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Retrospective Study

Prognostic factors of response to endoscopic treatment in painful chronic pancreatitis

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Abstract**AIM**

To evaluate the endoscopic treatment efficacy and

prognostic factors of long-term response to treatment for painful chronic pancreatitis.

METHODS

This retrospective analysis identified 168 patients with painful chronic pancreatitis hospitalized during January 2010-January 2015 in a Romanian tertiary referral center. Data on demographics, medical history, alcohol consumption, smoking habit, clinical parameters, type and number of endoscopic procedures and hospital admissions number were collected from the medical charts and analyzed. The absence or substantial reduction of pain (mild pain) at the end of the follow-up associated with the technical success of endotherapy was considered as clinical success.

RESULTS

Among the 168 patients with painful chronic pancreatitis admitted to our department during the study period, 39 (23.21%) had optimal response to the medical therapy. One hundred and twenty-nine patients required endoscopic treatment. The median follow-up period was 15 mo (range, 0-60 mo). Overall, technical success of endotherapy was achieved in 105 patients (81.39%). More than two-thirds of patients (82.78%) had substantial improvement of pain after the endoscopic treatment, including frequency and severity of the pain attacks. Patients younger than 40 years had significantly more successful endoscopic procedures ($P = 0.041$). Clinical success was higher in non-smoking patients ($P = 0.003$). The hospital admission rate was higher in patients with recognized alcohol consumption ($P = 0.03$) and in smokers ($P = 0.027$). The number and location of pancreatic stones and locations of strictures did not significantly influence the technical success ($P > 0.05$) or the clinical success ($P > 0.05$).

CONCLUSION

Younger age than 40 years can be considered an important factor positively influencing endoscopic treatment outcome in patients with painful chronic pancreatitis.

Key words: Pain; Chronic pancreatitis; Endoscopic procedures; Alcohol; Smoking; Hospital admission; Technical success; Clinical success

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Core tip: We evaluated the endoscopic treatment efficacy and prognostic factors of long-term response in painful chronic pancreatitis. Technical and clinical success was achieved in more than two-thirds of patients. Patients younger than 40 years had significantly more successful endoscopic procedures. Non-smoking patients had greater clinical success. Also, the hospital admission rate was higher in patients with recognized alcohol consumption and in smokers. Number and location of pancreatic stones and locations of strictures did not significantly influence the technical

or clinical success. Younger age can be considered an important factor that positively influences the endoscopic treatment outcome in these patients.

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INTRODUCTION

Patients with chronic pancreatitis (CP) often present with severe abdominal pain, resistant to common analgesics. The exact pathophysiology of CP is still unknown, being a debated subject^[1]. Increased intrapancreatic pressure within the parenchyma and/or pancreatic duct causing tissue ischemia (due to pancreatic duct strictures and stones), inflammation of the pancreas, and pancreatic and extrapancreatic complications^[1] (*i.e.*, pseudocysts, bile duct/duodenal strictures and peptic ulcers) are factors suggested as causing pain in CP.

The endoscopic treatment of painful CP remains a clinical challenge. The goals of endotherapy are to drain the pancreatic duct^[2], to reduce the frequency and the severity of the pain, and to resolve the local complications of the disease. Unfortunately, few data are available on the long-term efficacy of this endoscopic treatment. Most of the authors of the related literature consider that endoscopic retrograde cholangiopancreatography (ERCP) should be used as a first-line treatment in patients unresponsive to medical therapy. The efficacy of ERCP is comparable to that surgery, with a higher success rate in properly selected patients and a low morbidity rate. Moreover, it can be performed repeatedly and independently of patient age. In some cases it may be considered as a "bridge" to subsequent surgery^[3-5].

Several studies have identified the factors associated with a good long-term outcome of endoscopic treatment in painful CP, including cephalic intraductal stones, complete pancreatic clearance, absence of ductal stricture, and recent onset of disease^[6-9]. Also, cessation of alcohol consumption and of smoking is associated with a good outcome^[7,10]. Higher rates of clinical success have been associated with a short interval between the CP onset and endoscopic therapy and older age at the onset of disease^[7]. Different literature data have evidenced better results of surgery vs endoscopic treatment in terms of pain control^[11,12]. Regarding the short-term outcome, no significant differences have been found between endoscopic treatment and surgery in terms of hospitalization rate and medical costs. Instead, the hospitalization rate

and its duration were found to be significantly higher in patients with endoscopic treatment, regarding the long-term outcome compared to surgery^[13].

In this study, we considered our case experience from a referral tertiary center in Romania to evaluate the endoscopic treatment efficacy and prognostic factors of long-term response to treatment in patients with painful CP. Our intention was to determine whether ERCP maintains merits in the management of pain in CP and if there are some new clinical or endoscopic factors which might help to achieve long-term results.

MATERIALS AND METHODS

Patients

We retrospectively searched the medical database of our hospital (a tertiary referral center; Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania) to identify all patients with painful CP hospitalized for treatment in our Gastroenterology Department during January 2010-January 2015 ($n = 168$). Patients with good response to medical therapy and without required endotherapy were excluded from the study ($n = 39$). All patients who underwent endotherapy with treatment intention were included in the study ($n = 129$).

Data on demographics, medical history, clinical data (*i.e.*, abdominal pain pattern and severity, diarrhea, diabetes, jaundice), hospital admissions number, type and number of endoscopic procedures and complications of treatment were collected from the medical charts and analyzed. Alcohol consumption was defined as a daily intake of > 20 g of ethanol for both women and men. Cigarette smoking was defined as smoking at least 5 pack-years^[7].

The first parameter taken into account was abdominal pain relief in patients with pancreatic drainage. The pain character and intensity was quantified based on patients' medical records at study enrollment and at end of follow-up. No standardized instruments for pain quantifying, quality of life or psychosocial impact evaluation were used. In the medical records, the severity of pain was qualified as severe, moderate and/or mild with continuous or intermittent pattern.

Endoscopic treatment

All ERCPs and endoscopic procedures were performed by the same experienced endoscopist physician (> 600 ERCPs/year). According to the initial pancreatography findings, the patients with pancreatic drainage were divided into three different groups: patients with pancreatic strictures; patients with pancreatic intraductal stones; and patients with pancreatic strictures and intraductal stones. An efficient pancreatic sphincterotomy and/or successful stent placement across the strictures and/or intraductal stones removal was considered a technical success. Otherwise, the

endoscopic treatment was considered as a failure. Also, we considered any form of surgical drainage performed during the follow-up period as indicating failure of the endoscopic treatment. All instances of early complications (in first 24 h post-ERCP) were also noted.

In patients with intention to treat, the endoscopic treatment was considered as complete if no further ERCP session was required and if no pancreatic stents were *in situ* at the cut-off date (January 2015). Otherwise, endotherapy was considered as ongoing. The absence of significant reduction of pain (absent or mild pain) at the end of follow-up associated with the technical success of endotherapy was considered a clinical success. Treatment of concomitant bile duct strictures ($n = 35$) and pseudocysts ($n = 28$) were also noted. Considering biliary drainage, clinical success was noted in the case of jaundice improvement with the bile duct stricture waist disappearing.

According to the European Society of Gastrointestinal Endoscopy guidelines, in patients with pseudocysts, technical success was considered where at least one stent from a pancreatic pseudocyst to the digestive lumen was able to be inserted^[6] or by resolution of the fluid collection. Short-term clinical success was considered in the case of complete relief of the initial symptoms with a decrease in pseudocyst diameter of at least 30%-50% at 1 mo^[6]. For large ductal stones in the pancreatic head or body, one or multiple sessions of extracorporeal shock wave lithotripsy (ESWL) were performed. A third-generation electromagnetic lithotripter (Dornier MedTech, Weisling, Germany) was used, with the patient under general anesthesia.

Statistical analysis

Qualitative data is presented as counts and percentages. Quantitative data is presented as means and standard deviations for normally distributed data, and as medians and standard deviations and interquartile ranges or ranges for skewed distributions. Associations between qualitative variables were assessed with the chi-square test or Fisher's exact test. Comparisons between two groups of quantitative skewed data were performed with the Wilcoxon rank sum test, and comparisons between three groups with the Kruskal-Wallis test, followed by nonparametric post hoc tests.

For all statistical tests performed, we used the two-tailed *P*-value and an 0.05 level of significance. All analyses were computed with R environment for statistical computing and graphics version 3.2.3 (<http://www.R-project.org/>).

RESULTS

Clinical characteristics of patients

From January 2010 to January 2015, 168 patients with painful CP were admitted to our department.

Table 1 Demographic, etiological and clinical characteristics of patients at study entry, [*n* = 129, *n* (%)]

Sex as male/female	106 (82.17)/23 (17.83)
Age (mean ± SD, yr)	51.55 ± 11.34
Etiology	
Alcoholic	102 (79.07)
Autoimmune	2 (1.55)
Genetic	2 (1.55)
Idiopathic	13 (10.08)
Metabolic	3 (2.33)
Pancreas divisum	7 (5.43)
Pain pattern: continuous/intermittent	22 (17.05)/107 (82.95)
Pain intensity: severe/moderate	57 (44.19)/72 (55.81)
Diabetes	41 (31.78)
Diarrhea	63 (48.84)

Thirty-nine patients (23.21%) had optimal response to the medical therapy (*i.e.*, paracetamol, non-steroidal anti-inflammatory drugs, tramadol, co-medication for neuropathic pain, and pancreatic enzyme substitution) and they were excluded from the study. Thus, 129 patients were enrolled in the study. The mean age was 51.55 years (range, 15-82 years). One hundred and six were men (82.17%) and 23 were women (17.83%). Demographical, etiological and clinical data are shown in Table 1. Seventy-five patients (58.14%) were alcohol drinkers and 47 patients (36.43%) were smokers at study enrollment. The median follow-up period was 15 mo (range, 0-60 mo).

Endoscopic pancreatic drainage

During the study period a total of 265 ERCPs were performed, with a median of 2.8 procedures/patient. At the initial pancreatography, 89 patients (68.99%) had only pancreatic duct strictures, 17 patients had only intraductal pancreatic stones (13.18%) and 23 patients (17.83%) had both intraductal stones and strictures. Seven patients (5.43%) had pancreas divisum and were treated *via* the minor papilla.

Overall, technical success was achieved in 105 patients (81.39%). At the end of study, endoscopic treatment was completed in 103 patients and ongoing in 2 patients. Endotherapy failure was noted in 24 patients (18.6%). In 7 of these patients (29.16%) the endoscopic procedures could not be performed due to severe stenosis of the pancreatic duct and/or giant intraductal stones. The number and size of the intraductal pancreatic stones and the location of ductal stenosis did not significantly influence the clinical and technical success (Tables 2 and 3).

Early complications post-ERCP appeared in 7 patients (6.67%) who had technical success and in 2 patients (8.33%) who had failure of the endoscopic treatment. Acute pancreatitis post-ERCP was noted in 8 patients (6.2%) and post-sphincterotomy bleeding in 1 patient (0.77%). All complications were successfully managed conservatively.

Patients with at least one session of endoscopic treatment (*n* = 122): There were no statistically significant differences regarding the number of hospital admissions, the number of ERCP/patients and the number of endoscopic procedures between patients with technical success (86.06%) vs failure of endotherapy (13.93%) (Table 4). More than two-thirds of the patients with at least one session of endoscopic treatment (*n* = 101, 82.78%) had clinical success after the endoscopic treatment, including improvements in frequency and severity of pain attacks (Table 5).

Patients with pancreatic strictures alone at initial pancreatography (*n* = 85): In 23 patients (27.05%), a pancreatic sphincterotomy was the only sufficient procedure. Sixty-two patients (72.94%) required multiple procedures. Multiple pancreatic restenting sessions were performed in 6 patients (7.05%). The clinical success rate was 81.17% (*n* = 69) (Table 6).

Patients with pancreatic intraductal stones alone at initial pancreatography (*n* = 17): Two patients (11.76%) required initial ESWL followed by endoscopic stone extraction. To achieve stone clearance, multiple sessions of stone extraction were performed in all patients. The clinical success rate was 76.47% (*n* = 13) (Table 6).

Patients with pancreatic strictures and intraductal stones at initial pancreatography (*n* = 20): Multiple procedures were performed in all patients. Six patients (30%) required pancreatic restenting, five of who (25%) required multiple stone extraction sessions. Two patients still had pancreatic plastic stents in place at the end of the study period. The clinical success rate was 95% (*n* = 19) (Table 6). There were significant differences regarding the number of ERCP/patient between the group of patients with pancreatic strictures and those with strictures and stones ($P < 0.001$) and in terms of procedures/patient in all three groups ($P < 0.001$) (Table 6). No statistically significant differences were found regarding the mean age and severity of initial pain, technical success ($P = 0.995$) or clinical success ($P = 0.899$). However, the technical success was significantly higher in patients younger than 40-years-old ($P = 0.041$).

No statistically significant association was found between the continuation of alcohol drinking and clinical success ($P = 0.066$). In contrast, non-smoking patients had a higher rate of clinical success than their smoking counterparts ($P = 0.003$). Considered separately, patients without any alcohol consumption or smoking had a better prognosis than patients who had one or both addictions ($P = 0.007$) (Table 7). Alcohol drinkers (*n* = 75) had a higher hospital admission rate (4 vs 3, $P = 0.03$) than patients who were not alcohol drinkers (*n* = 54). The number of

Table 2 Technical and clinical success according to the initial pancreatography *n* (%)

	<i>n</i>	Technical success	Clinical success
All patients	129	105 (81.39)	101 (78.29)
Only pancreatic stones	17	14 (82.35)	13 (76.47)
Cephalic	16		
Non-cephalic	1		
Cephalic and non-cephalic	0		
Only pancreatic strictures	89	71 (79.77)	69 (81.18)
Cephalic	82		
Non-cephalic	5		
Cephalic and non-cephalic	2		
Pancreatic strictures + stones	23	20 (86.95)	19 (95)
Cephalic stones + cephalic strictures	19		
Cephalic stones + cephalic and non-cephalic strictures	2		
Cephalic and non-cephalic stones + cephalic strictures	2		

Table 3 Clinical and technical success according to number and size of stones *n* (%)

	Technical success				Clinical success			
	Yes ¹	No ²	OR (95%CI)	<i>P</i> -value	Yes ¹	No ²	OR (95%CI)	<i>P</i> value
Stone number, median (IQR)	2 (1-2)	1 (1-1.75)	0.28 (0.004-5.96)	0.39	2 (1-2)	1 (1-1)	0.36 (0.03-3.64)	0.098
Stone size, <i>n</i>	34	6			32	5		
5-10 mm, <i>n</i> = 14	12 (80)	3 (20)		0.073	11 (78.57)	3 (21.43)		0.346
< 5 mm, <i>n</i> = 23	22 (91.67)	2 (8.33)			21 (91)	2 (8.7)		
< 10 mm, <i>n</i> = 1	-	1			-	-		

¹Technical or clinical success achieved; ²Failure of endoscopic treatment and no pain improvement. IQR: Interquartile range.

Table 4 Hospital admissions and procedures in patients with endoscopic treatment (technical success *vs* failure of endoscopic treatment) (*n* = 122)

	Technical success		
	Yes, <i>n</i> = 105	No, <i>n</i> = 17	<i>P</i> value
Hospital admissions	3 (3-5)	3 (3-5)	0.728
ERCP/patient	2 (1-3)	2 (1-2)	0.605
Procedures/patient	3 (1-4)	2 (0-3)	0.055

Data are presented as median (IQR). IQR: Interquartile range; ERCP: Endoscopic retrograde cholangiopancreatography.

endoscopic procedures/patients was higher (3 *vs* 2) in alcohol drinkers, but not significantly (*P* = 0.249). In smokers (*n* = 47), the hospital admission rate was higher (4 *vs* 3, *P* = 0.027) than for patients who were non-smokers (*n* = 82) and the endoscopic procedures required was also greater (3 *vs* 2, *P* = 0.622). Newly diagnosed diabetes appeared in 14 patients (13.46%) with clinical success during follow-up.

Biliary drainage

During the follow-up period, 35 patients (28.68%) developed biliary stricture with jaundice. Biliary drainage was achieved using a single plastic biliary stent in 21 patients (60%) and simultaneous biliary plastic stents in 2 patients (5.71%). Multiple biliary

stent sessions were performed in 12 patients (34.29%). Covered self-expanding metallic stents (SEMS) were used in 2 patients (5.71%) who were deemed at high surgical risk. Biliary drainage was successful in 26 patients (74.29%) and failed in 9 patients (25.71%).

Pancreatic pseudocysts

Pancreatic pseudocysts were identified in 28 patients (22.95%). Transpapillary drainage was performed in 17 cases (60.71%) and transmural drainage in 9 cases (32.14%). In 1 patient (3.57%) the endoscopic approach could not be achieved due to the severe stenosis of the pancreatic duct and surgical drainage was indicated. Technical success was achieved in 96.43% cases (*n* = 27). Short-term clinical success was achieved in 26 patients (96.3%). Endoscopic ultrasound drainage was indicated in 1 patient because of an increase in the size of the pseudocyst and remarkable collateral circulation in the portal hypertension context.

Surgery

In 24 patients (18.6%) the endoscopic treatment failed and some form of surgery was performed during follow-up. In 7 patients, no endoscopic procedures were performed. The endoscopic treatment was converted to surgery in 17 patients (13.93%).

Table 5 Pain evolution in patients with endoscopic treatment [n = 122, n (%)]

	Technical success			P value
	Yes, n = 105	No, n = 17	OR (95%CI)	
Pain reduction	104 (99.05)	13 (76.47)	30.3 (2.7-1572.8)	0.001
Final pain				
Absent	52 (49.52)	1 (5.88)	Absent <i>vs</i> others:	< 0.001
Mild	49 (46.67)	5 (29.415)	15.4 (2.2-668.6)	
Moderate	4 (3.81)	11 (64.71)	Absent + mild <i>vs</i> moderate + severe:	
			42.8 (9.5-245.0)	
Severe	-	-		

Table 6 Endoscopic drainage (endoscopic retrograde cholangiopancreatography and procedures/patients) according to initial pancreatography changes (n = 122)

	Stones, n = 17	Strictures, n = 85	Strictures + stones, n = 20	P value
ERCP/patient ¹	2 (1-3)	2 (1-2) ^c	2 (2-3) ^c	< 0.001
Procedures/patient ¹	3 (2-5) ^a	2 (1-3) ^c	4 (3-4) ^{ac}	< 0.001
Only one procedure	0	23	0	< 0.001
Multiple procedures	17	62	20	< 0.001
Clinical success	13	69	19	0.221

¹Data are presented as median (IQR). ^aP < 0.05, *vs* the groups with Stones to the group Strictures + Stones had a; ^cP < 0.05, *vs* the groups with Strictures to the group Strictures + Stones had a. IQR: Interquartile range; ERCP: Endoscopic retrograde cholangiopancreatography.

DISCUSSION

Through this retrospective study, we obtained results of the endoscopic approach of painful CP patients in a tertiary referral center. Technical success was achieved in 81.39% of patients with significant improvement of pain experienced by more than two-thirds of the patients, including frequency and severity of pain attacks. About 50% of the patients were pain-free at the end of follow-up. We found that age under 40 years, no smoking, no alcohol consumption and multiple ERCP sessions are independent factors associated with a good response to the endoscopic treatment.

Few data are available on the long-term efficacy of endoscopic treatment in painful CP^[4,6-8,14,15]. Endoscopy societies recommend endoscopic drainage as first-line therapy in painful obstructive CP^[6,16]. Our study was conducted on a large group of patients with a median long-term follow-up and describes the new approach to the position of endotherapy in treatment of patients suffering from CP.

The aim of endotherapy is to decompress the main pancreatic duct by complete stone clearance and ductal drainage^[17]. The cause of pain in CP is multifactorial, explaining why symptom relief can be unsatisfying even if technical success is achieved^[16]. Surgery is indicated in patients with persistent pain that does not respond to medical and/or endoscopic treatment^[16], in patients with a heavy stone burden (especially in the body/tail of the pancreas with pancreatic ductal dilatation and/or strictures^[11,17,18]) or in the case of a suspected pancreatic inflammatory mass^[16]. Endotherapy should also be considered in patients at high surgical risk^[19].

There are several studies with good results regarding the long-term outcome after endoscopic treatment in painful CP^[4,7-8,14-15] with a median rate of endotherapy success of 83%^[6]. In our series, most patients required multiple procedures to obtain the goal of endoscopic therapy. In these patients, the pancreatography changes were more severe than those in patients with only a pancreatic sphincterotomy. There is one small series with a median of three stents for refractory pancreatic strictures showing good results after a mean follow-up

of 38 mo^[20], and three prospective series of the use of SEMS^[21,22]. The use of multiple large plastic stents and expandable metal mesh stents in the pancreatic duct is not yet considered standard of care^[16]. In a selected center with experience, ESWL of large pancreatic stones can lead to ductal clearance, as effective and more cost effective than the ERCP combination^[9,23]. Our center does not dispose of equipment for ESWL, and 2 patients with large intraductal stones with diameter > 15 mm, impacted upstream of a tight ductal stenosis benefited from this procedure in another center prior to endoscopic ductal clearance.

We found that the numbers of procedures and sessions of ERCP was statistically higher in patients with stones and strictures than in patients with stones or strictures alone. But, we did not find any correlation between the size and number of stones or the number and location of stenosis with technical or clinical success. Data showed that the cephalic stones^[9], complete pancreatic stone clearance and absence of main pancreatic duct stricture are the factors independently associated with long-term (≥ 2 years) pain relief following endoscopic therapy^[6,24,25]. A single stricture located in the pancreatic head is the ideal situation for endoscopic treatment compared to an isolated stricture in the tail or multiple strictures in the pancreas body^[24].

There are few data regarding the correlation between age of patient and technical or clinical success of endotherapy^[25]. Using a cut-off of 40 years for age, we noticed that younger patients had a better response to endoscopic treatment ($P = 0.041$). As far as we know, our study is the first described in the literature to evaluate the association of younger age and endoscopic technical success in patients with painful CP. We must emphasize that endoscopic treatment should be initiated earlier in young patients with painful CP in order to achieve better results.

Alcohol and smoking are independent risk factors of CP. Alcohol abuse causes pancreatic fibrosis by stellate cell activation^[26] and is an important factor for mortality in CP. Alcohol abstinence may help in providing pain relief^[16]. Smoking is an independent

Table 7 Smoking and alcohol drinking influence on clinical success and technical success [*n* = 122, *n* (%)]

	Technical success					Clinical success				
	Yes	No	OR (95%CI)	<i>P</i> value	<i>P</i> value overall	Yes	No	OR (95%CI)	<i>P</i> value	<i>P</i> value overall
Smoker only, <i>n</i> = 11	8 (66.67)	3 (33.3)	0.16 (0.02-1.15)	0.036		7 (63.64)	4 (36.36)	0.05 (0.001-0.59)	0.006	
Alcohol only, <i>n</i> = 36	31 (77.5)	5 (22.5)	0.27 (0.04-1.20)	0.064		30 (83.33)	6 (16.67)	0.13 (0.003-1.17)	0.048	
Non-smoker and non-alcohol, <i>n</i> = 40	39 (92.8)	1 (7.14)	-	-	0.103	39 (97.5)	1 (2.5)	-	-	0.007
Smoker and alcohol, <i>n</i> = 35	27 (77.1)	8 (22.8)	0.26 (0.04-1.23)	0.099		25 (71.43)	10 (28.5)	0.066 (0.001-0.52)	0.002	

risk factor for the development and progression of pancreatitis^[10,27] and carcinogenesis^[28]. It has been shown that abstinence not only slows the disease progression but also prevents complications such as pancreatic cancer^[29-31]. Cessation of alcohol has beneficial effects on clinical outcome and progression of painful CP^[30,31]. An association between smoking and CP pain has yet to be determined.

We found that patients without any alcohol consumption or smoking had better prognosis than patients who had one or both addictions, regarding clinical success ($P = 0.007$). Cigarette smoking was associated with a poor clinical outcome in our group. Furthermore, hospital admission rates were significantly higher in patients who continued alcohol drinking and smoking. Our results add new and important data regarding the association of smoking and CP pain and emphasized the importance of smoking and alcohol cessation in those patients.

Endoscopic drainage is also recommended as a first-line treatment in uncomplicated pancreatic pseudocysts^[32], with similar outcomes to surgery regarding the recurrence rate during long-term follow-up and better results in terms of mortality^[33,34], medical cost and quality of life^[35]. In our series, endoscopic drainage was feasible in almost all patients, and technical success was 96.43% with a short-term clinical success of 96.3%; similar results are in the literature^[36-39].

The success of endotherapy in biliary drainage in CP is poor in most of the published series, with a 10%-33% rate of stricture resolution^[40-47]. The choice between endoscopic and surgery drainage should be made according to the medical center's expertise, patient co-morbidities and compliance to repeat endoscopic procedures^[6]. Multiple simultaneous plastic stents reportedly have better results^[48-50] than single biliary plastic stenting. Recent data demonstrate good results using covered expandable metal stents^[51-54]. In our series, biliary drainage was successful in 74.29% of patients during follow-up. Multiple single biliary stent sessions were performed in 12 patients (34.29%)

and simultaneous biliary plastic stents in 2 patients (5.71%). Covered SEMS were used in 2 patients with multiple comorbidities and high surgical risk.

CP is a progressive inflammatory disease. Patients with long-term CP or extensive pancreatic resection can develop type 3 diabetes mellitus, characterized by a lack of insulin and other counter-regulatory islet hormones, such as glucagon^[55-57]. In our series, diabetes was present initially in one-third of patients. Newly diagnosed diabetes appeared in a quarter of patients with clinical success during follow-up. We speculate that endoscopic and clinical success do not stop the progression of exocrine and endocrine pancreatic deterioration.

Our study has several weaknesses that should be considered when interpreting our results. This is a retrospective study in a single tertiary academic center and can overestimate clinical success. We did not do use any objective assessment of pain control, standardized instruments for pain quantification, quality of life and psychosocial impact evaluation in patients with CP. Also, the continuing use of concomitant medical therapy was not followed. We consider that large, multicenter randomized studies are required to evaluate ERCP efficacy vs surgery in patients with painful CP without response to medical therapy.

In conclusion, endoscopic therapy in painful CP is effective and safe. Technical success was achieved in 81.39% of cases. Clinical success was achieved in 82.78% of the patients, with multiple endoscopic procedures being required in the majority of cases. Positive prognostic factors of response to endoscopic treatment are age under 40 years, no smoking, no alcohol consumption, and multiple ERCP sessions. Number and size of the intraductal pancreatic stones and the location of ductal stenosis did not significantly influence the clinical and technical success. Alcohol drinking and smoking should be recognized early and aggressively advised against to improve the quality of life and to reduce hospital admission. Endoscopic treatment should be considered as the first choice of

pain treatment, especially in younger patients.

COMMENTS

Background

The endoscopic management of patients with chronic pancreatitis (CP) pain is very challenging. The intraductal stone location, complete pancreatic clearance, absence of ductal stricture, recent onset of the disease and alcohol cessation are proven factors associated with a good long-term outcome of endoscopic treatment in painful CP. Other prognostic factors, such as young age and smoking cessation, are under investigation. In this retrospective study, we evaluated new clinical or endoscopic factors which might help to achieve long-term results.

Research frontiers

Few studies have evaluated the association of smoking with CP pain. No study to date has evaluated the prognostic role of younger age in patients with painful CP who undergo endoscopic treatment.

Innovations and breakthroughs

The results of this study underline the efficacy of endoscopic treatment in patients without response to medical therapy regarding pain relief, especially in younger patients. The authors have found that younger age, no smoking, no alcohol consumption, and multiple endoscopic retrograde cholangiopancreatography (ERCP) sessions are independent factors associated with a good response to endoscopic treatment.

Applications

Most patients with painful CP undergo endoscopic treatment as first step strategy. In the present study, the endoscopic treatment in young patients with painful CP might affect long-term clinical outcome.

Terminology

ERCP is an endoscopic procedure that combines the use of endoscopy and fluoroscopy to diagnose and treat certain problems of the biliary or pancreatic ductal systems (stones, strictures, pseudocysts, tumors).

Peer-review

This is a retrospective study discussing the efficacy of endoscopic therapy in chronic pancreatitis. Overall the study is well written. Results are clear and to the point.

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