World Journal of Gastrointestinal Surgery

World J Gastrointest Surg 2021 January 27; 13(1): 1-95





Published by Baishideng Publishing Group Inc

WJGS

World Journal of Gastrointestinal Surgery

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ABOUT COVER

Editorial board member of World Journal of Gastrointestinal Surgery, Dr. Raphael LC Araujo is a Professor of Liver Surgery at Federal University of São Paulo (UNIFESP -Brazil). After earning his medical degree from University of the State of Rio de Janeiro (2003), he undertook training in Surgical Oncology at AC Camargo Cancer Center. Afterwards, he spent two years (2010-2012) as Research Fellow in Hepatopancreatobiliary Service at Memorial Sloan-Kettering Cancer Center (New York, United States), working on multimodal approaches for hepatopancreatobiliary malignancies, mainly for colorectal liver metastases and pancreas cancer. Subsequently, he performed residency in Hepatopancreatobiliary Service at Hospital Paul Brousse (France; 2012-2013) and then earned both a PhD (2015) and post-doctorate (2017) degree in Gastroenterology from the University of São Paulo. (L-Editor: Filipodia)

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INDEXING/ABSTRACTING

The WJGS is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJGS as 1.863; IF without journal self cites: 1.824; Ranking: 109 among 210 journals in surgery; Quartile category: Q3; Ranking: 77 among 88 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Xiang Li; Editorial Office Director: Ya-Juan Ma.

NAME OF JOURNAL	INSTRUCTIONS TO AUTHORS
World Journal of Gastrointestinal Surgery	https://www.wjgnet.com/bpg/gerinfo/204
ISSN	GUIDELINES FOR ETHICS DOCUMENTS
ISSN 1948-9366 (online)	https://www.wjgnet.com/bpg/GerInfo/287
LAUNCH DATE	GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
November 30, 2009	https://www.wjgnet.com/bpg/gerinfo/240
FREQUENCY	PUBLICATION ETHICS
Monthly	https://www.wjgnet.com/bpg/GerInfo/288
EDITORS-IN-CHIEF	PUBLICATION MISCONDUCT
Shu-You Peng, Varut Lohsiriwat, Jin Gu	https://www.wjgnet.com/bpg/gerinfo/208
EDITORIAL BOARD MEMBERS	ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/1948-9366/editorialboard.htm	https://www.wjgnet.com/bpg/gerinfo/242
PUBLICATION DATE	STEPS FOR SUBMITTING MANUSCRIPTS
January 27, 2021	https://www.wjgnet.com/bpg/GerInfo/239
COPYRIGHT	ONLINE SUBMISSION
© 2021 Baishideng Publishing Group Inc	https://www.f6publishing.com

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World J Gastrointest Surg 2021 January 27; 13(1): 30-49

DOI: 10.4240/wjgs.v13.i1.30

ISSN 1948-9366 (online)

ORIGINAL ARTICLE

Retrospective Study

Pancreas-preserving duodenal resections vs pancreatoduodenectomy for groove pancreatitis. Should we revisit treatment algorithm for groove pancreatitis?

Vyacheslav Egorov, Roman Petrov, Aleksandr Schegolev, Elena Dubova, Andrey Vankovich, Eugeny Kondratyev, Andrey Dobriakov, Dmitry Kalinin, Natalia Schvetz, Elena Poputchikova

ORCID number: Vyacheslav Egorov 0000-0002-8805-7604; Roman Petrov 0000-0003-3872-7363; Aleksandr Schegolev 0000-0002-2111-1530; Elena Dubova 0000-0002-7115-538X; Andrey Vankovich 0000-0001-6240-1588; Eugeny Kondratyev 0000-0001-7070-3391; Andrey Dobriakov 0000-0002-1773-2916; Dmitry Kalinin 0000-0001-6247-9481; Natalia Schvetz 0000-0002-0846-8850; Elena Poputchikova 0000-0002-8533-4629.

Author contributions: Egorov V contributed to idea, surgery, acquisition, analysis and interpretation of data, writing the paper; Petrov R and Vankovich A contributed to surgery, acquisition, analysis and interpretation of data, paper revision; Kondratyev E contributed to acquisition, analysis and interpretation of radiological data, paper revision; Schegolev A, Dubova E, Dobriakov A, Kalinin D, Schvetz N, and Poputchikova E contributed to pathological examination, acquisition, analysis and interpretation of pathohistological data, paper revision.

Institutional review board

statement: The study was reviewed and approved by the Ethics Committee of Ilyinskaya Vyacheslav Egorov, Roman Petrov, Department of Surgical Oncology, Ilyinskaya Hospital, Moscow 143421, Russia

Aleksandr Schegolev, V. I. Kulakov Research Center for Obstetrics, Ministry Hlth Russian Federat, VI Kulakov Res Ctr Obstet Gynecol & Perinatol, Moscow 119526, Russia

Elena Dubova, Department of Pathology, Buranazian Federal Medical and Biological Center of the Federal Medical and Biological Agency of Russian Federation, Moscow 143421, Russia

Andrey Vankovich, Department of HPB Surgery, Moscow Clinical Research Center, Moscow 111123, Russia

Eugeny Kondratyev, Department of Radiology, Vishnevsky Institute of Surgery, Ilyinskaya Hospital, Moscow 143421, Russia

Andrey Dobriakov, Natalia Schvetz, Elena Poputchikova, Department of Pathology, Bakhrushin Brothers Moscow City Hospital, Moscow 107076, Russia

Dmitry Kalinin, Department of Pathology, Vishnevsky Institute of Surgery, Ilyinskaya Hospital, Moscow 117997, Russia

Corresponding author: Vyacheslav Egorov, MD, PhD, Associate Professor, Department of Surgical Oncology, Ilyinskaya Hospital, Rubliovskoye predmestiie 2-2, Moscow 143421, Russia. egorov12333@gmail.com

Abstract

BACKGROUND

The management of cystic dystrophy of the duodenal wall (CDDW), or groove pancreatitis (GP), remains controversial. Although pancreatoduodenectomy (PD) is considered the most suitable operation for CDDW, pancreas-preserving duodenal resection (PPDR) has also been suggested as an alternative for the pure form of GP (isolated CDDW). There are no studies comparing PD and PPDR for this disease.

AIM



Hospital, approval No. 03-01-SG/2020 of January 14, 2020.

Informed consent statement:

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The

authors have no conflicts of interest.

Data sharing statement: No additional data are available.

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Manuscript source: Unsolicited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: Russia

Peer-review report's scientific quality classification

Grade A (Excellent): 0 Grade B (Very good): B Grade C (Good): 0 Grade D (Fair): 0 Grade E (Poor): 0

Received: August 3, 2020 Peer-review started: August 3, 2020 First decision: September 17, 2020 Revised: September 22, 2020 Accepted: December 2, 2020 Article in press: December 2, 2020 Published online: January 27, 2021

P-Reviewer: Zhao CF S-Editor: Huang P L-Editor: Webster JR

To compare the safety, efficacy, and short- and long-term results of PD and PPDR in patients with CDDW.

METHODS

A retrospective analysis of the clinical, radiologic, pathologic, and intra- and postoperative data of 84 patients with CDDW (2004-2020) and a comparison of the safety and efficacy of PD and PPDR.

RESULTS

Symptoms included abdominal pain (100%), weight loss (76%), vomiting (30%) and jaundice (18%) and data from computed tomography, magnetic resonance imaging, and endoUS led to the correct preoperative diagnosis in 98.8% of cases. Twelve patients were treated conservatively with pancreaticoenterostomy (n = 8), duodenum-preserving pancreatic head resection (n = 6), PD (n = 44) and PPDR (n= 15) without mortality. Weight gain was significantly higher after PD and PPDR and complete pain control was achieved significantly more often after PPDR (93%) and PD (84%) compared to the other treatment modalities (18%). New onset diabetes mellitus and severe exocrine insufficiency occurred after PD (31% and 14%), but not after PPDR.

CONCLUSION

PPDR has similar safety and better efficacy than PD in patients with CDDW and may be the optimal procedure for the isolated form of CDDW. The pure form of GP is a duodenal disease and PD may be an overtreatment for this disease. Early detection of CDDW provides an opportunity for pancreas-preserving surgery.

Key Words: Groove pancreatitis; Cystic dystrophy of the duodenal wall; Pancreaspreserving duodenectomy; Pancreas-preserving duodenal resection; Chronic pancreatitis; Pancreatoduodenectomy

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Core Tip: This is a retrospective study that compared the safety, efficacy, short- and long-term results of pancreatoduodenectomy (PD) and pancreas-preserving duodenal resections (PPDR) in patients with groove pancreatitis (GP). Although PD is a conventional option for GP management, PPDR has been suggested as a treatment alternative for the pure form of GP in the early stage of this disease. Evaluation of these two treatment modalities has shown that PPDR for the pure form of GP is similar in terms of safety and better in efficacy compared to PD performed for GP. The key aim of this study is to demonstrate that PPDR may be the treatment of choice for the pure form of GP, which is a disease of the duodenum; early detection of GP makes preservation of the pancreas possible, and prolonged conservative treatment in early GP may lead to the development of segmental and diffuse pancreatitis, which may deprive patients of the pancreas-preserving option; PD is an overtreatment for the pure form of GP, since it involves resection of undamaged pancreas, which means that PPDR may be an alternative treatment procedure for GP.

Citation: Egorov V, Petrov R, Schegolev A, Dubova E, Vankovich A, Kondratyev E, Dobriakov A, Kalinin D, Schvetz N, Poputchikova E. Pancreas-preserving duodenal resections vs pancreatoduodenectomy for groove pancreatitis. Should we revisit treatment algorithm for groove pancreatitis? World J Gastrointest Surg 2021; 13(1): 30-49 URL: https://www.wjgnet.com/1948-9366/full/v13/i1/30.htm

DOI: https://dx.doi.org/10.4240/wjgs.v13.i1.30

INTRODUCTION

Cystic dystrophy of the duodenal wall (CDDW) is a relatively rare form of chronic pancreatitis (CP). It is mainly observed in middle-aged men and manifests with abdominal pain, weight loss, and occasionally vomiting and jaundice^[1-7]. In the



P-Editor: Li JH



literature, it has also been referred to as groove pancreatitis (GP)^[8-11], periampullary duodenal wall cyst^[12], adenomyoma^[13,14], paraduodenal pancreatitis (PP)^[15-17], and pancreatic hamartoma of the duodenum^[18-20]. All these terms refer to the same histology, each one putting the emphasis on one of its different manifestations: Fibrotic inflammatory changes of the duodenal wall, spread of fibrosis to the groove area (thin area between the pancreas, common bile duct and duodenum) and common bile duct opening, duodenum wall thickening accompanied by intramural cyst formation, Brunner's gland hyperplasia and fragments of ectopic pancreatic tissue with myoid cells infiltrating the duodenal wall^[1,2,8,9,15].

This entity was first described as "cystic dystrophy" of the duodenal wall in 1970 by Potet et al^[1]. Stolte et al^[8] in 1982 and Becker et al^[9] in 1991 used the term GP, dividing it into "pure" and "segmental" forms. The "pure" form of the disease (which correlates to the isolated form of CDDW in the original description^[1]) refers to the condition where only cicatricial changes occur in the duodenum and area of the groove between the duodenum and the pancreas, while the pancreatic parenchyma remains intact. The "segmental" form of the disease is characterized by both the fibrotic changes of the groove, as well as signs of CP (fibrosis, pancreatic calculi, cysts, and changes of the duct of Wirsung) in the head of the pancreas or in the whole gland. In 2004, Adsay et al[15] introduced the notion of "paraduodenal pancreatitis," also discriminating two types of the disease: "Pure" and "Segmental"^[17]. When considering groove, or PP, some authors also divide it into solid and cystic forms, depending on whether only fibro-inflammatory thickening of the medial duodenal wall is present or whether this thickening is accompanied by cystic transformation^[15-17]. Therapeutic approaches to treatment remain controversial, as well as the opinions on its primary cause, but today pancreatoduodenectomy (PD) is considered preferable and even a first-line treatment option for CDDW^[4,6,10,11,17,21-24]. Pancreas-preserving duodenal resection (PPDR) was introduced into practice in 2009^[25], and the objectives of this study were a comparison of the safety and efficacy of PD and PPDR in patients with CDDW.

MATERIALS AND METHODS

Patients and methods

A retrospective analysis of pre- and post-treatment data of 84 consecutive patients with CDDW treated by our group between February 2004 and April 2020 was performed. Patients with the so-called "solid type" of groove or PP were not included, as thickening (*i.e.*, inflammatory infiltration) of the medial duodenal wall in such patients may be the consequence, rather than the cause of chronic or acute inflammation of the pancreas. Intraoperative and short- and long-term postoperative data of the patients who underwent PD (n = 44) and PPDR (n = 15) were compared.

Patient information included demographic data, medical history, history of alcohol consumption and smoking and information on pancreatic endocrine and exocrine insufficiency. All blood tests and imaging studies were performed according to standard protocols.

All the cases were discussed at multidisciplinary meetings, which included experts in gastroenterology, pancreas surgery, radiology, oncology and endocrinology. Primary operative procedures were all elective. In all patients, initial treatment was conservative, which included smoking and alcohol cessation, analgesics, proton pump inhibitors, short- or long-acting somatostatin analogues, nutritional support and pancreatic enzyme replacement therapy (PERT), along with endoscopic procedures, including endoscopic ultrasonography, stenting, fine-needle aspiration and/or core $needle\ biopsy^{[4,6,10,16,17]}.\ Indications\ for\ surgical\ intervention\ were\ conservative\ and/or$ endoscopic treatment failure manifested by persistence of pain, duodenal obstruction, jaundice and (in one case) suspected tumor^[4,6,16,17]. The choice of the type of surgery changed with time, as our insight into the nature of the disease evolved. Patient flow is shown in Figure 1.

The procedures performed have been described in detail in our previous publications^[6,25] and elsewhere. These included internal drainage of the main pancreatic duct^[7,16,17], duodenum-preserving pancreatic head resection (DPPHR)^[26,27], pylorus-preserving (ppPD) and classical PD (Whipple procedure), Nakao procedure (PD modification)^[24], and PPDR^[6,25].

The diagnosis in all 59 patients who underwent PD and PPDR was clinically, radiologically and histologically confirmed. Eighteen patients (37%) demonstrated symptoms and signs of the isolated form of CDDW, as shown by computed tomography (CT) (Figure 2A and B), magnetic resonance imaging (MRI) and/or



Duodenum-preserving pancreatic head resection, n = 6





Figure 2 Isolated form of cystic dystrophy of the duodenal wall. Arterial phase. Coronal view. A: Deformation and thickening of the medial wall of the duodenum (D), major papilla surrounded by well-defined cysts located in the submucosa (DD). The gastroduodenal artery is shifted forward and to the left, lying in the groove between the unaffected pancreatic head (P) and duodenal wall; B: Unchanged orthotopic pancreas. Only the duodenum and the groove are involved. SMA: Superior mesenteric artery; GDA: Gastroduodenal artery; RGEA: Right gastro-epiploic artery.

endoscopic ultrasonography (Figure 3A and B) (i.e., considerable (> 10 mm) thickening of the duodenal wall containing cystic cavities, separation of duodenal wall changes from the intact pancreas and antero-medial displacement of the gastroduodenal artery with respect to the pathological focus within the duodenum)^[3,28,29].

Histological diagnosis of CDDW was based on the detection of a cystic cavity or cavities in the duodenal wall, completely isolated from the pancreas, surrounded by areas of inflammation, fibrosis, and Brunner's gland hyperplasia. These cavities could contain fragments of ectopic pancreatic tissue, being postnecrotic cysts, or distended ectopic pancreatic ducts with preserved or desquamated epithelium (Figure 4A-D).

The diagnosis of CP in the orthotopic gland was based on the criteria presented elsewhere^[1,2,8,15]. When histologic examination of the duodenum and/or pancreas was not possible during the course of management of CDDW (n = 25), the diagnosis was based on pathognomonic findings of CT, MRI, and endoscopic ultrasonography according to the Cambridge and Rosemont criteria^[3,4,6,10,17,28,29-32]. PPDR was considered possible and indicated if only the duodenum was involved and in the absence of pancreatic duct calculi or calcification, cysts and fibrotic changes in the pancreatic parenchyma (Cambridge Class 0-1 and/or less than three Rosemont criteria)^[10,30-32].



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Figure 3 Duodenoscopy and endosonography. Isolated form of the cystic dystrophy of the duodenal wall with unchanged orthotopic pancreas (P). A: Duodenal wall cyst (DWC) within the submucosa and muscularis of the diffusely thickened duodenal wall (DW); B: Multiple DWCs in the submucosa and muscularis surrounding the major papilla in the diffusely thickened DW. DWC: Duodenal wall cyst; DW: Duodenal wall.

Pancreas-preserving surgery for CDDW was described previously^[6,25], and we want to note a few details (Figure 5A-D). If the affected area of the second duodenal portion does not exceed 4 cm, a segmental resection of this part of the duodenum followed by duodeno-duodenostomy is possible. However, tension may be a limitation for this type of reconstruction, especially if the inflammatory zone spreads wider. In this case, intestinal interposition can be an option (Figure 5B), as well as classical duodenectomy (Figure 5C) or Roux-en-Y reconstruction (Figure 5D).

If inflammatory and fibrotic changes around the duodenum are moderate, it is possible to remove all the walls of the duodenal cyst without causing damage to the pancreas (Figure 4C)^[25]. However, when significant fibrosis is present, it is preferable to keep the medial cystic wall intact to prevent possible damage to the pancreatic head^[6]. This does not predispose to relapse, since the cysts lack epithelium due to chronic inflammation. Intraoperative biopsy of the resected portion of the duodenum is essential to exclude malignancy^[33-35].

When inflammation and fibrosis extended beyond the second portion of the duodenum, we opted for the standard subtotal duodenectomy described by Chung et al^[36] (Figure 5A and B)^[37].

If the cyst extended to the first portion of the duodenum and/or stomach or if there was a peptic duodenal, pyloric or pre-pyloric ulcer, an antrectomy or pylorus resection with subsequent Roux-en-Y reconstruction was performed. Roux-en-Y reconstruction after ppPD PPDR is also an option if the surgeon sees reasons to separate the biliopancreatic tract from the food passage (Figure 5C).

All patients suffering from exocrine insufficiency received mini-microspheres of pancreatin (Creon[®]) at doses eliminating diarrhea, at least 200000 U/d before surgery. Pancreatin was continued for three months following the operation, at 240-320000 U/d. PERT was stopped if no signs of pancreatic insufficiency were observed after surgery.

The results of CDDW treatment were monitored for a period of 3 to 188 mo. The





Figure 4 Microphotograph and resected specimen. A: Microphotograph of the isolated form of the cystic dystrophy of the duodenal wall. Heterotopia of the pancreatic tissue in the duodenal wall. Ectopic pancreatic tissue (EP), dilated ducts of the ectopic pancreas (EPD) and acini (A) in the duodenal wall, M: Duodenal muscle layer fibers; SM: Duodenal submucosa; Muc: Duodenal mucosa. Hematoxylin-eosin, × 100; B: Microphotograph of the isolated form of the cystic dystrophy of the duodenal wall. Cyst in the duodenal wall formed by a dilated duct of the ectopic gland (EPD) with the foci of preserved epithelium (arrows). Hematoxylin-eosin, × 50; C: Cystic dystrophy of the duodenal wall associated with chronic pancreatitis in the pancreatic head (segmental form of groove pancreatitis). Resected specimen after Whipple procedure in a 47-year-old male. There are multiple cysts within the thickened, chronically inflamed duodenal wall of the second portion of the duodenum (arrowheads) without dilation of the common hepatic (yellow arrow) and main pancreatic (black arrow) ducts. Chronic inflammation in the pancreatic head with necrotic mass (thick blue arrow) makes pancreas-preserving surgery unjustified and pancreatoduodenectomy the surgery of choice; D: Isolated form of the cystic dystrophy of the duodenal wall = pure form of groove pancreatitis. Due to unchanged orthotopic gland, pancreas-preserving duodenal resection was performed in a 53-year-old male. Resected 6-cm specimen of the second part of the duodenum with major papilla (thick yellow arrow) and large scar-sided cyst of the medial duodenal wall with the remainder of the ectopic pancreatic tissue inside. A forceps was introduced into the duodenum to show the absence of communication between the duodenal lumen and the lumen of the cyst (white arrow).

following information was recorded: Initial body weight, body weight at presentation, weight loss prior to the treatment, weight changes after 12-24 mo following surgery or treatment initiation (*i.e.*, when most notable body weight changes are generally observed). Body weight and weight gain were defined based on the data acquired at the visit or provided in an information letter.

The pain level and rate were assessed using the Izbicki score^[88]. Patients were contacted by telephone between the beginning and the end of July 2020 to evaluate the clinical, imaging and laboratory data.

Statistical analysis

All data distribution was evaluated by the Shapiro-Wilk test of normality in frequentist statistics. Demographic or clinical characteristics such as the average age, the proportion of subjects of each sex, the symptoms, *etc.*, have been reflected by non-parametric descriptive statistics. The mean in variables was expressed as the median (Me) and interquartile range (LQ-UQ). Subgroups were compared using the Mann-Whitney and Kruskal-Wallis tests, as appropriate. P = 0.05 was considered statistically significant, and confidence intervals were calculated at 95%. All statistical analyses were performed using the SPSS software program, version 20.0 (SPSS, Chicago, IL, United States).

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Figure 5 Isolated form of the cystic dystrophy of the duodenal wall. Scheme of the pancreas-preserving resection of the second portion of the duodenum (A) with reconstruction by direct duodeno-jejunostomy (B), intestinal interposition (C) or Roux-en-Y method (D). CBD: Common bile duct; MPD; Main pancreatic duct.

RESULTS

The patient flow chart is presented in Figure 1. The treatment types and short- and long-term results are shown in Table 1.

By April 2020, only 12 patients were left in the conservative therapy group due to rejection of surgery. One patient died of heart failure after two myocardial infarctions 7 years after the onset of the disease. Although the patients in this subgroup did not undergo surgery, 2 of them died during observation and 6 complications were observed: Migration of a stent that drained the duodenal wall cyst into the duodenal lumen (n = 1), gastrointestinal bleeding associated with NSAID administration (n = 4), and ectopic pancreas malignization with multiple liver metastases and death after 7 years of monitoring and 10 years of the disease. Pain completely resolved in 5 patients in this subgroup but at the expense of "burning out" of the pancreas, which

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Table 1 Short- and long- term results of cystic dystrophy of the duodenal wall treatment (2004-2019)									
Type of treatment	n	¹ Morbidity <i>n</i> (%)	Full pain control, <i>n</i> (%)	Steatorrhea, <i>n</i> (%)	New DM, <i>n</i> (%)				
Conservative	12	5 (42%)	5 (42)	4 (33)	6 (50)				
Draining OP	8	1/1 (12.5/12.5%)	2 (25)	2 (25)	2 (25)				
DPPHR	6	1/2 (17/34%)	2 (33)						
PD	44	12/7 (27/16%)	37 (84)	6 (14)	12 (31)				
PPDR	15	4/1 (27/7%)	14 (93)						

¹Postoperative complications are shown as minor/major (Dindo-Clavien I-II/III-IV).

DPPHR: Duodenum-preserving pancreatic head resection; PD: Pancreatoduodenectomy; PPDR: Pancreas-preserving duodenal resection; DM: Diabetes mellitus; Draining OP: Pancreatico- and/or cystoenterostomy.

manifested with exocrine and endocrine insufficiency. The median time of follow-up in this subgroup was 93 mo (LQ-UQ: 78-111).

With the exception of one patient from the conservative therapy subgroup (ASA class III), all other patients had ASA class II physical status.

Draining procedures were carried out between 2004 and 2008, when we treated CDDW by the methods traditionally used for CP. In this subgroup, only 2 of 8 patients became pain-free, but due to a "burned out" pancreas, both patients developed diabetes and exocrine insufficiency. Postoperatively, two patients developed gastrointestinal hemorrhage. In 2008, we stopped performing draining procedures because of their inefficiency. However, all patients in this subgroup refused reoperation. One patient died 10 years after surgery due to heart failure. Median follow-up before surgery was 48 mo (LQ-UQ: 42-66) and after surgery was 142 mo (LQ-UQ: 123-144).

Six patients with CDDW associated with diffuse CP underwent DPPHR due to substantial enlargement of the pancreatic head. One patient was subjected to ppPD with pain relapse one year after the DPPHR. Three patients developed post-operative complications (gastrointestinal bleeding, grade B pancreatic fistula and acute pancreatitis). Only two patients achieved complete pain relief. None suffered from or developed exocrine insufficiency or diabetes. Median follow-up before surgery was 36 mo (LQ-UQ: 29-48) and after surgery was 120 mo (LQ-UQ: 105-133).

The three aforementioned subgroups did not include patients with the isolated form of CDDW.

The PD group included 29 ppPD, 11 classic PDs, and 4 Nakao procedures (Tables 2 and 3). Three patients underwent surgery for an isolated form of CDDW and the rest for CDDW associated with CP. Complete pain control was achieved in 84% of these patients. Seven patients (17%) developed major postoperative complications: Grade B pancreatic fistula (n = 3), gastrointestinal bleeding (n = 1), grade B delayed gastric emptying (n = 6) and intraoperative ureter electric trauma in the presence of pronounced retroperitoneal fibrosis (n = 1). Pancreatic fistulas developed only in patients with isolated CDDW. In one patient (No. 43), early ductal adenocarcinoma was found in an ectopic pancreas. Four patients had steatorrhea, and 5 had either diabetes or glucose intolerance prior to surgery. Twelve patients developed new diabetes and 6 developed steatorrhea after surgery. One patient in this group had ankylosing spondylitis. One patient died from myocardial infarction 14 years after PD, and four patients died 5.5, 5.5, 11 and 14.5 years after surgery of unknown cause. Four patients were lost to follow-up 185, 167, 164 and 159 mo after surgery. Median followup was 42 mo (LQ-UQ: 36-60) pre-operatively and 98 mo (LQ-UQ: 67-138) postoperatively. Thirty-seven patients (84%) were alcohol drinkers, and 33 (75%) were tobacco users before surgery After surgery, seven patients still smoke, and five still drink. After surgery, six patients had episodes of pancreatitis and 4 of them were hospitalized at least once due to this reason.

PPDR group. Tables 4 and 5 present demographic data, operative details, complications, and monitoring notes for patients undergoing PPDR. All patients were males with a mean age of 44.7 years (28-62 years). The mean body weight loss was 15.9 kg (5-44 kg). All patients suffered from pain of varying severity. Constant or frequent debilitating pain was recorded in 7 patients (46.6%). In 4 patients (26.6%), vomiting was associated with duodenal obstruction, whereas 3 patients (20%) had obstructive jaundice. Seven patients (46.6%) were addicted to alcohol, and 9 (60%) were active

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Table 2 Demographic data and symptoms before and after pancreatoduodenectomy for cystic dystrophy of the duodenal wall, July 2020

No.	Age	Pain	Vomi- ting	Jaundice	Weight Ioss, kg	Weight gain after surgery, kg	Weight gain after surgery, %	PERT after surgery	Pain after surgery, status, events	Treatment before surgery, mo	Follow-up after surgery, mo, status, events
1	44	37.8	-	+	6	9	150	Yes	No, DM	72	188, NA
2	49	63	-		12	5	41	Yes	No, drinking, NDM	84	151, death of unknown cause
3	56	73.8	-		9	9	100	Yes	No, steatorrhea. Smoking, DM	54	166, death of MI
4	49	37.8	+	+	10	8	80	Yes	No, NDM	96	170, NA
5	55	81.3	+	+	12	6	50	Yes	31.5, drinking, NDM, steatorrhea	79	167, NA
6	52	73.8	-		12	9	75	Yes	No	50	162, NA
7	39	73.8	-		15	11	73	Yes	31.5, smoking, DM	60	167
8	43	63	+++		21	10	48	Yes	No	48	164
9	55	73.8	+++		18	13	72	Yes	No, smoking	38	162
10	39	63	++		17	12	71	No	No	60	156
11	57	73.8	-		6	6	100	Yes	No, NDM	8	69, death of unknown cause
12	40	73.8	-		11	8	78	Yes	No	36	155
13	51	77.5	-		10	6	60	Yes	37.8	36	152
14	61	81.3	++		8	6	75	Yes	No, steatorrhea, NDM	48	132, death of unknown cause
15	49	73.8	+++		14	8	57	Yes	37.8, NDM	72	147
16	48	77.5	++	+	12	7	58	Yes	31.5, drinking, smoking	31	147
17	40	63	+		13	7	54	No	no	60	141
18	53	77.5	-		7	7	100	Yes	no	48	129
19	59	31.5	+	+	13	9	69	Yes	No, steatorrhea	36	126
20	46	77.5	-		12	7	58	Yes	No	36	120
21	45	73.8	++		8	5	62.5	Yes	No, drinking	41	117
22	59	73.8	++		5	5	100	Yes	No	62	111
23	50	31.5	-		5	7	140	Yes	No, smoking	48	107
24	53	81.3	+++		16	9	56	Yes	No	66	105
25	47	37.8	++	+	10	8	80	Yes	No	54	103
26	44	63	-		10	7	70	Yes	No	48	101
27	46	63	+++		19	10	52	Yes	No, steatorrhea, NDM	36	97
28	51	63	+++		14	11	78.6	Yes	No	36	93
29	37	77.5	+++		15	9	60	No	No	40	93
30	54	73.8	++		10	8	80	Yes	No, DM	48	69, death of unknown cause
31	52	31.5	-	+	12	8	67	Yes	No, drinking, NDM	66	85
32	53	67.5	-		12	10	83	Yes	31.5	24	85
33	49	77.5	++		15	6	40	Yes	No, steatorrhea	12	79



34	46	81.3	+		13	9	69	Yes	No	9	69
35	48	37.8	++	+	15	10	67	Yes	No	16	69
36	50	63	++		14	9	64	Yes	No	32	69
37	51	81.3	-		7	6	86	Yes	No, smoking	39	60
38	58	31.5	-		11	8	73	Yes	No, NDM, smoking	42	57
39	54	37.8	-		12	8	67	Yes	No	30	52
40	49	73.8	++		8	6	75	Yes	No	36	45
41	47	77.5	++		7	6	86	Yes	No, DM	120	20
42	58	37.8	-		12	8	67	Yes	No, NDM	72	18
43	47	73.8	+		11	1	9	Yes	No, NDM	66	13
44	45	77.5	+++		21	5	23	Yes	No	63	6

Median preoperative follow-up was 42 mo (LQ-UQ: 36-60). All the patients, except two are males. Pain was assessed by the Izbicki score^[38]. DM: Diabetes mellitus; NDM: New diabetes mellitus; PERT: Pancreatic enzyme replacement therapy; NA: Not by April 2020.

> tobacco users before surgery. After surgery, three patients still smoke and one still drinks. There were no patients with exocrine or endocrine insufficiency either before or after surgery.

> The main diagnostic imaging modalities included MRI (n = 13), CT (n = 14), and endoscopic ultrasound (EUS, n = 11). In all patients, CDDW was diagnosed prior to surgery. In the isolated form of CDDW, no or minimal abnormalities of the pancreas were observed and only the duodenum was involved. Main pancreatic duct dilation (> 4 mm) was observed in 6 patients (40%) and common bile duct dilation (> 10 mm) in 8 patients (53%). Minor duodenal papilla was not detected. Accessory pancreatic duct (Santorini's duct) dilation or impairment was not observed. This subgroup included one patient with essential hypertension (No. 14) and two patients (No. 4 and No. 12) with ankylosing spondylitis. PPDR were standard (Chung et al^[36]) in 7 patients (46.6%) who were reconstructed with duodeno-duodenal anastomosis in 2 (13.3%), intestinal interposition in 2 (13.3%) and Roux-en-Y reconstruction in 4 (26.6%) (Table 2). No postoperative mortality occurred in any of the groups.

> In all patients with isolated CDDW, macroscopic and microscopic examinations demonstrated intramural duodenal cysts completely separated from the pancreatic head and Brunner's gland hyperplasia of varying severity. The cysts were located in the medial (n = 14) and anterolateral duodenal walls (n = 1), abutted (n = 7) and surrounded the main pancreatic duct (MPD) (n = 5) and, in three cases, extended from the second portion of the duodenum towards the stomach. In 8 patients (53%) ectopic pancreatic tissue was identified at pathology, one of them with PanIN II. In 7 patients, the cysts matched the characteristics of postnecrotic cysts or were characterized as a dilated pancreatic duct with preserved or desquamated epithelium (Figure 2).

> Four patients in this group developed minor complications (Clavien-Dindo grade I), and one patient (No. 4) suffered major postoperative complications (33.3%). All minor complications were grade A pancreatic fistulas (No. 3, No. 6, No. 10, and No. 14). Average length of hospital stay (with the exception of patient No. 4) was 15 (11-21) d (Table 3).

> Patient No. 4 was reoperated on 19 d after PPDR with intestinal interposition due to leakage and bleeding from the proximal duodeno-enteranastomosis. This complication was successfully treated with antrectomy and Roux-en-Y reconstruction. The rest of the patients were discharged without complications, and there were no readmissions within the next 90 d.

> Patient No. 12 developed recurrent gastric bleeding due to rupture of a splenic artery aneurysm 46 mo after PPDR, having been asymptomatic all this period. Splenic artery aneurysm rupture led to retroperitoneal hematoma, splenic vein thrombosis, sinistral portal hypertension, acute gastric varices formation and hemorrhage. This delayed complication was successfully treated with distal pancreatectomy and splenectomy. Currently, the patient remains asymptomatic. In this case, the decision regarding the primary operation was based on non-contrast MRI and EUS findings due to the patient's allergy to intravenous contrast. Therefore, it is unclear whether the aneurysm developed after surgery or existed before.

Table 3 Operative data and complications of pancreatoduodenectomy for cystic dystrophy of the duodenal wall (July, 2020)							
No.	Procedure	Blood loss, mL	Time, min	Postop stay	Morbidity (Clavien-Dindo)		
1	pPD	130	290	16	Grade I, DGE A		
2	pPD	150	310	11	No		
3	pPD	50	230	14	No		
4	PD	460	370	31	Grade IV, GI bleeding		
5	pPD	500	350	18	Grade I, pneumonia		
6	PD	120	305	10	No		
7	pPD	150	290	10	No		
8	pPD	100	280	10	Grade I, DGE A		
9	PD	230	300	12	No		
10	pPD	50	185	25	Grade III, POPF B		
11	PD	100	340	12	No		
12	pPD	100	270	14	No		
13	pPD	130	220	15	Grade I, DGE A		
14	pPD	140	280	16	Grade I, Lymphorrhea		
15	pPD	50	270	11	No		
16	PD	50	280	12	No		
17	pPD	120	210	36	Grade III, POPF B, DGE B		
18	pPD	70	225	10	No		
19	PD	750	480	41	Grade III, ureter intraoperative trauma, DGE B		
20	pPD	100	200	9	No		
21	pPD	100	200	7	No		
22	pPD	150	240	14	No		
23	Nakao	100	330	27	Grade III, DGE B		
24	pPD	50	230	16	Grade I, short-term bile leakage		
25	pPD	50	280	11	No		
26	Nakao	100	350	12	Grade I, DGE A		
27	pPD	120	250	10	No		
28	pPD	140	260	9	No		
29	pPD	50	170	28	Grade III, POPF B, DGE B		
30	Nakao	100	310	14	Grade I, short-term bile leakage		
31	PD	120	290	12	No		
32	Nakao	100	320	13	No		
33	pPD	100	190	27	Grade III, DGE B		
34	pPD	100	300	10	Grade I, lymphocele		
35	PD	100	320	11	No		
36	pPD	350	310	11	Grade I, wound infection		
37	pPD	50	300	13	No		
38	pPD	50	270	12	No		
39	pPD	50	240	14	Grade I, DGE A		
40	pPD	50	230	11	Grade I, POPF A		
41	PD	100	230	10	No		

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42	pPD	150	410	12	No
43	PD	270	390	11	No
44	PD	250	440	10	No

PD: Pancreatoduodenectomy; pPD: Pylorus-preserving pancreatoduodenectomy; DGE A: Delayed gastric emptying A; GI: Gastrointestinal; POPF B: Postoperative pancreatic fistula grade B.

Table 4 Demographic data and symptoms before and after pancreas-preserving duodenal resections for isolated form of cystic dystrophy of the duodenal wall (pure form of groove pancreatitis), July 2020

No.	Age	Pain	Vomit	Jaundice	Weight loss, kg	Weight gain after surgery, kg	Weight gain after surgery, %	PERT after surgery	Pain after surgery, status, events	Treatment before surgery, mo	Follow-up after surgery, mo
1	53	31.5	+++	+	44	46	105	No	No	9.5	127
2	43	37.8	+++	+	21	18	86	No	No	10	124
3	47	62.5	-		18	16	89	No	No	13	118
4	45	81.3	+++		23	16	70	Yes	Pain 26.3, still drinking	7	116
5	41	62.5	+		11	8	73	No	No	11	110
6	46	62.5	+		9	8	89	No	No	8	108
7	28	67.5	-		5	3	60	No	No	8.5	104
8	30	73.8	-		6	8	75	No	No	9	103
9	56	77.5	-		14	10	71	No	No, smoking	10.5	101
10	40	68.8	+		12	8	67	No	No, smoking	12	98
11	44	81.3	-		7	8	114	No	No	13.5	97
12	52	37.8	+++		31	24	77	No	GI bleeding -DP 46 mo after surgery, no symptoms	11.5	89
13	29	77.5	+		6	8	86	No	No, smoking	11	68
14	62	68.8	+	+	11	11	100	No	No	5	65
15	55	77.5	++		21	12	57	No	No	7	31

All the patients were males. Pain assessed by the Izbicki score^[38]. PERT: Pancreatic enzyme replacement therapy; GI: Gastrointestinal; DP: Distal pancreatectomy.

> Median follow-up prior to surgery was 10 mo (LQ-UQ: 8-12), and after surgery was 81 mo (LQ-UQ: 70-93). Currently, 14 of 15 patients have no complaints or symptoms (93.3%, Table 1). One patient (No. 4) with ankylosing spondylitis experienced a significant decrease in the frequency and intensity of pain episodes, despite regular alcohol consumption. All remaining patients had no episodes of pancreatitis or hospitalizations due to pancreatitis.

> Short- and long-term results after PD and PPDR are shown in Tables 6-8. Follow-up before PPDR (Figure 6) was considerably shorter compared to other procedures.

DISCUSSION

Today, most pancreatologists recognize CDDW as a distinct form of CP^[10,11]. Various terms have been used to define this condition, but all refer to the same set of clinical and histologic manifestations with typical imaging diagnostic criteria^[3,28,29]. Despite the increasing number of publications on CDDW, it is difficult to define its true incidence and prevalence. Based on the data of large series from specialized centers, CDDW is identified in 13%-24% of patients who undergo surgery for CP; whereas the isolated form of CDDW (pure form of GP) was present in 22%-37% of all CDDW cases

Table 5 Operative data and complications of pancreas-preserving duodenal resection, performed for isolated form of cystic dystrophy of the duodenal wall (July, 2020)

No.	PPDR	Blood loss, mL	Time, min	Postop stay, d	Morbidity (Clavien-Dindo)
1	Intest pouch	150	280	14	No
2	Standard	200	310	15	No
3	DDA	50	250	21	Grade I, POPF A
4	Intest pouch	50	270	39	Grade IV, upper DJA leakage, converted in Roux-en-Y
5	Standard	100	270	12	No
6	DDA	50	260	18	Grade I, POPF A
7	Standard	50	220	12	No
8	Standard	150	245	12	No
9	Standard	100	235	11	No
10	Standard	100	200	17	Grade I, POPFA
11	Roux-en-Y	50	215	14	No
12	Standard	100	215	16	No
13	Roux-en-Y	50	195	15	No
14	Roux-en-Y	50	230	14	Grade I, POPF A
15	Roux-en-Y	50	225	16	No
	Mean value	87			

PPDR: Pancreas-preserving duodenal resection; DDA: PPDR with duodeno-duodeno anastomosis reconstruction; DJA: Duodenojejunoanastomosis; Intest pouch: Pancreas-preserving duodenal resection with intestinal interposition reconstruction; Standard: Classical pancreas-preserving duodenal resection with one duodeno-jejuno anastomosis; Roux-en-Y: Pancreas-preserving duodenal resection with Roux-en-Y reconstruction; POPF: Postoperative pancreatic fistula.

Table 6 Pancreatoduodenectomy and pancreas-preserving duodenal resection for cystic dystrophy of the duodenal wall, comparison of demographic data and symptoms

PPDR	PD	P M-W value
15	44	
45 (40-52)	49 (46-54)	0.09
69 (62.5-77.5)	73.8 (63-73.8)	0.08
12 (7.5-21)	12 (10.5-13)	0.52
5 (33)	18 (41)	0.53
3 (25)	8 (18)	1
10 (8-12)	45 (36-57)	0 ¹
	PPDR 15 45 (40-52) 69 (62.5-77.5) 12 (7.5-21) 5 (33) 3 (25) 10 (8-12)	PPDR PD 15 44 45 (40-52) 49 (46-54) 69 (62.5-77.5) 73.8 (63-73.8) 12 (7.5-21) 12 (10.5-13) 5 (33) 18 (41) 3 (25) 8 (18) 10 (8-12) 45 (36-57)

¹Difference is significant.

All data are presented as Me (95% CI). PD: Pancreatoduodenectomy; PPDR: Pancreas-preserving duodenal resection.

(Table 9).

At the time when we were not aware of the cause of CDDW and thought that the cystic lesion of the duodenal wall originated from the pancreatic head, we performed operations relevant to conventional CP, such as longitudinal pancreaticojejunostomy, pancreaticocystostomy and DPPHR. Due to high complications and low efficacy rates, we stopped practicing this procedure in any type of CDDW.

A comparison of short- and long-term results of the two most efficient methods of CDDW treatment, namely PD and PPDR (Tables 6-8 have shown that both groups were similar in most of the parameters. Preoperative follow-up in the PD group was



Table 7 Pancreas-preserving duodenal resections and pancreatoduodenectomy for cystic dystrophy of the duodenal wall, comparison of intraoperative data and complications

Variables	PPDR	PD	P M-W value				
n	15	44					
Blood loss, mL	50 (50-100)	50 (100-125)	0.10				
Time, min	235 (215-270)	275 (240-290)	0.05				
Hospital stay, d	15 (13-17)	12 (11-14)	0.03				
Morbidity (Clavien-Dindo > III), n (%)	1 (6)	6 (14)	0.67				

PD: Pancreatoduodenectomy; PPDR: Pancreas-preserving duodenal resection.

Table 8 Pancreas-preserving duodenal resection vs pancreatoduodenectomy for cystic dystrophy of the duodenal wall, long term results

Variables	PPDR	PD	P M-W value
n	15	44	
Weight gain, kg	10 (8-16)	8 (7-9)	0.01
Weight gain, %	77 (70-89)	69 (63-75)	0.03
Pain after surgery, n (%)	1 (6)	5 (11.4)	0.66
New DM, <i>n</i> (%)		12 (31)	0.00^{1}
PERT, <i>n</i> (%)	1 (6)	43 (98)	0.00^{1}
Follow-up, mo	89 (78-100)	105 (80-134)	0.15

¹Difference is significant.

All data are presented as Me (95%CI). PERT: Pancreatic enzyme replacement therapy; DM: Diabetes mellitus.

Table 9 Literature review of the largest series of cystic dystrophy of the duodenal wall treatment PPDR² Ref. Year CDDW patients (n) Pure form of CDDW Surgery¹ PD² Stolte et al^[8] 1982 30 11 (37%) $30(100\%^{1})$ 30 (100%) Jouannaud et al^[4] 2006 23 0 $14 (61\%^{1})$ 10 (71%) Rebours et al^[5] 2007 105 30 (29%) 29 (28%) 17 (59%) Tison *et al*^[35] 2007 9 5 (56%) $9(100\%^{1})$ 9 (100%) de Pretis et al^[17] 2017 57 (69.5%¹) 51(89%) 82 22 (27%) Our data 82 18 (22%) 70 (85%) 42 (60%) 15 (21%) Overall 331 209 159 15 86

¹% of all patients.

²% of all surgical procedures.

CDDW: Cystic dystrophy of the duodenal wall; PD: Pancreatoduodenectomy; PPDR: Pancreas-preserving duodenal resection.

significantly longer because of long-lasting efficient conservative treatment, including endoscopic options. Patients in the PPDR subgroup were operated on much earlier due to intensive and/or frequent pain, with such CDDW complications as duodenal obstruction and jaundice. There were no significant differences in intraoperative details and short-term results. In spite of the advantages of PPDR in this data sample, transfer to the general population did not reveal significant differences in morbidity, which was probably due to the small number of cases. Hospital stay was not significantly longer in the PPDR group, depending mainly on the peculiarities of the

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Figure 6 Duration of preoperative treatment of patients with cystic dystrophy of the duodenal wall. Preoperative treatment before pancreaspreserving duodenal resection was significantly shorter when compared with the other subgroups (explanations in the text). PPDR: Pancreas-preserving duodenal resection; DPPHR: Duodenum-preserving pancreatic head resection.

Russian Federation health care system relating to new treatment methods (Table 6).

Postoperative absolute and relative weight gain were higher in the PPDR group compared to the PD group, but not significantly so. New onset diabetes mellitus never occurred in the PPDR group, which was significantly better compared to 31% after PD. No patient required PERT after PPDR, which was significantly different compared to the PD group, where only two patients were PERT-free (Table 7). Six of our 44 patients (14%) suffered pain recurrence after PD, which is comparable to the results of the Italian studies (18.75%)^[17].

Only one major complication was recorded after PPDR: Leakage of the proximal duodenojejunostomy, and it was caused by marked fibrosis of the duodenal bulb, due to a long history of peptic ulcer disease. This observation changed our practice so that patients with a history of peptic ulcer disease were subsequently subjected to Roux-en-Y reconstruction with no serious complications since then. It is important to note that a significant history of peptic ulcer is common in patients with CDDW due to stenosis of the second portion of the duodenum. One other remote complication was splenic artery aneurysm rupture, which occurred in one case four years after PPDR. The aneurysm was not detected before surgery, since no contrast CT had been carried out. The patient underwent distal pancreatectomy and subsequently returned to normal life. All minor complications were confined to short-term grade A pancreatic fistulas, which might have occurred due to suturing normal pancreatic parenchyma. After PPDR, all patients except one, achieved long-term improvement. No patients developed endocrine or exocrine pancreatic insufficiency due to preservation of the whole gland, which was only mildly affected.

As for derivative procedures, they were quite effective in the French experience^[5], but in the Italian study^[17], they failed in more than 60% of patients, which is very similar to our results.

Based on our data (Table 1) and the works of Italian and French colleagues^[4,17], conservative treatment (including endoscopic) and draining procedures are ineffective when damaged pancreatic tissue is present in the context of CDDW, although there have been some reports of short-term positive results^[7,17,23,39,40].

In our series, neither minor duodenal papilla, nor Santorini's duct alterations were detected in the PPDR subgroup during pathologic examination. This corresponds to the radiological data by Wagner *et al*^[41] and to Stolte *et al*^[8] and Becker et al's^[9] histologic evidence. The latter also demonstrated that, in cases of CDDW, the minor duodenal papilla detection rate is 31%, which corresponds to the minor duodenal papilla distribution in the general population. All these findings are important to the surgeon making the decision to save or not to save the pancreas, and they do not argue for the importance of minor duodenal papilla and Santorini's duct pathology in the development of CDDW.

The efficacy of pancreas-preserving duodenectomy for the isolated form of CDDW (



i.e., pure form of GP) is important evidence indicating that, in the early stages of the disease the lesion is located in the duodenum, rather than in the pancreas or paraduodenal area.

It is worth mentioning that the imaging characteristics of CDDW are quite specific, so that preoperative diagnosis has become increasingly reliable^[3,28,29,42,43]. Eighty three of 84 patients were diagnosed as having CDDW prior to the operation and only one was operated on due to "impossibility to rule out duodenal or pancreatic head tumor." The same "learning curve" for radiologists is mentioned by our Italian colleagues^[16].

The possibility of malignant transformation in ectopic pancreatic tissue should never be ruled out, although there have been only 15 such cases reported^[30,31,32]. In our pool of 84 patients, one in the conservative therapy subgroup died of metastatic cancer of the ectopic pancreas, early cancer was found in the ectopic pancreas after PD in a second, and PanIN II epithelial dysplasia of the ectopic pancreas was diagnosed after PPDR in a third patient^[27].

The limitations of the work are its retrospective design and the impossibility to compare PD and PPDR for the isolated form of CDDW only because of conventional practice and relative rarity of the disease. We tried to be strict in selecting only patients who abstained from smoking and alcohol consumption, but due to legislation in Russia, it is impossible to use opioids for CP treatment. As a result, we had to operate on patients with intractable pain. The same is true for such complications of CDDW as jaundice and duodenal obstruction, even if patients are still smoking and drinking.

The point of interest is the association of CDDW and ankylosing spondylitis in three patients in our series, which could be a topic of subsequent research.

In summary, CDDW is a distinctive form of CP. Its peculiarity lies in the fact that no or minimal damage to the orthotopic (main) pancreas occurs in its isolated form, while further development of the disease leads to involvement of the pancreas. The success of PPDR and the decreased probability of disease progression from its isolated form to segmental and, then, diffuse pancreatitis after PPDR, indicate that in the cases of CDDW: (1) PPDR may be the treatment of choice for the isolated form of CDDW; (2) Isolated CDDW, or the pure form of GP, is a disease of the duodenum; (3) Early detection of CDDW makes preservation of the pancreas possible; (4) PD appears to be overtreatment for the isolated form of CDDW, since it involves resection of undamaged pancreatic head parenchyma; (5) Prolonged conservative treatment in cases of the isolated form of CDDW may lead to the development of segmental and diffuse pancreatitis, which may deprive patients of the pancreas-preserving option; and (6) The abovementioned points make PPDR an alternative treatment for CDDW (GP).

Comments

Potet *et al*^[1] and Stolte *et al*^[8] and Becker *et al*^[9] demonstrated that clinical and pathologic manifestations of GP might occur with no pancreas involvement. In these cases, the pathologic process is localized in the duodenum as intramural duodenal cysts, chronic inflammation of ectopic pancreatic tissue in the duodenal wall, and perifocal fibrosis. These observations are also supported by other studies^[2-9,34]. This led to the conclusion that the pure form was an initial stage of GP, which is supported by our data regarding a much shorter time between the onset of the disease and the operation in the PPDR subgroup (Figure 6). Therefore, the disease is referred to by different authors as the isolated cystic form of CDDW^[1,2-7], pure form of GP^[8,9], or pure form of PP^[17]. The groove between the duodenum and pancreas has no organs to be inflamed, and this leads to fibrotic changes of the groove; therefore, its cicatrization may only be caused by the involvement of adjacent organ(s). If we do not detect considerable alterations of the pancreatic head, but do detect changes in the duodenal wall, it would be reasonable to assume that inflammation of the duodenal wall caused cicatrization of the groove and the development of other symptoms. This means that the involvement of the duodenum is the primary factor, while damage to the pancreas comes second. The idea that CDDW, GP or PP is a duodenal disease is not new. All main investigators of the subject^[5,8,15-17] unambiguously spoke about this. Some misunderstandings appeared when the pathologic examination was carried out in a series that only included cases of advanced disease (for example, 21 specimens in[15], or 20 specimens from 10 hospitals^[4]). In all other large series, we can find specimens with isolated forms of CDDW (pure forms of GP) (Table 9). The organ of disease origin is impossible to establish in advanced stages with associated severe CP of the main gland^[4,15,42,43].

These observations lead to two conclusions. The first is the adoption of a legitimate term to refer to the condition. If this stage of the disease is called groove or PP, we describe pancreatitis with no pancreatitis, since all alterations are concentrated in the



duodenum. It does not seem reasonable to refer to a disease located in the duodenum as inflammation of the pancreas^[44]. Along with that, CDDW sounds like a diagnosis referring to a specific organ and incorporation of this term appears as a more logical alternative. The second conclusion is that the removal of the damaged area (*i.e.*, partial or total duodenectomy) may be the best possible method of treatment of the pure form of GP or PP^[27].

It is important to differentiate between the pure and segmental forms of GP (isolated form of CDDW) in order not to confuse "typical signs or symptoms of the disease"[45,46]. These two forms of the disease may demonstrate the same clinical manifestations, but different typical signs, and based on the aforementioned data, may be treated differently.

CONCLUSION

The following conclusions were drawn: (1) PPDR may be the treatment of choice for the isolated form of CDDW; (2) Isolated CDDW, or the pure form of GP, is a disease of the duodenum; (3) Early detection of CDDW makes preservation of the pancreas possible; (4) PD appears to be overtreatment for the isolated form of CDDW, since it involves resection of undamaged pancreatic head parenchyma; (5) Prolonged conservative treatment in the isolated form of CDDW may lead to the development of segmental and diffuse pancreatitis, which may deprive patients of the pancreaspreserving option; and (6) the abovementioned points make PPDR a procedure that is changing the treatment of CDDW (GP).

ARTICLE HIGHLIGHTS

Research background

Today most pancreatologists recognize groove pancreatitis as a distinct form of chronic pancreatitis, but the natural history of the disease and the optimal time for surgery are unknown.

Research motivation

To understand the best technique and timing of pancreas-preserving procedures for groove pancreatitis (GP).

Research objectives

To compare the results of conventional (Whipple procedure) and organ-preserving surgery for the treatment of GP.

Research methods

A retrospective comparison of the different conservative and surgical modalities for the treatment of GP in 84 patients.

Research results

Timely pancreas-preserving procedures for GP are safe and provide better long-term results compared to conventional surgery, which is usually used at the late stages of the disease.

Research conclusions

Pancreas-preserving duodenal resection (PPDR) may be the treatment of choice for the isolated form of GP; the pure form of GP is a disease of the duodenum, early detection of which makes preservation of the pancreas possible; prolonged conservative treatment in the isolated form of GP may lead to the development of segmental and diffuse pancreatitis, which may deprive patients of the pancreas-preserving option; timely performed PPDR is a treatment-changing procedure for GP.

Research perspectives

If the author's approach is widely accepted, more patients with GP will have the chance to save their pancreas, and prospective comparative trials will be possible on the above mentioned subject.



ACKNOWLEDGEMENTS

The authors would like to express appreciation to Löhr M, Rebours V and Tsiotos G for review and correction of the manuscript, to Bystrovskaya E for endoscopic and endoUS pictures, and to Maslennikov V for his drawings.

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