HHS Public Access

Author manuscript

Pancreas. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Pancreas. 2017 July ; 46(6): 764–769. doi:10.1097/MPA.0000000000000848.

Therapeutic Endoscopic Retrograde Cholangiopancreatography in Pediatric Patients with Acute Recurrent and Chronic Pancreatitis: Data from the INSPPIRE (*IN*ternational *S*tudy group of *P*ediatric *P*ancreatitis: *I*n search for a cu*RE*) Study

David M. Troendle, MD[1], **Douglas S. Fishman, MD**[2], **Bradley A. Barth, MD, MPH**[1], **Matthew J. Giefer, MD**[3], **Tom K. Lin, MD**[4], **Quin Y. Liu, MD**[5], **Maisam Abu-El-Haija, MD**[4], **Melena D. Bellin, MD**[6], **Peter R. Durie, MD**[7], **Steven D. Freedman, MD, MPH**[8], **Cheryl Gariepy, MD**[9], **Tanja Gonska, MD**[7], **Melvin B. Heyman, MD, MPH**[10], **Ryan Himes, MD**[2], **Sohail Z. Husain, MD**[11], **Soma Kumar, MD**[12], **Mark E. Lowe, MD, PhD**[11], **Veronique D. Morinville, MD**[13], **Chee Y. Ooi, MBBS, PhD**[14], **Joseph Palermo, MD**[4], **John F. Pohl, MD**[15], **Sarah Jane Schwarzenberg, MD**[6], **Steven Werlin, MD**[16], **Michael Wilschanski, MD**[17], **M. Bridget Zimmerman, PhD**[18], and **Aliye Uc, MD**[19]

[1]Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, USA

[2]Section of Pediatric Gastroenterology and Nutrition, Baylor College of Medicine, Houston, TX, USA

[3]Department of Pediatrics, Seattle Children's Hospital, Seattle, WA, USA

[4]Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[5]Department of Medicine and Pediatrics, Cedars-Sinai Medical Center, Los Angeles, CA, USA

[6]Department of Pediatrics, University of Minnesota, University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota, USA

[7]Department of Paediatrics, University of Toronto, and Research Institute, The Hospital for Sick Children, Toronto, ON, Canada

[8]Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

[9]Department of Pediatrics, The Ohio State University and Nationwide Children's Hospital, Columbus, OH, USA

[10]Department of Pediatrics, University of California at San Francisco, San Francisco, CA, USA

Corresponding author: Aliye Uc, M.D., BT1120-C JPP Stead Family Department of Pediatrics, The University of Iowa Carver College of Medicine, 200 Hawkins Drive, Iowa City, IA 52242; Tel: (319) 384-6032; Fax:(319) 353-8967; aliye-uc@uiowa.edu.

Conflicts of Interest: DSF is a consultant for Pentax Medical Imaging, Cook Medical, Norgine Pharmaceuticals, and UpToDate. TKJ receives research funding from Vertex Pharmaceuticals and is a consultant for Glaxo Smith Kline Inc., Pfizer and the Cystic Fibrosis Foundation. MBH is an editor for the Journal of Pediatric Gastroenterology and Nutrition and receives royalties from UpToDate. MEL is on the board for the National Pancreas Foundation and a consultant for AbbVie, Inc and Nordmark. MDB in on the board for ARIEL, is a consultant for AbbVie, and receives grant funding from Dompe. JFP is on the editorial board for Practical Gastroenterology and a member of the Speaker's bureau for Medical Education Resources Inc. SJS is a consultant for the Cystic Fibrosis Foundation and AbbVie and receives grant support from the Cystic Fibrosis Therapeutic Network. AU is a board member for the American Board of Pediatrics, Sub-board of Pediatric Gastroenterology. For the Remaining authors, no conflicts were declared.

[11]Department of Pediatrics, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA

[12]Department of Pediatrics, Rady Children's Hospital, San Diego, CA, USA

[13]Department of Pediatrics, Montreal Children's Hospital, McGill University, Montreal, QC, Canada

[14]Faculty of Medicine, School of Women's and Children's Health, University of New South Wales and Sydney Children's Hospital Randwick, Sydney, Australia

[15]Division of Pediatric Gastroenterology, University of Utah, Salt Lake City, UT, USA

[16]Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI, USA

[17]Department of Pediatric Gastroenterology, Hadassah Hebrew University Hospital, Jerusalem, Israel

[18]Department of Biostatistics, University of Iowa College of Public Health, Iowa City, IA, USA

[19]Stead Family Department of Pediatrics, University of Iowa Carver College of Medicine, Iowa City, IA, USA

Abstract

Objectives—To characterize utilization and benefit of therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in children with acute recurrent pancreatitis (ARP) or chronic pancreatitis (CP).

Methods—From August 2012 to February 2015, 301 children with ARP or CP were enrolled in the INSPPIRE study. Physicians reported utilization and benefit of therapeutic ERCP at enrollment. Differences were analyzed using appropriate statistical methods.

Results—117 children (38.9%) underwent at least one therapeutic ERCP. The procedure was more commonly performed in children with CP compared to ARP (65.8% vs 13.5%, $p<0.0001$). Utility of therapeutic ERCP was reported to be similar between ARP and CP (53% vs 56%, $p=0.81$) and was found to be helpful for at least one indication in both groups (53 of 99 patients, 53.5%). Predictors for undergoing therapeutic ERCP were: presence of obstructive factors in ARP and CP, Hispanic ethnicity, or white race in CP.

Conclusions—Therapeutic ERCP is frequently utilized in children with ARP or CP and may offer benefit in selected cases, specifically if ductal obstruction is present. Longitudinal studies are needed to clarify the efficacy of therapeutic ERCP and to explore subgroups that might have increased benefit from such intervention.

Keywords

endotherapy; children; bile stent; pancreatic stent; bile ducts; pancreatic ducts

INTRODUCTION

Acute pancreatitis (AP) in children was considered to be uncommon, but its incidence is now recognized to approach that reported in adults.[1–3] While many children recover without long-term effects, a subset of patients will have further episodes of pancreatitis and/or

develop chronic pancreatitis (CP). With advanced non-invasive imaging modalities, endoscopic retrograde cholangiopancreatography (ERCP) is infrequently utilized solely as a diagnostic modality. However, ERCP is frequently applied as a therapeutic modality to manage patients with sequelae of acute recurrent pancreatitis (ARP) and CP. Endoscopic intervention such as therapeutic ERCP have traditionally been undertaken after failure of non-invasive maneuvers such as eliminating possible instigating environmental factors, or when medication trials are ineffective and before more invasive surgical interventions are pursued.

The literature regarding ARP and CP in the pediatric population is sparse, and even less data are published on appropriate interventions to ameliorate or prevent recurrences of pancreatitis or consequences of CP.[4–7] Given its favorable benefit/risk profile compared with surgical interventions, therapeutic ERCP is still recommended by most experts to be the first reasonable approach to treat select patients, for example with CP.[8] Collaborative efforts among adult providers have led to significant advances in understanding etiologies and clinical outcomes from surgical and endoscopic interventions in adult patients with ARP and CP.[9,10]

The INSPPIRE (**IN**ternational **S**tudy group of **P**ediatric **P**ancreatitis: **I**n search for a cu**RE**) consortium was formed to address gaps in knowledge of pediatric ARP and CP. The present study analyzes baseline information entered on patients in this database to describe the utilization and efficacy of endoscopic intervention on pediatric patients with ARP or CP as reported by the providers responsible for patient enrollment. We identify predictors of therapeutic ERCP utilization and report its utility.

MATERIAL AND METHODS

Study Design and Participants

Demographic and clinical data were collected from 16 institutions using patient/parent and physician questionnaires for children who fulfilled the criteria for ARP or CP and were ≤19 years of age at the time of enrollment, as previously described.[11]. Patient information was entered into the REDCap™ (Research Electronic Data Capture[12], Vanderbilt University, Nashville, TN) database from September 2012 to July 2015, and represented baseline information of the INSPPIRE cohort. All centers obtained Institutional Review Board approval or the equivalent for their country. These 301 subjects (155 ARP and 146 CP) have been reported in different contexts in previous reports.[13,14]

Definitions

The definitions utilized for ARP and CP have previously been described.[15] In summary, ARP was defined as at least 2 distinct episodes of AP with complete resolution of pain (>= 1-month pain-free interval between diagnoses of AP) or complete normalization of pain and serum pancreatic enzymes levels (amylase and lipase) before the subsequent episode of AP was diagnosed. CP was diagnosed when pancreatic imaging findings suggestive of CP were identified in the setting of either chronic pancreatic type pain, evidence of exocrine pancreatic insufficiency or endocrine pancreatic insufficiency. Suggestive imaging findings

of CP included: ductal changes (irregular contour of the main pancreatic duct or its radicles; intraductal filling defects; calculi, stricture or dilation) or parenchymal changes (generalized or focal enlargement, irregular contour [accentuated lobular architecture], cavities, calcifications, heterogeneous echotexture). Imaging modalities may include computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreagraphy (MRCP), ERCP; transabdominal ultrasound (US); or endoscopic ultrasound (EUS) (in which at least 5 EUS features [as defined by the Rosemont classification[16]] must be fulfilled).

Statistical Analysis

Differences were compared using Fisher's exact test or chi square test for categorical variables depending on sample size and the student t-test for continuous variables. All differences were considered significant at a two-sided $p<0.05$. Data were analyzed utilizing SAS 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

We analyzed the 301 patients entered into the INSPPIRE database as of July 2015; 155 (51.5%) were diagnosed with ARP and 146 (48.5%) with CP. Patient characteristics are presented in Table 1. Therapeutic ERCP was undertaken in 117 (38.9%) of patients.

Of the 155 children with ARP, 21 (13.5%) underwent therapeutic ERCP. The results of a univariate analysis evaluating predictors for application of therapeutic ERCP in patients with ARP are included in Table 2. Children suspected to have obstructive factors contributing to their disease process were significantly more likely to undergo therapeutic ERCP.

Of the 146 patients with CP, 96 (65.8%) underwent therapeutic ERCP. Patients with CP were more likely to undergo therapeutic ERCP compared with ARP (65.8% vs 13.5%, $p<0.0001$). The results of a univariate analysis evaluating predictors for utilization of therapeutic ERCP in patients with CP were included in Table 3. Children who were of Hispanic ethnicity, white race, and those who were suspected to have obstructive factors contributing to their disease process were significantly more likely to have therapeutic ERCP. In contrast, patients with alcohol exposure or autoimmune pancreatitis were significantly less likely to have therapeutic ERCP. Table 4 shows benefit of various endoscopic interventions reported by the physician questionnaires. While therapeutic ERCP, particularly pancreatic interventions such as sphincterotomy, stone removal and stenting, was utilized more commonly in the CP group, its efficacy was not significantly different comparing patients with ARP and those with CP. Biliary stenting was infrequently performed in both cohorts.

DISCUSSION

In our cohort, therapeutic ERCP was relatively infrequently performed in our patients with ARP, especially compared with patients with CP. When utilized in patients with ARP, therapeutic ERCP was done more frequently in patients with obstructive factors or pancreatic anatomical anomalies. Otherwise, therapeutic ERCP was not utilized as frequently in patients with other contributing variables causing pancreatitis. Over half of the

patients with ARP who had a therapeutic ERCP performed were reported to have improvement of symptoms. Our study volume was similar to one of the largest pediatric ERCP studies for pediatric pancreatitis by Agarwal et al, who described 221 ERCPs in 172 children, of whom 19 had ARP.[6] Of these 19 children, 63% were reported to have improvement of symptoms after therapeutic ERCP, similar to our observed rate of improvement of 56%. Otto et al also evaluated a large series of pediatric ERCP for pancreatitis and found a similar rate of children with anatomical abnormalities (13/106) contributing to recurrent pancreatitis, but their study did not evaluate the effectiveness of ERCP guided endotherapy for relief of symptoms in children with ARP or CP.[17] Cote et al demonstrated that biliary sphincterotomy alone may be as effective as dual biliary and pancreatic sphincterotomy to prevent AP episodes in adult patients with idiopathic ARP.[18] Unfortunately, the small number of sphincterotomies performed in our ARP cohort did not allow us to perform an analogous analysis, but the reported utility of biliary and pancreatic sphincterotomies in our cohort were similar (60% for biliary vs 50% for pancreatic). From our data, although therapeutic ERCP was used much less frequently in children with ARP compared with CP, its benefit in children with ARP was similar to those with CP. Whether therapeutic ERCP should be utilized at a greater frequency in managing children with ARP remains to be determined, but evidence should best come from longitudinal prospective studies evaluating the outcomes of such intervention.

Similar to the pediatric INSPPIRE consortium, several adult centers in a collaborative effort formed the North American Pancreatitis Study 2 (NAPS2) and first published on their collective data on ARP and CP in adult patients in 2008.[9] This was soon followed by a focused analysis of the NAPS2 data assessing the pattern of use of therapeutic ERCP and surgical therapies and their perceived effectiveness for only CP as based on completed physician questionnaires.[10] In the present study from the pediatric-based INSPPIRE consortium, a similar analysis was performed yielding specific data for CP, but also included ARP (Tables 2 thru 4), but limited to only therapeutic ERCP. Several key comparisons between the current INSPPIRE CP data and that from the NAPS2 cohort are notably important to highlight. Despite notable differences in the mean ages of the patients (12 yrs in INSPPIRE vs 49 yrs in NAPS2) and primary identified risk factors (genetics/obstructive factors in INSPPIRE vs alcohol in NAPS2) the utilization of therapeutic ERCP (66% for INSPPIRE vs 61% for NAPS2) and the perceived utility of this therapy (53% for INSPPIRE vs 43% for NAPS2) were remarkably similar for patients with CP in both cohorts.[10] Interestingly, biliary interventions were performed more often in the adult NAPS2 cohort compared with the current pediatric data (biliary sphincterotomy: 42% vs 26 %, biliary stenting: 14% vs 8%) possibly reflective of the less frequent occurrence of CP-related biliary strictures encountered in pediatric patients. In contrast, pancreatic interventions such as pancreatic stenting and stone removal were performed more often in the INSPPIRE cohort (44% and 22%, respectively) compared with the NAPS2 cohort (36% and 11%, respectively) possibly reflecting the fact that obstructive pathology within the pancreatic duct were more frequently identified in pediatric cohort as well. These differences in therapeutic ERCP utilization between adult and pediatric cohorts deserve further study, as they may provide clues into differences in underlying mechanisms of disease, disease progression, and which subgroups of patients may be more amenable to specific endoscopic interventions. These

differences are also important to consider as endoscopists performing therapeutic ERCP in children attempt to apply the relatively abundant adult literature in this area to pediatric patients in which a paucity of literature currently exists for the purpose of guiding management decisions.

In uncomplicated CP, several adult studies have shown that therapeutic ERCP can be helpful in improving the chronic pain associated with this disease.[19–21] The technical goals of therapeutic ERCP in CP typically include alleviating pancreatic ductal obstructions due to stones or strictures, stenting of the main pancreatic duct and treatment of regional complications such as peri-pancreatic fluid collections and strictures of the intra-pancreatic portion of the bile duct. Clinical guidelines by the European Society of Gastrointestinal Endoscopy suggest that therapeutic ERCP should be considered as a first-line treatment for patients with uncomplicated CP.[8] However, others advocate for reserving this intervention for those with imaging-proven main pancreatic duct obstruction.[22] In our study cohort, a majority of children with CP who undergo therapeutic ERCP are suspected to have pancreaticobiliary obstruction. Adult studies have also shown that benign biliary strictures, such as those seen in CP, are very responsive to endoscopic stenting, with response rates between 80–90%.[23–25] As mentioned previously, this intervention was rarely undertaken in our pediatric cohort and curiously only 3 of the 10 children with CP who had biliary stents placed were reported to benefit from this intervention. We are unable to account for this discrepancy; however, it is possible that the diminutively sized biliary tree of the pediatric-aged patients may preclude some of the effective stenting therapies developed in adults (i.e. placement of multiple plastic or fully covered metal biliary stents).

As previously described by the INSPPIRE consortium, genetic mutations in pancreatitis-related genes are frequently identified in pediatric ARP and CP.[13] Limited retrospective studies have suggested that therapeutic ERCP may be effective at decreasing rates of recurrent pancreatitis and help manage chronic pain for these patients.[5,7] Although therapeutic ERCP offers an effective alternative to treat the disease sequelae in this subgroup, it does not address the underlying genetic defect. Therefore, care should be taken in equating technical procedural success with improvements in pain and quality of life. The relatively invasive nature of therapeutic ERCP and the potential for adverse events invokes the need for ongoing studies to examine the long term effects of these procedures in children with ARP and CP. Unfortunately, the retrospective nature of our data collection regarding pain did not allow us to comment on patient or family perceptions as to whether or not therapeutic ERCP led to any tangible benefits in this regard. However, the majority of physician respondents believed that therapeutic ERCP was helpful for their patients although this result may be skewed due to bias on behalf of the provider. Clearly, prospective studies are still warranted to determine the effects of therapeutic ERCP on pain and quality of life in children with ARP and CP. Of particular interest is elucidating where in the treatment paradigm therapeutic ERCP should be considered for various subgroups of patients in relation to other potential treatment modalities such as medications, extracorporal shockwave lithotripsy, surgical interventions and total pancreatectomy with auto islet cell transplantation.

This study has several significant limitations that need to be taken into consideration. Subjects were recruited from tertiary care centers which may introduce referral bias towards children with more severe and disabling forms of ARP and CP. Another limitation is the subjective nature of procedural effectiveness that was utilized. In addition, the timing of the intervention in relation to the assessment of procedural effectiveness was not standardized as all patients were analyzed at enrollment. It is hoped that by incorporating annual follow-up questionnaires as well as more objective measures of effectiveness such as rates of recurrent pancreatitis, pain medication utilization, school days missed among others into the longitudinal INSPPIRE database will help overcome these limitations as the consortium continues its study of pediatric ARP and CP in a systematic manner. Nevertheless, the large number of well-phenotyped pediatric patients with ARP and CP allowed us to assess therapeutic ERCP utilization in these patients and gain insight into its perceived effectiveness according to providers.

In summary, this study is unique in that it is the first multicenter assessment of therapeutic ERCP utilization and perceived benefit in pediatric patients with ARP and CP. We document that therapeutic ERCP is more commonly undertaken in patients with CP compared with ARP, and in those identified to have obstructive factors contributing to their disease burden. Further systematic investigation is needed in this area, including prospective comparative studies evaluating therapeutic interventions in ARP and CP incorporating assessment of outcomes including qualify of life after these interventions.

Acknowledgments

Sources of funding: This work was supported by NIH DK096327, DK108334 (AU); National Pancreas Foundation (AU); UL1 TR000442 (CTSA). The sponsors of this study (NIH) did not participate in the study design, collection of data, writing of the report, or the decision to submit this manuscript for publication.

Roles: The concept for the manuscript was developed by DMT, DSF and AU with all authors contributing at a face-to-face meeting and online. The first draft was written by DMT, BAB, DSF, MJG, TKL and QYL. Statistical analysis by MBZ. The manuscript was reviewed, edited, and the final version approved by all authors.

References

1. Corfield AP, Cooper MJ, Williamson RC. Acute pancreatitis: a lethal disease of increasing incidence. Gut. 1985; 26:724–729. [PubMed: 4018637]
2. Nydegger A, Heine RG, Ranuh R, et al. Changing incidence of acute pancreatitis: 10-year experience at the Royal Children's Hospital, Melbourne. J Gastroenterol Hepatol. 2007; 22:1313–1316. [PubMed: 17489962]
3. Morinville VD, Barmada MM, Lowe ME. Increasing incidence of acute pancreatitis at an American pediatric tertiary care center: is greater awareness among physicians responsible? Pancreas. 2010; 39:5–8. [PubMed: 19752770]
4. Li ZS, Wang W, Liao Z, et al. A long-term follow-up study on endoscopic management of children and adolescents with chronic pancreatitis. Am J Gastroenterol. 2010; 105:1884–1892. [PubMed: 20216535]
5. Ceppa EP, Pitt HA, Hunter JL, et al. Hereditary pancreatitis: endoscopic and surgical management. J Gastrointest Surg. 2013; 17:847–856. [PubMed: 23435738]
6. Agarwal J, Nageshwar Reddy D, Talukdar R, et al. ERCP in the management of pancreatic diseases in children. Gastrointest Endosc. 2014; 79:271–278. [PubMed: 24060520]
7. Oracz G, Pertkiewicz J, Kierkus J, et al. Efficiency of pancreatic duct stenting therapy in children with chronic pancreatitis. Gastrointest Endosc. 2014; 80:1022–9. [PubMed: 24852105]

8. Dumonceau J-M, Delhaye M, Tringali A, et al. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2012; 44:784–800. [PubMed: 22752888]

9. Whitcomb DC, Yadav D, Adam S, et al. Multicenter approach to recurrent acute and chronic pancreatitis in the United States: the North American Pancreatitis Study 2 (NAPS2). Pancreatology. 2008; 8:520–531. [PubMed: 18765957]

10. Glass LM, Whitcomb DC, Yadav D, et al. Spectrum of use and effectiveness of endoscopic and surgical therapies for chronic pancreatitis in the United States. Pancreas. 2014; 43:539–543. [PubMed: 24717802]

11. Morinville VD, Lowe ME, Ahuja M, et al. Design and implementation of INSPPIRE. J Pediatr Gastroenterol Nutr. 2014; 59:360–364. [PubMed: 24824361]

12. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42:377–381. [PubMed: 18929686]

13. Kumar S, Ooi CY, Werlin S, et al. Risk Factors Associated With Pediatric Acute Recurrent and Chronic Pancreatitis: Lessons From INSPPIRE. JAMA Pediatr. 2016; 170:562–9. [PubMed: 27064572]

14. Schwarzenberg SJ, Bellin M, Husain SZ, et al. Pediatric Chronic Pancreatitis Is Associated with Genetic Risk Factors and Substantial Disease Burden. J Pediatr. 2015; 166:890–896.e1. [PubMed: 25556020]

15. Morinville VD, Husain SZ, Bai H, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. J Pediatr Gastroenterol Nutr. 2012; 55:261–265. [PubMed: 22357117]

16. Catalano MF, Sahai A, Levy M, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. Gastrointest Endosc. 2009; 69:1251–1261. [PubMed: 19243769]

17. Otto AK, Neal MD, Slivka AN, et al. An appraisal of endoscopic retrograde cholangiopancreatography (ERCP) for pancreaticobiliary disease in children: our institutional experience in 231 cases. Surg Endosc. 2011; 25:2536–2540. [PubMed: 21359895]

18. Coté GA, Imperiale TF, Schmidt SE, et al. Similar efficacies of biliary, with or without pancreatic, sphincterotomy in treatment of idiopathic recurrent acute pancreatitis. Gastroenterology. 2012; 143:1502–1509.e1. [PubMed: 22982183]

19. Díte P, Ruzicka M, Zboril V, et al. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy. 2003; 35:553–558. [PubMed: 12822088]

20. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis. N Engl J Med. 2007; 356:676–684. [PubMed: 17301298]

21. Cahen DL, Gouma DJ, Laramée P, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. Gastroenterology. 2011; 141:1690–1695. [PubMed: 21843494]

22. Bor R, Madácsy L, Fábián A, et al. Endoscopic retrograde pancreatography: When should we do it? World J Gastrointest Endosc. 2015; 7:1023–1031. [PubMed: 26322155]

23. Costamagna G, Pandolfi M, Mutignani M, et al. Long-term results of endoscopic management of postoperative bile duct strictures with increasing numbers of stents. Gastrointest Endosc. 2001; 54:162–168. [PubMed: 11474384]

24. Draganov P, Hoffman B, Marsh W, et al. Long-term outcome in patients with benign biliary strictures treated endoscopically with multiple stents. Gastrointest Endosc. 2002; 55:680–686. [PubMed: 11979250]

25. Catalano MF, Linder JD, George S, et al. Treatment of symptomatic distal common bile duct stenosis secondary to chronic pancreatitis: comparison of single vs. multiple simultaneous stents. Gastrointest Endosc. 2004; 60:945–952. [PubMed: 15605010]

TABLE 1

Patient Characteristics

Total	**N (%)**
Age at enrollment, mean (SD), y	11.9 (4.6)
Age at first attack, mean (SD), y	8.7 (4.9)
Sex, female	172 (57)
Ethnicity, Hispanic	63/276 (23)
Race, n = 265	
White	214 (81)
Multi-racial	20 (8)
Black	10 (4)
Asian	14 (5)
Other	7 (3)
ARP	155 (52)
CP	146 (48)
Exocrine insufficiency	46/259 (18)
Endocrine insufficiency	13/278 (5)
Risk factors	
Toxic-metabolic	23/195 (12)
•Medications	7/287 (2)
•Ethanol exposure	4/287 (1)
•Active smoker	24/269 (9)
•Passive smoke exposure	30/220 (14)
Autoimmune	97/296 (33)
Obstructive factors	
Genetic risk factors	
•*PRSS1*	65/196 (33)
•*SPINK1*	35/177 (20)
•*CFTR*	54/193 (28)
•*CTRC*	9/121 (7)
Therapies Attempted	194/294 (66)
•Medical therapies	145/289 (50)
•Therapeutic ERCP utilization	117/301 (39)
•Surgery (non-TPIAT)	61/292 (21)
•TPIAT	29/291 (10)

SD: standard deviation, ARP: acute recurrent pancreatitis, CP: chronic pancreatitis, *PRSS1:* protease, serine 1, *SPINK1:* serine peptidase inhibitor, Kazal type 1, *CFTR:* cystic fibrosis transmembrane conductance regulator, *CTRC:* chymotrypsin C, ERCP: endoscopic retrograde cholangiopancreatography, TPIAT: total pancreatectomy and islet autotransplantation.

TABLE 2

Predictors of Therapeutic Endoscopy Utilization in Pediatric ARP

Variables	Underwent therapeutic-ERCP, n=21 n (%)	No therapeutic-ERCP, n=134 n (%)	*P*
Sex, female	14 (67)	74 (55)	0.325
Ethnicity, Hispanic	(n=20) 11 (55)	(n=125) 93 (74)	0.074
Race	(n=17)	(n=121)	
White	14 (82)	98 (81)	0.414
Multi-racial	3 (18)	9 (7)	–
Black	0 (0)	5 (4)	–
Asian	0 (0)	7 (6)	–
Other	0 (0)	2 (2)	–
Age at first acute attack, mean (SD), y	(n=18) 9.1 (5.1)	(n=122) 9.0 (5.0)	0.967
Exocrine insufficiency	0/16 (0)	2/111 (2)	1.0
Endocrine insufficiency	0/19 (0)	6/122 (5)	1.0
Alcoholic	0/19 (0)	2/131 (2)	1.0
Active smoker	0/20 (0)	1/130 (1)	1.0
Passive smoking exposure	1/19 (5)	11/121 (9)	1.0
Autoimmune pancreatitis	3/13 (23)	13/99 (13)	0.394
Other autoimmune diseases	3/19 (16)	11/124 (9)	0.400
Genetic Risk Factors:			
PRSS1	0/11 (0)	15/77 (19)	0.199
SPINK1	3/10 (30)	7/68 (10)	0.113
CFTR	3/10 (30)	27/79 (34)	1.0
CTRC	0/6 (0)	5/42 (12)	1.0
Obstructive factors	14/21 (67)	36/131 (27)	0.0004 *
Pancreas divisum	4/20 (20)	9/126 (7)	0.081
Sphincter of Oddi disorders	3/20 (15)	2/124 (2)	0.019 *
Gallstones	3/19 (16)	6/128 (5)	0.093
Pancreatic duct mal-union	2/20 (10)	5/126 (4)	0.245
Duct obstruction	0/20 (0)	1/128 (1)	1.0
Annular pancreas	0/20 (0)	3/128 (2)	1.0
Choledochal cyst	3/20 (15)	2/128 (2)	0.018 *
Medications			
Pain medications	7/13 (54)	34/102 (33)	0.217
Medical therapies	8/19 (42)	36/130 (28)	0.198
Pancreatic enzymes	7/19 (37)	25/130 (19)	0.130

Variables	**Underwent therapeutic-ERCP, n=21 n (%)**	**No therapeutic-ERCP, n=134 n (%)**	***P***
Pancreatic enzymes (not for PI)	7/19 (37)	24/130 (18)	0.076
Vitamins/anti-oxidants	1/18 (6)	11/127 (9)	1.0
Steroids	0/18 (0)	0/125 (0)	–
Octreotide	0/19 (0)	2/128 (2)	1.0

*Statistically significant.

ARP: acute recurrent pancreatitis, SD: standard deviation, PRSS1: protease, serine 1, *SPINK1:* serine peptidase inhibitor, Kazal type 1, *CFTR:* cystic fibrosis transmembrane conductance regulator, *CTRC:* chymotrypsin C, PI: pancreatic insufficiency, ERCP: endoscopic retrograde cholangiopancreatography.

TABLE 3

Predictors of Therapeutic Endoscopy Utilization in Pediatric CP

Variables	Underwent therapeutic ERCP, n=96 (%)	No therapeutic ERCP, n=50 (%)	*P*
Sex, female	60 (62)	24 (50)	0.093
Ethnicity, Hispanic	(n=85) 19 (22)	(n=46) 3 (7)	0.021 *
Race	(n=80)	(n=47)	0.010 *
White	68 (85)	34 (72)	–
Multi-racial	4 (5)	4 (8)	–
Black	6 (6)	0 (0)	–
Asian	1 (1)	6 (13)	–
Other	2 (3)	3 (7)	–
Age at first acute attack, mean (SD), y	(n=81) 8.3 ± 4.6	(n=38) 8.1 ± 4.9	0.827
Age at first diagnosis CP, mean (SD), y	(n=72) 9.7 ±4.4	(n=32) 11.3 ± 4.6	0.106
Exocrine insufficiency	29/89 (33)	15/43 (35)	0.793
Endocrine insufficiency	6/93 (6)	1/44 (2)	0.429
Alcoholic	1/90 (1)	4/47 (9)	0.028 *
Active smoker	1/90 (1)	2/47 (4)	0.271
Passive smoking exposure	9/84 (11)	3/45 (7)	0.540
Autoimmune pancreatitis	2/68 (3)	12/40 (30)	<0.0001 *
Other autoimmune diseases	5/92 (5)	3/46 (7)	1.0
Genetic Risk Factors:			
PRSS1	34/75 (45)	16/33 (48)	0.762
SPINK1	16/69 (23)	9/30 (30)	0.473
CFTR	14/71 (20)	10/33 (30)	0.233
CTRC	4/53 (8)	0/20 (0)	0.570
Obstructive factors	38/95 (38)	9/49 (18)	0.009 *
Pancreas divisum	16/91 (18)	6/49 (12)	0.408
Sphincter of Oddi disorders	2/91 (2)	0/48 (0)	0.545
Gallstones	5/92 (5)	1/47 (2)	0.664
Pancreatic duct mal-union	5/91 (5)	1/48 (2)	0.664
Duct obstruction	4/93 (4)	0/48 (0)	0.299
Annular pancreas	1/93 (1)	0/48 (0)	1.0
Choledochal cyst	2/93 (2)	0/48 (0)	0.548
Medications			
Pain medications	42/73 (58)	20/36 (56)	0.844
Medical therapies	72/94 (77)	29/46 (63)	0.093

Variables	**Underwent therapeutic ERCP, n=96 (%)**	**No therapeutic ERCP, n=50 (%)**	***P***
Pancreatic enzymes	55/93 (59)	22/46 (48)	0.060
Vitamins/anti-oxidants	14/89 (16)	6/45 (13)	0.713
Steroids	3/90 (3)	5/45 (11)	0.116
Octreotide	4/89 (4)	1/46 (2)	0.661

*Statistically significant.

CP: chronic pancreatitis, SD: standard deviation, PRSS1: protease, serine 1, SPINK1: serine peptidase inhibitor, Kazal type 1, CFTR: cystic fibrosis transmembrane conductance regulator, CTRC: chymotrypsin C, ERCP: endoscopic retrograde cholangiopancreatography.

TABLE 4

Benefit of Endoscopic Interventions in Pediatric ARP and CP

Intervention	ARP, n = 155 n (%)	CP, n = 146 n (%)	*P*
Therapeutic ERCP performed	21 (14)	96 (66)	<0.0001 *
Helpful for at least one indication	9/16 (56)	44/83 (53)	0.812
Biliary sphincterotomy performed	11/151 (7)	36/136 (26)	<0.0001 *
Helpful	6/10 (60)	12/30 (40)	0.300
Biliary stenting performed	2/151 (1)	11/138 (8)	0.006 *
Helpful	2/2 (100)	3/10 (30)	–
Pancreatic sphincterotomy performed	4/151 (3)	68/138 (49)	<0.0001 *
Helpful	2/4 (50)	33/66 (50)	–
Pancreatic duct stenting performed	6/151 (4)	60/137 (44)	<0.0001 *
Helpful	2/5 (40)	28/57 (49)	–
Pancreatic stone removal performed	1/151 (1)	30/137 (22)	<0.0001 *
Helpful	1/1 (100)	18/18 (100)	–

* Statistically significant.

ARP: acute recurrent pancreatitis, CP: chronic pancreatitis, ERCP: endoscopic retrograde cholangiopancreatography.