

Comparison of the Profile and Management of Chronic Pancreatitis between China and Western Countries: A Single-Center Experience and Literature Review

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Objective: The etiology, clinical presentation, diagnosis, and treatment strategies of chronic pancreatitis (CP) vary significantly between countries. Specifically, the etiology and surgical approaches to treating CP differ between China and Western countries. Therefore, this study aims to compare the disparities in CP profiles and management based on our single-center experience and recent data from the West.

Methods: From January 2007 to December 2017, a total of 130 consecutive patients with histologically confirmed chronic pancreatitis (CP) underwent surgical treatment at the First Affiliated Hospital of Nanjing Medical University. The clinical features, etiology, risk factors, and operative procedures of these CP patients were analyzed and compared with recent data from Western countries.

Results: Our patient cohort was predominantly male (3.19:1), with a median age of 50.2 ± 9.8 years. Upper abdominal pain was the most common symptom, present in 102 patients (78.5%). The most common etiology was obstructive factors (47.7%), followed by alcohol (34.6%). The incidence of genic mutation was 2%, significantly lower than rates reported in Western research. Steatorrhea, weight loss, and jaundice were present in 6.9%, 18.5%, and 17.7% of patients, respectively. Pancreatic cysts or pseudocysts were diagnosed in 7 patients (5.4%). The following procedures were performed: Partington procedure in 33 patients (25.4%), Frey procedure in 17 patients (13.2%), Berne procedure in 5 patients (3.9%), Beger procedure in 1 patient (0.8%), pancreaticoduodenectomy in 17 patients (13.1%), pylorus-preserving pancreaticoduodenectomy in 18 patients (13.9%), middle pancreatectomy in 1 patient (0.8%), and distal pancreatectomy in 9 patients (6.9%). Choledochojejunostomy was performed in 14 patients (10.8%), gastroenterostomy in 2 (1.5%), and 15 patients (11.5%) underwent aspiration biopsy.

Conclusion: Our study confirms that, etiologically, obstructive chronic pancreatitis (CP) is more frequent in the Chinese population than in Western populations. Although diagnostic instruments and operative procedures in China and Western countries are roughly comparable, slight differences exist in relation to diagnostic flowcharts/criteria and the indications and optimal timing of surgery.

Keywords: chronic pancreatitis; risk factors; treatment; surgery

Introduction

Chronic pancreatitis (CP) is a progressive, chronic disease with a global estimated incidence of 9.62 per 100,000 population [1]. Prevalence rates ranging from 36 to 125 per 100,000 population have been reported in the United States of America (USA), China, Japan, and India, with the highest prevalence noted in India [2]. There is considerable variation among countries in the etiology, clinical presenta-

tion, diagnosis, and treatment strategies of CP, particularly concerning etiology and surgical treatment between China and Western countries. However, these differences have not been formally addressed [3]. Thus, this study aims to compare disparities in the profiles and management of CP based on experiences within a single center and recent reports in the literature from Western countries.

Methods

From January 2007 to December 2017, a total of 130 consecutive patients with histologically confirmed chronic pancreatitis (CP) underwent surgical treatment at The First Affiliated Hospital of Nanjing Medical University, a tier-3A referral hospital in Nanjing, China. All data were extracted, and events were assessed based on patients' medical records. The clinical features, etiology, risk factors, and operative procedures of the 130 CP patients were analyzed. Additionally, we screened for the R122H and N29I

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Table 1. Clinical features of patients with chronic pancreatitis.

Clinical features	Data
Total patients (n)	130
Mean (SD) age	50.2 ± 9.8 years
M:F (ratio)	3.19:1
Upper abdominal pain	102 (78.5%)
Steatorrhea	9 (6.9%)
Weight loss	24 (18.5%)
Jaundice	23 (17.7%)
Diabetes mellitus	36 (27.7%)
Median (range) duration of symptom	2 (1–144) months

Table 2. Etiology and risk factors of chronic pancreatitis.

Etiology and risk factors	n (%)
Non-alcoholic chronic pancreatitis	85 (65.4%)
Obstructive factors (biliary disease)	62 (47.7%)
Others	23 (17.7%)
Alcoholic chronic pancreatitis (alcohol intake > 80 g/day for males or 60 g/day for females >2 years)	45 (34.6%)
Smokers (>10 cigarette per day for >2 years)	53/130 (40.8%)
Alcoholic chronic pancreatitis and smokers	42/45 (93.3%)
Idiopathic chronic pancreatitis and smokers	11/85 (12.9%)

mutations of the cationic trypsinogen (PRSS1) gene and the N34S mutation of the serine protease inhibitor Kazal type 1 (SPINK1) gene in 100 randomly selected patients from the 130, with an additional 100 healthy subjects serving as controls. Each patient’s history of alcohol intake, including duration and daily amount, was obtained. Alcoholism was defined as a daily intake of >80 g/day for males and >60 g/day for females for more than two years. Similarly, each patient’s smoking history, including duration and daily quantity smoked, was recorded, with smokers defined as those with a daily intake of ≥10 cigarettes for over two years. Indications for surgery included CP with large (>1 cm) and numerous (i.e., more than three) pancreatic stones, complex strictures (bile duct stenosis, pancreatic duct stenosis), an inflammatory head mass, disease limited to the pancreatic tail, or suspicion of malignancy. This study was approved by the Ethics Committee of our institution (Ethics number: 2017-SR-288).

Categorical and continuous variables were presented as frequency (percentage) or mean ± standard deviation, or median (interquartile range) where appropriate. The data were analyzed using SPSS software version 24.0 (IBM, Armonk, NY, USA).

Results

A total of 130 consecutive patients with chronic pancreatitis (CP) who had undergone surgical treatment were enrolled in our study. Table 1 summarizes their clinical features. Our patient cohort was predominantly male (99 patients, i.e., 76.2%), with a median age of 50.2 ± 9.8 years. Upper abdominal pain was the most common symptom, present in 102 patients (78.5%); 28 patients (21.5%) reported no pain.

Table 3. Procedures of CP patients.

Procedures	n (%)
Drainage procedures	
Partington	33 (25.4%)
Resectional procedures	
PD	17 (13.1%)
PPPD	18 (13.9%)
MP	1 (0.8%)
DP	9 (6.9%)
Procedures combining Drainage and resection	
Frey	17 (13.2%)
Bern	5 (3.9%)
Beger	1 (0.8%)
Other procedures	
Biopsy	15 (11.5%)
Choledochojejunostomy	14 (10.8%)
Gastroenterostomy	2 (1.5%)

CP, chronic pancreatitis; PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; MP, middle pancreatectomy; DP, distal pancreatectomy.

Steatorrhea was present in 9 cases (6.9%), weight loss in 24 (18.5%), and jaundice in 23 (17.7%). Among the 130 patients, 36 (27.7%) had diabetes mellitus. A pancreatic cyst or pseudocyst was diagnosed in 7 patients (5.4%).

The etiology and risk factors of the 130 CP patients are listed in Table 2. A history of smoking was present in 53 patients (40.8%), while 45 patients (34.6%) had a history of alcohol consumption.

The procedures received by the 130 CP patients are summarized in Table 3. The Partington procedure was per-

formed in 33 (25.4%) patients, the Frey procedure in 17 (13.2%), the Berne procedure in 5 (3.9%), the Beger procedure in 1 (0.8%), pancreaticoduodenectomy (PD) in 17 (13.1%), pylorus-preserving pancreaticoduodenectomy (PPPD) in 18 (13.9%), middle pancreatectomy (MP) in 1 (0.8%), and distal pancreatectomy (DP) in 9 (6.9%). Cholecystojejunostomy was performed in 14 patients (10.8%), gastroenterostomy in 2 (1.5%), and 15 patients (11.5%) underwent aspiration biopsy.

Genetic mutations were identified in only two patients from the CP group, including one with the R122H mutation of PRSS1 and one with the N34S mutation of SPINK1. No genetic mutations were detected in the 100 healthy subjects.

Discussion

Chronic pancreatitis is characterized by fibrosis and irreversible destruction of the pancreatic parenchyma. It is caused by excessive alcohol consumption, genetic mutations, and other risk factors, such as cholelithiasis, resulting in exocrine and endocrine insufficiency in the end stage. Approximately 80% of patients with CP present with recurrent or chronic upper abdominal pain [1]. Up to 50% of all patients with CP undergo surgical treatment at some point during their disease to obtain pain relief and improve their quality of life [4]. Our study aims to identify the differences in characteristics and surgical strategies of CP between China and the West.

Historically, excess alcohol consumption has been the most common etiology of CP, diagnosed in 42% to 77% of CP patients in Western countries [2]. In a recent multicenter study involving 1158 patients from the USA, the three most common etiologies of CP identified were alcohol (49.4%), idiopathy (24.6%), and genetic mutations (8.4%) [5]. However, many studies from China indicate a strong association between biliary tract diseases and CP [3], a phenomenon not widely reported elsewhere. One retrospective multicenter analysis in China reported that the main etiologies of CP found were alcohol (35.11%), biliary diseases (34.36%), hereditary factors (7.22%), and idiopathy (12.90%) [6]. In another study involving 2,037 patients with CP from China, only 19.8% had alcoholic CP [7]. The most common etiologies identified in our study were obstructive factors (47.7%) and alcohol (34.6%). However, we observed that the frequency of alcohol-related CP increased from 11.7% to 43.0% between the first and last five-year periods of 2007 to 2017, while the frequency of obstructive CP decreased from 74.3% to 38.9%. The changing trends of CP etiologies identified in our study suggest that alcohol consumption may gradually replace biliary diseases as the leading cause of CP in China.

Genetic factors also contribute to CP development, with mutations in cationic trypsinogen (PRSS1), serine protease inhibitor Kazal type 1 (SPINK1), and carboxypeptidase A1 (CPA1) being the most important genetic risk factors [8]. In this study, we tested for the R122H and N29I mutations

of the PRSS1 gene and the N34S mutation of the SPINK1 gene in 100 patients randomly selected from among the 130 patients with CP in the study sample and 100 healthy subjects. Genetic mutations were identified in only two patients from the CP group, including one R122H mutation of PRSS1 and one N34S mutation of SPINK1. No genetic mutations were detected in the 100 healthy subjects. In a study involving 134 patients from the USA who had undergone genetic testing, 88 pathogenic genetic variants were found in 64 patients (47.8%) with idiopathic CP, including 10 (7.5%) PRSS1 and 22 (16.4%) SPINK1 variants [9]. The incidence rate of genetic mutation was significantly higher in CP patients in the USA than in our study.

As of now, there is no universal consensus on the definition of chronic pancreatitis (CP), especially in the early stages of the disease [10]. Diagnostic criteria typically rely on end-stage features consisting of irreversible changes, which may be morphological (such as calcifications, ductal abnormalities) or histological (such as fibrosis, atrophy), with or without other accompanying features (e.g., pain, acute pancreatitis), and include organ dysfunction (e.g., diabetes, exocrine insufficiency) and impaired quality of life [11]. The comparison made in this study indicates that China is not significantly different from Western countries regarding the diagnostic guidelines for CP [12, 13]. However, slight differences were found in the details. For example, the Chinese diagnostic guidelines include major and minor diagnostic criteria: a diagnosis of CP can be confirmed by one major diagnostic criterion or by at least two minor diagnostic criteria. This approach is clear and easy to implement but also carries the potential for misdiagnosis. In contrast, the diagnostic guidelines of the American Pancreatic Association emphasize that patients should not be labeled as having CP without sufficient evidence, suggesting a cautious approach of not definitively diagnosing CP but recommending longitudinal follow-up with serial imaging and physiological testing until definitive evidence is present [10].

The main principles of surgical therapy for chronic pancreatitis (CP) aim to relieve symptoms, especially pain, improve pancreatic functions, enhance quality of life, and treat complications [12–14]. The indications for surgical treatment for CP in China are largely similar to those in Western countries, primarily including the following aspects: (i) intractable pain; (ii) symptomatic local complications of adjacent organs, such as bile or pancreatic duct stenosis, duodenal stenosis, pancreatic pseudocyst, and gastrointestinal hemorrhage; and (iii) suspicion of neoplasm. The principal surgical strategies available for CP include drainage procedures (e.g., Partington procedure), resectional procedures (e.g., pancreaticoduodenectomy (PD) or pylorus-preserving pancreaticoduodenectomy (PPPD)), and a combination of the two (e.g., Beger or Frey procedure). Among the 130 patients in our study, 33 (25.4%) underwent drainage procedures, 45 (34.6%) underwent resectional procedures, and 23 (17.7%) underwent procedures

combining drainage and resection. In a retrospective analysis of chronic pancreatitis-related surgical procedures based in the USA, 24.4% of patients underwent drainage procedures and 21.6% underwent pancreatectomies [15]. The frequencies of different operative procedures were comparable. However, among patients who underwent drainage procedures and pancreatectomies, 72.7% had a pancreatic cyst or pseudocyst, a much higher proportion than the 5.4% of patients in our study. Additionally, according to multivariate modeling, a pancreatic cyst or pseudocyst is an extremely strong predictor of surgical management, which partly suggests different emphases in the detail of indications for surgery between Western countries and China (as represented in our study population).

The correct timing for operative management of chronic pancreatitis (CP) remains controversial [16]. In many centers in China, surgical treatment is typically recommended when a patient's pain cannot be alleviated without the use of opioids, and endoscopic interventions have proven ineffective [13]. However, a growing body of studies in Western countries suggests that early surgery is preferable to surgery at a more advanced stage of the disease in terms of optimal long-term pain relief, reduced risk of postoperative pancreatic exocrine insufficiency (PEI), and long-term improvement in quality of life [17–22]. An individual patient data meta-analysis (IPDMA) of raw data from two randomized controlled trials, including 406 patients, demonstrates that early surgery resulted in an increased likelihood of complete pain relief (RR 1.67 [1.09–2.56], $p = 0.02$), a reduced risk of pancreatic insufficiency, and low re-intervention rates [17–19]. This new insight may warrant further research to confirm these findings in China.

Conclusion

This study has confirmed that, etiologically, obstructive chronic pancreatitis (CP) is more prevalent among the Chinese population compared to Western populations. While diagnostic instruments and operative procedures were found to be roughly comparable between the two regions, slight differences were identified in diagnostic flowcharts/criteria and indications, as well as the optimal timing of surgery.

Availability of Data and Materials

The datasets used or analysed during the current study are available from the corresponding authors on reasonable request.

Author Contributions

YYZ, HYL: Data collection and analysis, article writing; JLF, LLZ: Research design and guidance, paper revision, financial support; DQJ, JCH, ZJY, QGK, YMW, FMY: research implementation, data collection, analysis. All authors contributed to editorial changes in the manuscript. All

authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of our institution (Ethics number: 2017-SR-288). Informed patient consent was obtained for this study in accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Xiao AY, Tan MLY, Wu LM, Asrani VM, Windsor JA, Yadav D, et al. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. *The Lancet. Gastroenterology & Hepatology*. 2016; 1: 45–55.
- [2] Singh VK, Yadav D, Garg PK. Diagnosis and Management of Chronic Pancreatitis: A Review. *JAMA*. 2019; 322: 2422–2434.
- [3] Jha AK, Goenka MK, Goenka U. Chronic pancreatitis in Eastern India: Experience from a tertiary care center. *Indian Journal of Gastroenterology: Official Journal of the Indian Society of Gastroenterology*. 2017; 36: 131–136.
- [4] Dua MM, Visser BC. Surgical Approaches to Chronic Pancreatitis: Indications and Techniques. *Digestive Diseases and Sciences*. 2017; 62: 1738–1744.
- [5] Wilcox CM, Sandhu BS, Singh V, Gelrud A, Abberbock JN, Sherman S, et al. Racial Differences in the Clinical Profile, Causes, and Outcome of Chronic Pancreatitis. *The American Journal of Gastroenterology*. 2016; 111: 1488–1496.
- [6] Wang LW, Li ZS, Li SD, Jin ZD, Zou DW, Chen F. Prevalence and clinical features of chronic pancreatitis in China: a retrospective multicenter analysis over 10 years. *Pancreas*. 2009; 38: 248–254.
- [7] Hao L, Wang LS, Liu Y, Wang T, Guo HL, Pan J, et al. The different course of alcoholic and idiopathic chronic pancreatitis: A long-term study of 2,037 patients. *PLoS One*. 2018; 13: e0198365.
- [8] Löhner JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United European Gastroenterology Journal*. 2017; 5: 153–199.

- [9] Jalaly NY, Moran RA, Fargahi F, Khashab MA, Kamal A, Lennon AM, *et al.* An Evaluation of Factors Associated With Pathogenic PRSS1, SPINK1, CTFR, and/or CTRC Genetic Variants in Patients With Idiopathic Pancreatitis. *The American Journal of Gastroenterology*. 2017; 112: 1320–1329.
- [10] Duggan SN, Ní Chonchubhair HM, Lawal O, O'Connor DB, Conlon KC. Chronic pancreatitis: A diagnostic dilemma. *World Journal of Gastroenterology*. 2016; 22: 2304–2313.
- [11] Machicado JD, Yadav D. Epidemiology of Recurrent Acute and Chronic Pancreatitis: Similarities and Differences. *Digestive Diseases and Sciences*. 2017; 62: 1683–1691.
- [12] Conwell DL, Lee LS, Yadav D, Longnecker DS, Miller FH, Morteale KJ, *et al.* American Pancreatic Association Practice Guidelines in Chronic Pancreatitis: evidence-based report on diagnostic guidelines. *Pancreas*. 2014; 43: 1143–1162.
- [13] Zou WB, Ru N, Wu H, Hu LH, Ren X, Jin G, *et al.* Guidelines for the diagnosis and treatment of chronic pancreatitis in China (2018 edition). *Hepatobiliary & Pancreatic Diseases International: HBPD INT*. 2019; 18: 103–109.
- [14] Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE, *et al.* Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatology: Official Journal of the International Association of Pancreatology (IAP) ... [et Al.]*. 2017; 17: 720–731.
- [15] Bliss LA, Yang CJ, Eskander MF, de Geus SWL, Callery MP, Kent TS, *et al.* Surgical management of chronic pancreatitis: current utilization in the United States. *HPB: the Official Journal of the International Hepato Pancreato Biliary Association*. 2015; 17: 804–810.
- [16] Kempeneers MA, Issa Y, Ali UA, Baron RD, Besselink MG, Büchler M, *et al.* International consensus guidelines for surgery and the timing of intervention in chronic pancreatitis. *Pancreatology: Official Journal of the International Association of Pancreatology (IAP) ... [et Al.]*. 2020; 20: 149–157.
- [17] Yang CJ, Bliss LA, Schapira EF, Freedman SD, Ng SC, Windsor JA, *et al.* Systematic review of early surgery for chronic pancreatitis: impact on pain, pancreatic function, and re-intervention. *Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract*. 2014; 18: 1863–1869.
- [18] Cahen DL, Gouma DJ, Nio Y, Rauws EA, Boermeester MA, Busch OR, *et al.* Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *New England Journal of Medicine*. 2007; 356: 676–684.
- [19] Díte P, Ruzicka M, Zboril V, Novotný I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy*. 2003; 35: 553–558.
- [20] Ahmed Ali U, Nieuwenhuijs VB, van Eijck CH, Gooszen HG, van Dam RM, Busch OR, *et al.* Clinical outcome in relation to timing of surgery in chronic pancreatitis: a nomogram to predict pain relief. *Archives of Surgery (Chicago, Ill.: 1960)*. 2012; 147: 925–932.
- [21] Ke N, Jia D, Huang W, Nunes QM, Windsor JA, Liu X, *et al.* Earlier surgery improves outcomes from painful chronic pancreatitis. *Medicine*. 2018; 97: e0651.
- [22] Yang CJ, Bliss LA, Freedman SD, Sheth S, Vollmer CM, Ng SC, *et al.* Surgery for chronic pancreatitis: the role of early surgery in pain management. *Pancreas*. 2015; 44: 819–823.

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