyst", "Choledochal cyst", "Stenosis", "Stricture", and "Complication" for studies published between 1973 and 2022. The relevant cohorts of PAS were systematically searched for clinical presentation and outcomes.

Results The search strategy identified 795 reports. Seventy studies met the defined inclusion criteria, reporting a total of 206 patients with PAS. There is no prospective study in this search. The incidence of PAS was 2.1%. The proportion of Todani classification of the patient with PAS was higher in type IV-A with significant difference (2.0% in type I and 10.1% in type IV-A ($p=0.001$)). Fourteen studies reported a comparison between hepaticojejunostomy and hepaticoduodenostomy. There was no significant difference between the two groups ($p=0.36$). Four studies reported the diameter of the anastomosis at the primary surgery. The mean diameter was 12.5 mm. Nine studies reported a comparison between laparoscopic surgery and open surgery. Pooled odds ratio of PAS did not show a statistical difference ($p=0.29$).

Conclusions This study suggests that close careful follow-up is important in the patients with type IV-A of CC who underwent excision surgery, considering the possibility of PAS.

Keywords Choledochal cyst · Postoperative anastomotic strictures

Introduction

A choledochal cyst (CC) is a congenital hepatic bile duct anomaly related to a pancreaticobiliary maljunction [1–3]. The standard treatment for CC is total excision of the cyst and resection of the extrahepatic bile duct with bilioenteric anastomosis separating the mutual countercurrents of bile and pancreatic juice [4].

Most frequent late postoperative complications among patients with CC include cholangitis, hepatobiliary malignancies, and postoperative anastomotic strictures (PAS) [1]. PAS is a well-known complication after correcting CC. Although the exact cause of PAS is unknown, various risk factors such as Todani classification type IV-A [5], hepaticoduodenostomy (HD) [6], laparoscopic surgery [7], and narrow anastomosis [8] have been known to be associated with PAS. As far as we know, there is no report with a cumulative analysis of these risk factors of PAS. This systematic review and meta-analysis aimed to investigate the risk factors of PAS following surgical correction of CC in children.

✉ Takashi Doi
doitak@hirakata.kmu.ac.jp

[1] Division of Pediatric Surgery, Department of Surgery, Kansai Medical University, Osaka, Japan

Material and methods

Study selection

A systematic literature search was performed in the PubMed, CINAHL, Cochrane Library, and Ichushi-web electronic database using the combinations of the following terms "Congenital biliary dilatation", "choledochal cyst", "Stenosis", "Stricture", and "Complication" for studies published between 1973 and 2022. The relevant cohorts of PAS were systematically searched for clinical presentation and outcomes. Reference lists of relevant articles were manually searched for further cohorts. Duplicates were deleted. The resulting publications were reviewed in detail for clinical features and type of operation performed.

Data extraction

The relevant articles were reviewed by title, keywords, and abstracts by the authors (RT, HN, and TD) and a full-text assessment of selected articles was performed.

Inclusion criteria and exclusion criteria

The inclusion criteria were the study that reported pediatric patients with PAS after correcting CC and the study that was written in English or Japanese. The exclusion criteria were the study that reported adult patients with PAS or the study did not mention the age of the patients clearly.

Statistical analysis

A systematic review and meta-analysis were conducted based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. Pooled odds ratios (OR) were calculated for dichotomous variables using the Mantel–Haenszel method, and pooled mean differences were measured for continuous variables using the inverse variance method in meta-analysis. The odds ratio represents the odds of an adverse event occurring in the treatments. The confidence interval (CI) was established at 95%, a p value of less than 0.05 was considered statistically significant, and an odds ratio of less than 1 favored the treatment group.

Statistical heterogeneity was assessed using I^2. A fixed effects model was used if $I^2 < 50\%$, and a random effects model was used if $I^2 \geq 50\%$. Statistical analysis was conducted by Review Manager 5.4 (Cochrane Collaboration).

Results

The initial search yielded a total of 795 publications, of which 772 were identified by electronic database searching and 23 from cross-referencing (Fig. 1). After confirmation of duplicate listed articles, 625 titles, keywords, and abstracts were screened. Of these, 403 non-relevant studies were excluded. The remaining 223 publications were assessed in full text for eligibility and 152 articles were excluded because they did not address any of the selection criteria. In total, data from 70 studies [1, 3, 6–8, 10–74] (published between 1976 and 2022) met the defined inclusion criteria and were included in the cumulative analysis (Table 1). All 70 included studies are retrospective studies.

Characteristics of patients

The total number of PAS was 206, with an incidence of 2.1%. The mean age at the radical surgery for the patient without PAS was 43.66 months old, and 84.13 months old for the patient with PAS. Statistical evaluation was not possible because of the small number of cases. Four studies reported the diameter of the anastomosis at the primary surgery. The mean diameter was 12.5 mm.

Todani classification

Fifteen studies reported the Todani classification with 51 of 206 PAS patients. There were 21 cases with type I and 30 cases with Type IV-A. In particular, six studies compared the patient with PAS and without PAS regarding the Todani classification. The incidences of PAS were 2.0% in Type I and 10.1% in Type IV-A, respectively. Meta-analysis did not show a significant difference between the 2 groups [OR 0.09, 95% CI (0.02 0.40), $p = 0.001$] (Fig. 2).

Hepaticojejunostomy (HJ) versus HD

Fourteen studies reported a comparison between HJ and HD, including 1333 patients (824 underwent HJ and 509 underwent HD). The total number of PAS was 30 (22 underwent HJ and 8 underwent HD). Meta-analysis did not show a significant difference between the two groups [OR 1.02, 95% CI (0.62 2.60), $p = 0.51$] (Fig. 3).

Laparoscopic versus open

Nine studies reported a comparison between laparoscopic surgery and open surgery, including 1534 patients (761 underwent laparoscopic surgery and 773 underwent open surgery). The total number of PAS was 33 (13 underwent laparoscopic surgery and 20 underwent open surgery).

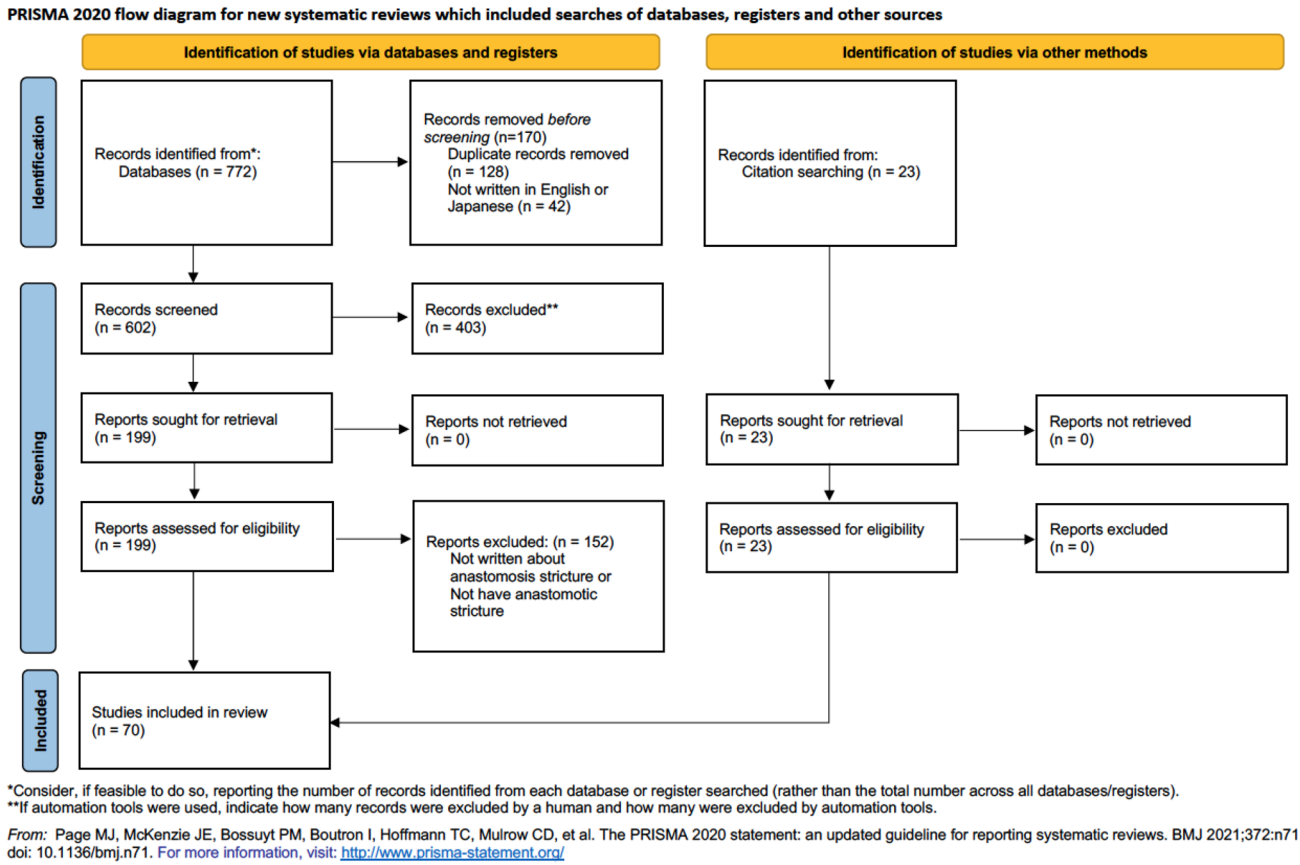

Fig. 1 This is an information flow diagram, demonstrating the process of selection and exclusion of articles from the literature search for the purposes of systematic review and meta-analysis

Meta-analysis did not show a significant difference between the two groups [OR 1.43, 95% CI (0.34 5.96), $p = 0.63$] (Fig. 4).

Treatments

Fifty-one studies reported the treatment of PAS. Thirteen patients were treated with endoscopic balloon dilatation, and 136 patients were treated with surgical revision of anastomosis.

Discussion

The present study was the first systematic review and meta-analysis to focus on the exact cause of PAS following the correction of CC. The cumulative incidence of PAS was 2.1%. Several reports suggested the cause of PAS such as Todani classification type IV-A, laparoscopic surgery, HD, and narrow anastomosis. In the present study, pooled data analysis has revealed that Todani classification Type IV-A was a significantly higher risk of PAS.

Todani classification type IV-A was the dilatation in the common bile duct and intrahepatic bile duct. Kim et al. [5] reported the risk factors of PAS in the adult patient and suggested that PAS could be influenced by type IV-A. Miyano et al. [75] reported that the pathological findings of the cystic type of CC showed atrophy of the lamina propria and prominent inflammatory cell infiltration. Kim et al. [5] also investigated the pathological findings of the bile duct and the cyst excised in the patient with PAS in the adult. They showed no significant differences in the thickness of cyst wall, fibrosis, loss of smooth muscle, and loss of mucosa between the patient with PAS and not [5]. On the other hand, they reported that there was a significant difference in the infiltration of inflammatory cells in the patient with PAS in adults [5]. In our study, although incidence of PAS in type IV-A was statistically higher than type I, it was unable to evaluate the inflammation of the cyst wall because only a few papers investigated the cyst wall in detail pathologically (e.g., pathological findings, inflammatory cytokines, and characterization of T-cell populations).

Yamataka et al. [25] reported that there were no PAS in the patients with CC whose ages were 5 years old or

Table 1 Study Characteristics

No.	Author	Year	Country	Number of patients with anastomotic stenosis
1	Barlow. B	1976	US	3
2	Miyano. T	1980	Japan	1
3	Lilly. J	1985	US	1
4	Todani. T	1988	Japan	2
5	Oweida. S	1989	US	1
6	Ohi. R	1990	Japan	1
7	Joseph. V.T	1990	Sungapare	3
8	Hamada. Y	1992	Japan	2
9	Todani. T	1992	Japan	8
10	Consentino. C	1992	US	1
11	Hata. Y	1993	Japan	2
12	Chijiwa. K	1993	Japan	2
13	Kamiyama. T	1994	Japan	4
14	Todani. T	1995	Japan	8
15	Nakamura. T	1996	Japan	2
16	Miyano. T	1996	Japan	3
17	Uno. K	1996	Japan	1
18	Saing. H	1996	Hong Kong	1
19	Saing. H	1997	HongKong	3
20	Yamataka. A	1997	Japan	2
21	Redkar.R	1998	UK	1
22	Hamada. Y	1998	Japan	1
23	Saing. H	1998	Hong Kong	1
24	Todani. T	1998	Japan	9
25	Watanabe. Y	1999	Japan	1
26	Fu. M	2000	China	8
27	Kubota. A	2004	Japan	2
28	Gardikis. S	2005	Greece	1
29	Kidogawa. H	2009	Japan	1
30	Foo. D	2009	China	1
31	She. W	2009	Hong Kong	2
32	Kim. J W	2010	Korea	1
33	Mukhopadhyay. B	2011	India	3
34	Diao. M	2011	China	12
35	Santore. M	2011	USA	2
36	Tang. S	2011	China	1
37	Germani. M	2011	Argentina	1
38	Chang. E	2012	Korea	1
39	Liem. N	2012	Vietnam	2
40	Urushihara.N	2012	Japan	5
41	Ono. S	2013	Japan	1
42	Acker. S	2013	US	1
43	Alizai. N	2014	UK	1
44	Li. S	2014	China	1
45	Son. TN	2014	Vietnam	1
46	Qiao. G	2015	China	6
47	Kim. N Y	2015	Korea	1
48	Senthilnathan. P	2015	India	1
49	Diao. M	2015	China	14
50	Yeung. F	2015	China	5
51	Dalton. B	2016	US	1
52	Yu. B	2016	China	5
53	Diao. M	2016	China	19
54	Hamada.Y	2017	Japan	1
55	Eijnden. M	2017	Netherlands	4
56	Miyano. G	2017	Japan	2
57	Sheng. Q	2017	China	5
58	Zhang. B	2019	China	1
59	Xie. X	2020	China	3
60	Yeung. F	2020	HongKong	4
61	Zhuansun. D	2020	China	4
62	Zheng. J	2020	UK	4
63	Amano. H	2021	Japan	4
64	Hyvärinen. I	2021	Finland	2
65	Miyake. H	2021	Japan	1
66	Ohyama. K	2021	Japan	1
67	Chi. S	2021	China	1
68	Tainaka. T	2022	Japan	3
69	Guan. X	2022	China	1
70	Lin. S	2022	China	1

younger. It has been reported that inflammation of the cyst wall was milder in the younger patient than 10 years old and more severe in the older patient with CC, indicating that histological damage to the common hepatic duct was more severe in older pediatric patients and adults [25]. In the present study, there was a trend that the age at the radical surgery in the patients with PAS was higher than the patient without PAS. However, a statistical analysis was not appropriate due to the small number of samples.

It was thought that HD was more prone to ascending cholangitis and thus to PAS [37, 76], but Todani et al. [77] found no difference in the frequency of ascending cholangitis between HD and HJ, and some surgeons [2, 69] also found no difference in the frequency of PAS between HD and HJ. Similarly, in a systematic review by Narayanan et al. [78] comparing HD and HJ, there was no significant difference in the frequency of PAS. In the present meta-analysis, no significant difference between HJ and HD.

The laparoscopic procedure has been getting adopted as the initial treatment for CC world wide since Farello et al. [79] reported the laparoscopic procedure for CC in 1995. Some surgeons are concerned about the disadvantages of the laparoscopic procedures for pediatric patients with CC due to small operative space, risk of injury to vital structures, and low quality of the anastomosis. Xie et al. [7] reported

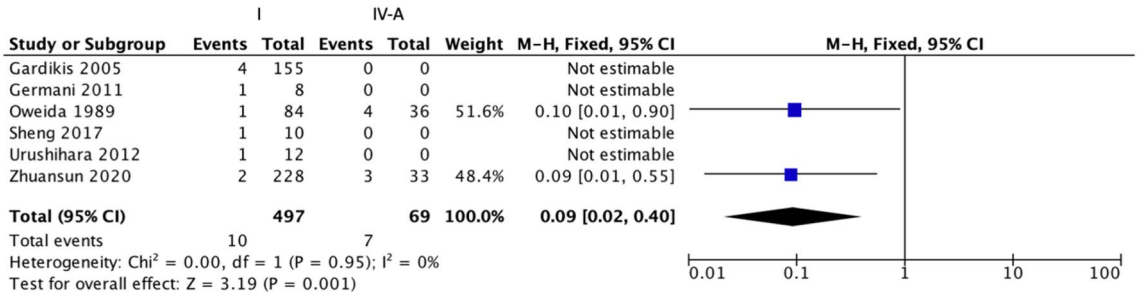

Fig. 2 Forest plots on the incidence of PAS between type I and type IV-A

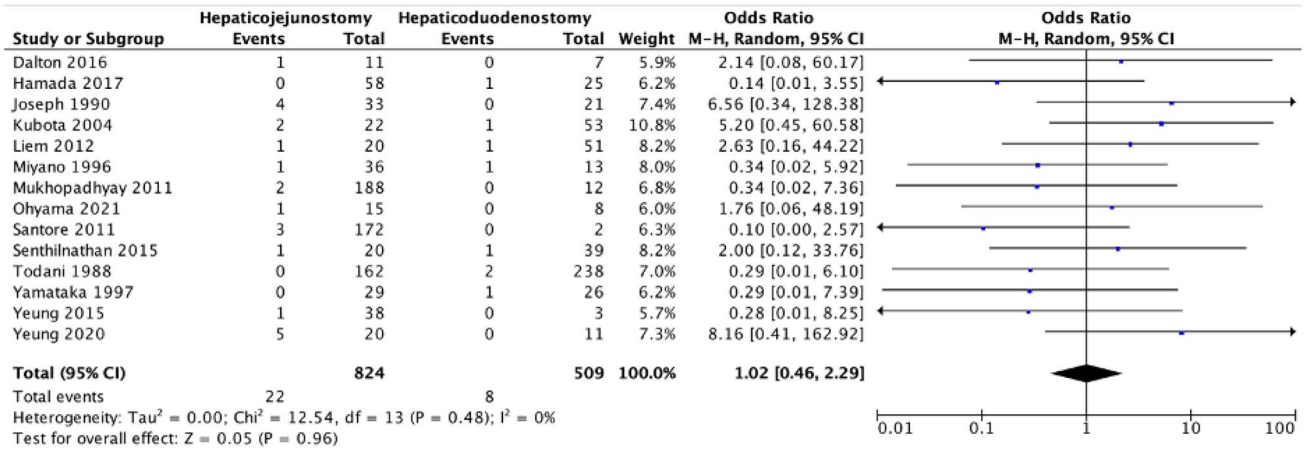

Fig. 3 Forest plots on the incidence of PAS between hepaticojejunostomy and hepaticoduodenostomy

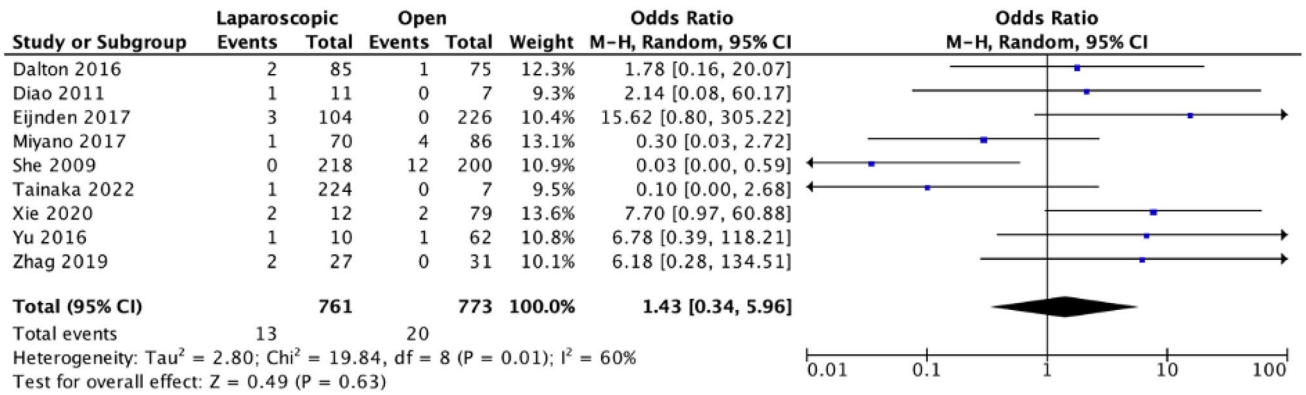

Fig. 4 Forest plots on incidence of PAS between laparoscopic surgery and open surgery

that the rate of PAS in the laparoscopic procedures was higher than in open procedures, but there was no significant difference, while Diao et al. [27] concluded that laparoscopic procedures were safe and effective, with lower morbidities of not only PAS, but also bile lake, intrahepatic stone formation, intrahepatic reflux, cholangitis, pancreatic leak, pancreatitis, and intestinal obstructions. Our meta-analysis showed no significant difference between laparoscopic procedures and open procedures.

Todani et al. [6] reported the creation of a wide anastomotic stoma was essential to prevent ascending cholangitis resulting in PAS. Kubota et al. [73] reported a case of PAS with an anastomotic diameter of 12 mm, which seemed to be sufficient, and in their case, intraoperative cholangiography

showed stenosis at the bifurcation of the right and left hepatic ducts, where cholangitis occurred, which may have spread to the anastomosis and resulted in PAS. In our study, the mean diameter of anastomoses was 12.5 mm, but there were few articles reporting the detail of cholangitis and the information on intrahepatic bile duct stenosis.

There were some limitations in this study. First, there were no randomized controlled trials that met our criteria. Second, there were variations in surgical techniques among facilities, and unified procedures could not be used to evaluate the results.

Based on this study, we plan to conduct further investigation focusing on (1) therapeutic strategies for PAS, (2) the pathological evaluation of the cyst wall in patients with PAS, and (3) looking for the adequate timing of the radical surgery for patients with CC.

In conclusion, this study suggests that close careful follow-up is essential in patients with type IV-A of CC who underwent excision surgery, considering the possibility of PAS. Since the age at the radical surgery would be associated with the inflammation of the cyst wall, further studies must be required in the future.

Author contributions R.T., H.N., and T.D. wrote the main manuscript text and R.T., S.Y., T.O., and R.S. prepared figures and table. All authors reviewed the manuscript.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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