

# CHRONIC PANCREATITIS: INDICATIONS FOR SURGERY AND LONG-TERM OUTCOME EVALUATION CRITERIA

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**Key words:** chronic pancreatitis, treatment, ductal hypertension, surgery indications, long-term results assessment

Indications for surgery in patients with chronic pancreatitis (CP) are known to be a complex integrative process involving primarily the dynamics of preceding conservative treatment with determining its effectiveness and, moreover, reflecting the degree of subjectivity in the decision of such an important change in the treatment, as many aspects of this problem are rather debatable [1, 4].

Existing criteria for indications for surgical treatment in the vast majority belong to the category of absolute ones: severe pain, evident enlargement of Wirsung's duct, the presence of stones in it, stricture formation, cystic transformation of parenchyma, obstructive duodenal stenosis, obstructive jaundice due to the compression of the intrapancreatic part of choledoch by the enlarged head of the pancreas («inflammatory mass»), etc. [5, 6, 8]. There is no doubt that surgical interventions in patients with CP are usually performed for absolute indications on the background of primarily known decompensated forms of the functional state of pancreas, namely exocrine function [2, 3]. With this in mind, development of indications for surgery in the earlier stages of the disease is still being debatable, as well as the development of a universal grading scale of long-term results of surgical or conservative treatment of CP, allowing to answer the question on the basis of what criteria can we distinguish good, satisfactory and unsatisfactory results to compare, for example, different methods of surgical interventions (parenchyma-preserving resection, draining, endoscopy, etc.) or methods of therapeutic intervention [7, 9, 10].

**Aim of research** is to clarify the indications for surgical treatment of patients with CP on the basis of the leading factors in the pathogenesis of this nosology with the development of evaluation criteria summarizing long-term results.

**Patients and methods.** 122 patients with CP were operated, including 103 (84.4%) men and 19 (15.6%) women with a mean age of patients equal to 45 years. Alcoholic etiology of CP was detected in 79 (64.8%), CP after acute pancreatitis (pancreatic necrosis) — in 29 (23.8%), biliary genesis — in 6 (4.9%), idiopathic — 8 (6.6%). In the examination of patients for hyperparathyroidism (serum ionized calcium, parathyroid hormone) no one case of hyperparathyroid etiology of CP was fixed. Increasing diameter of the Wirsung's duct was following: 4-8 mm — in 65 (53.3%), 8-12 or more — in 57 (46.7%). By forms of CP (classification by A. A. Shalimov et al., 1997) distribution was the following: pseudotumorous — in 39 (31.9%), calculous — in 40 (32.8%), fibrocystic — 17 (13, 9%), fibro-degenerative involving adjacent organs and violation of their functions — in 26 (21.4%).

All the patients reported abdominal pain and various manifestations of exocrine pancreatic insufficiency, endocrine abnormalities were found in 79 (64.8%).

Patients underwent computed tomography, ultrasound, including dopplerography of celiac trunk and branches of the portal vein, endoscopic examination, including endoscopic retrograde cholangiopancreatography; we determined endogenous insulin, C-peptide, glycosylated hemoglobin, tumor marker CA 19-9, pancreatic fecal elastase-1; by histochemical and immunohistochemical methods, we determined the prevalence of fibrosis, collagen I, III, IV type,  $\alpha$ -SMA-positive stellar cells in intraoperative pancreatic sections taken from the head, body and tail. In the long-term perspective results of treatment were assessed by the criteria elaborated in the clinic, as well as by the international questionnaires MOS SF-36 and EORTC QLQ-C30 STO22, evaluating the quality of life of patients.

In 64 (52.5%) patients (main group) we performed parenchyma-preserving surgery developed and patent-protected in Ukraine: Longitudinal total pancreatowirsungoduodenopapillotomy with longitudinal pancreatojejunal duodenostomy by Roux. In 58 (47.5%) patients (comparison group) we performed

resection surgery (pyloro-preserving pancreatoduodenal resection surgery by Beger and Frey).

Statistical analysis was performed with the use of Microsoft Excel 2010 application.

**Results and discussion.** According to the analysis, surgical CP treatment is carried out upon various complicated forms and, as a rule, with existing evident exocrine and/or endocrine dysfunctions on the background of severe pain syndrome. At the present stage the surgical treatment of CP requires not only the effective elimination of complications, but also the strict preservation of functional reserve of the pancreas, existing at the time of operation (exocrine, endocrine function). In addition, surgical treatment should be determined by a low mortality and a minimum frequency of postoperative complications.

Unfortunately, this approach is largely only declared and yet has virtually no practical implementation, if we consider the problem from the standpoint of late referral of patients for surgical treatment in the form of running decompensated forms and conducting almost "operations of despair" on this background.

The results of numerous studies presented at the recent European pancreatic meetings (EPC 2009-2012) and World Congress on hepatopancreatobiliary surgery (ICPBA 2010, 2012) indicate a dominant role of ductal hypertension in the development all the adverse effects of the clinical course of CP. Complete elimination of ductal hypertension plays a crucial role in preserving the pool of acinar cell mass of the pancreas, remaining before surgery, which determines the degree of exocrine insufficiency (from mild to severe). On this basis, there is no doubt that the indications for surgical treatment and modern surgical interventions in patients with CP should be strictly justified and organ-preserving, avoiding even minimal loss of body parts.

In the conducted research, indications for surgery in patients with CP were considered from surgical positions of problem vision, because expressed conservatism, which is typical for gastroenterology, with rare exceptions allows timely surgical treatment. However, incorrect indications and particularly

inappropriate choice of the surgical method often entail inefficiency and sometimes deterioration of the patient after surgery, thereby increasing the skepticism of gastroenterologists.

Modern classification of CP, including the last one — M-ANNHEIM (2007), have vague and non-specific character of indications for surgical treatment, presenting rather a set of non-binding recommendations. This happens because of the lack of classifications with a key point of a particular type of treatment (conservative and surgical). Such a core basis in the classification should be an assessment of the severity of pancreatic ductal hypertension and determining the etiology of CP.

With this in mind, any etiological variant of CP with ductal hypertension (proposed concept) should be potentially referred to the "surgical" type. We propose an algorithm of diagnostic and treatment process based on the conducted analysis. By generally accepted international classification TIGAR-O (2001), based on exhaustive information about the etiological aspects of CP, it is necessary to add etiological thesis for each section: a) without ductal hypertension; b) with ductal hypertension. Exactly such an approach originally disciplines the doctor and strictly makes him/her perform all the necessary protocol (screening) volume of diagnostic methods for the proof: pancreatic ductal hypertension — yes or no.

Thus, the etiological CP variants without ductal hypertension are fully within the competence of a gastroenterologist (pancreatologist), while the volume of screening studies should include a standard ultrasound and CT of the abdomen with a focus on the pancreas, fibrogastroduodenoscopy with a detailed examination of the major duodenal papilla, X-ray examination of the stomach and duodenum with barium, the definition of pancreatic elastase-1 in feces and glycemic profile. Complex and invasive methods at this stage are not prescribed, but if in the future there are progressive negative changes of clinical manifestations of CP, the appointment of these examinations should be coordinated with the surgeon.

At the same time, all CP variants with signs of ductal hypertension, defined on the basis of the volume of screening studies, require a joint appointment with the surgeon of further complicated and invasive diagnostic methods, including, if

necessary, ERCP, MRCP, endoscopic ultrasound with pancreatic biopsy, analysis of tumor marker CA 19-9, parathyroid hormone, lipid profile, endogenous insulin, C-peptide, IgG, conducting genetic examination (if possible). The task of such an extended study ("surgical" screening) is to determine (search) the anatomical and morphological changes of the pancreas.

Increasing diameter of the main pancreatic duct (MPD) is a strong evidence of ductal hypertension, but this exceptionally valuable phenomenon should be considered only in conjunction with other criteria mentioned above, linking them with the data on the degree of the exocrine and endocrine insufficiency (yes or no?), the presence of pain syndrome. Enlargement of MPD in combination with one, or even two signs (e.g., pain, exo-, endocrine insufficiency) is a decisive argument for surgical treatment, with a significant expansion of the diameter of the MPD to be considered less than 5 mm (Marseilles-Cambridge classification criteria for imaging, 1996). Such action algorithm eliminates undue inertia in observing the patients upon the presence of proven major phenomena of "surgical" CP (pain, increased MPD, the initial manifestation of exo- and/or endocrine insufficiency).

Definition of objective criteria of surgical treatment of CP patients in the long term is of primary importance. In the conducted work, we stated in the form of indisputable fact that it was impossible to regain lost function of the pancreas, if by the time of surgery there had been a loss of significant part of acinar cell mass, which determined those functions. The task of the surgeon in this difficult clinical situation is to eliminate pain and arising forms of CP complications, not worsening functional reserve of the pancreas (exo-, endocrine function) remained by the time of operation. It is the preservation of the remaining functional reserve of the pancreas on the background of elimination of abdominal pain is one of the main criteria for a good result, and it needs to be confirmed in long-term period documentally (relevant research methods), as well as through an independent self-assessment of the patient (quality of life based on specific questionnaires MOS SF-36, EORTC QLQ-C30 STO22). Reformatting the criteria of surgical treatment is essential for the progress of the treatment of CP as a whole.

Proceeding from this, developed at the clinic criteria of effective surgical treatment of patients with CP in the long-term period are:

1. *Good result*: the absence of abdominal pain syndrome observed before surgery; indicators of exocrine and/or endocrine pancreatic functions such as before surgery or better; absence of CP complications, serving as an indication for primary surgery.
2. *Satisfactory result*: absence or observation of abdominal pain syndrome of constant or recurrent nature, but much lower intensity than before the operation; indicators of exocrine and/or endocrine pancreatic functions are worse than before the surgery, but don't require a radical revision of corrective therapy (increasing doses of enzyme preparations in 2 times, the transition to insulin or increasing insulin doses); relapse of CP complications, but it is oligosymptomatic and doesn't require reoperation.
3. *Unsatisfactory result*: abdominal pain syndrome recurred after surgery or remained almost the same; indicators of exocrine and/or endocrine pancreatic functions were significantly deteriorated that required a radical revision of corrective therapy in the form of higher doses of enzyme preparations in 2 or more times, transfer to insulin or increasing doses of insulin; relapse of CP complications of symptomatic nature and requiring invasive procedures or reoperation.

According to the conducted research, good results in the long-term period were observed in 92.6% of patients who underwent parenchyma-preserving surgery; satisfactory — in 4 (7.4%); unsatisfactory results weren't marked. At the same time, good results after resection operations were found only in 53.1% of patients, satisfactory results — in 32.7%, and unsatisfactory — 14.3%.

**Conclusions.** CP patients receive unreasonably prolonged conservative treatment, often leading to functional insufficiency (exocrine and endocrine).

There is no proper continuity between conservative and surgical treatment.

Restructured TIGAR-O classification with amendments defines the direction of the dynamic and healing process in CP, specifying the indications for surgical treatment.

Criteria for assessing the long-term results of surgical CP treatment should maximize objective evaluation of anatomical and functional changes in the pancreas, which determine the quality of life of the patient.

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122 patients with complicated chronic pancreatitis were operated on. This article presents the critical analysis of negative consequences of chronic pancreatitis conservative therapy. They are conditioned in some degree by imperfection of current classifications of chronic pancreatitis. We propose special diagnostic algorithm paying precise attention to surgery indications and assessment criteria of long-term results of surgical treatment that objectify patients' life quality assessment.