News of European pancreatology
(by materials of the 51st Meeting of the European Pancreatic Club)

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On June 26-29, 2019, the 51st meeting of the European Pancreatic Club (EPC) was held in Bergen (Norway), which was attended by 670 delegates from 45 countries. Let's start with the achievements of the Ukrainian Pancreatic Club. Our Club is still the largest in Europe. At the meeting in Bergen, we presented 38 works in the form of oral and poster presentations from 25 authors. Ukraine entered the top ten most active countries in terms of the number of reports submitted. The delegation of Ukraine was represented by 23 pancreatologists. Now let us briefly describe the results of some studies that have attracted our attention.

Etiopathogenetic studies

Among the many studies in the field of fundamental pancreatology, the work of F. Viecelli et al. (Italy), whose authors studied the presence of a genetic predisposition capable of causing the development of chronic pancreatitis (CP). Scientists retrospectively analyzed the frequency of genetic mutations in patients with CP (n=276) and found that 66 (24%) patients are carriers of at least one mutation: in 42 (60%) cases, a CFTR gene mutation was recorded, in 21 (30%) cases — SPINK1, in 7 (10%) cases — PRSS1. The early onset of CP (patient's age up to 30 years), a burdened family history of pancreatitis, the presence of calcifications in the pancreas (pancreas) as a bovine eye (Fig. 1) were predictors of the presence of genetic mutations.

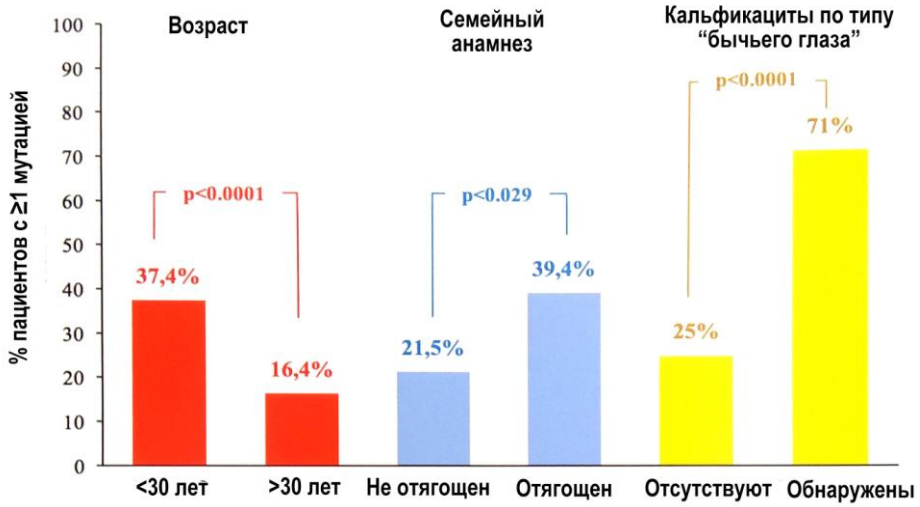


Fig. 1. Genetic mutation predictors for CP (according to F.Viecelli et al., 2019 [1])

Such calcifications are characterized by a weakening of the degree of calcification in the center due to the low content of calcium in it (Fig. 2).

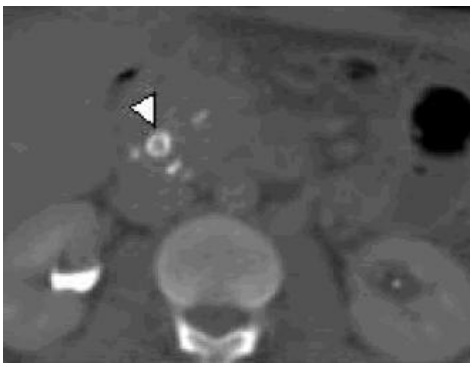


Fig. 2. Pancreatic calcification “bull’s eye”

Mutations were most often detected in patients with idiopathic CP (Fig. 3). The authors concluded that genetic testing of all patients with idiopathic CP is necessary, as well as in the presence of the above predictors.

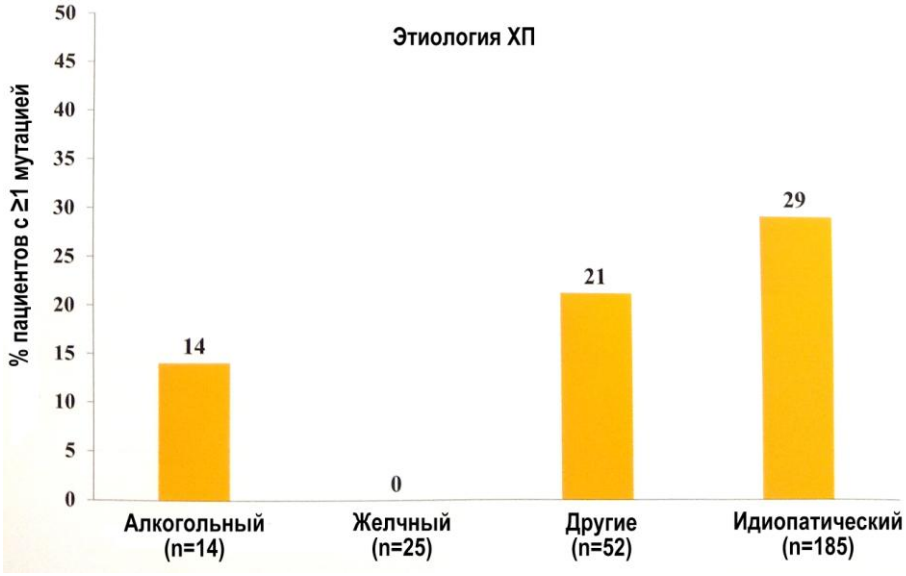


Fig. 3. Frequency of detection of mutations depending on the etiology of CP (according to F. Viecelli et al., 2019 [1])

The delegates of EPC 2019 paid close attention to the lectures of P. Bork, which revealed the role of the digestive tract microbiota in the development and progression of pancreatic adenocarcinoma. This topic has been widely discussed in the scientific community for several decades. In particular, a detailed literature review was recently published in which the dominant hypotheses on the role of intestinal microbiota in the pathogenesis of AP, CP, and pancreatic cancer are presented (Fig. 4).

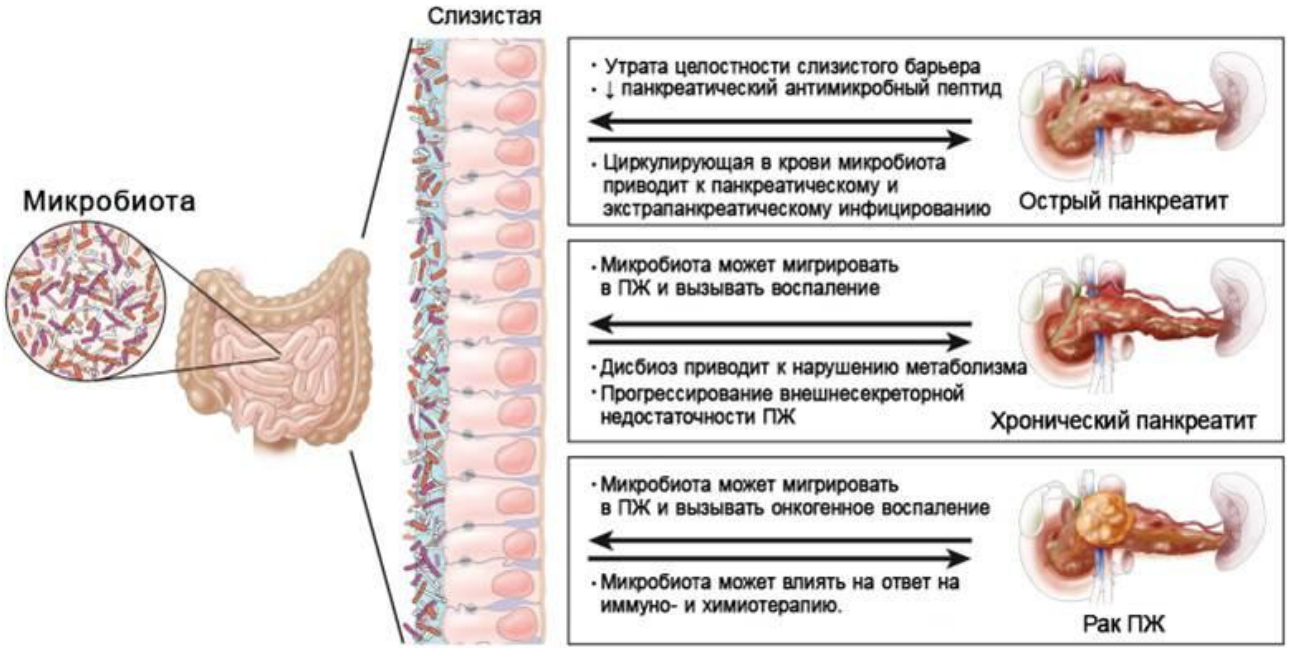


Fig. 4. The main directions of the pathogenesis of AP, CP, pancreatic cancer with the participation of intestinal microbiota (according to V. S. Akshintala et al., 2019 [2])

The main pathogenic microorganisms of the oral cavity involved in carcinogenesis include P. gingivalis, Fusobacterium, N. elongata, S. mitis. It has been proven that H. pylori infection is associated with an increased risk of pancreatic adenocarcinoma. Hepatotropic viruses have a potential role in the formation of pancreatic adenocarcinoma, although there is no direct evidence of their direct involvement (Fig. 5). Representatives of the genus Enterobacter, strains of Enterococcus and E. coli contribute to the growth of pancreatic adenocarcinoma (shown in the experiment). Numerous bacteria have been found in the pancreatic tissue inhibiting the effect of chemotherapy drugs.

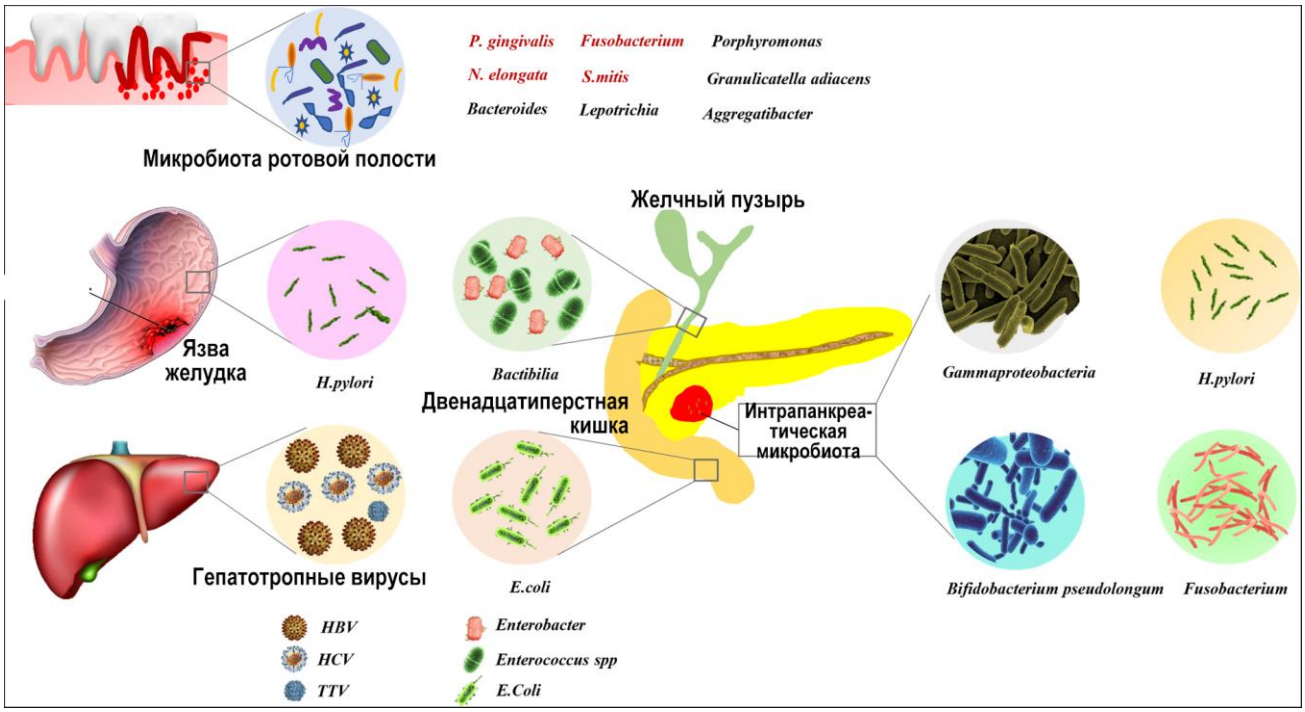


Fig. 5. Microbiota associated with pancreatic adenocarcinoma (according to M. Y. Wei et al., 2019 [7])

The role of microbiota in pancreatic carcinogenesis is discussed. According to the existing hypothesis, the microbiota colonizes the pancreas, forms a phenotype tolerant to adenocarcinoma through dysregulation of stellate cells and polarization of M2 macrophages. This leads to inhibition of cytotoxic CD8 and CD4-Th1 and a progressive increase in tumor size. In the absence of microbiota in the pancreatic tissue, macrophages of M1 are activated and tumor growth is suppressed (Fig. 6).

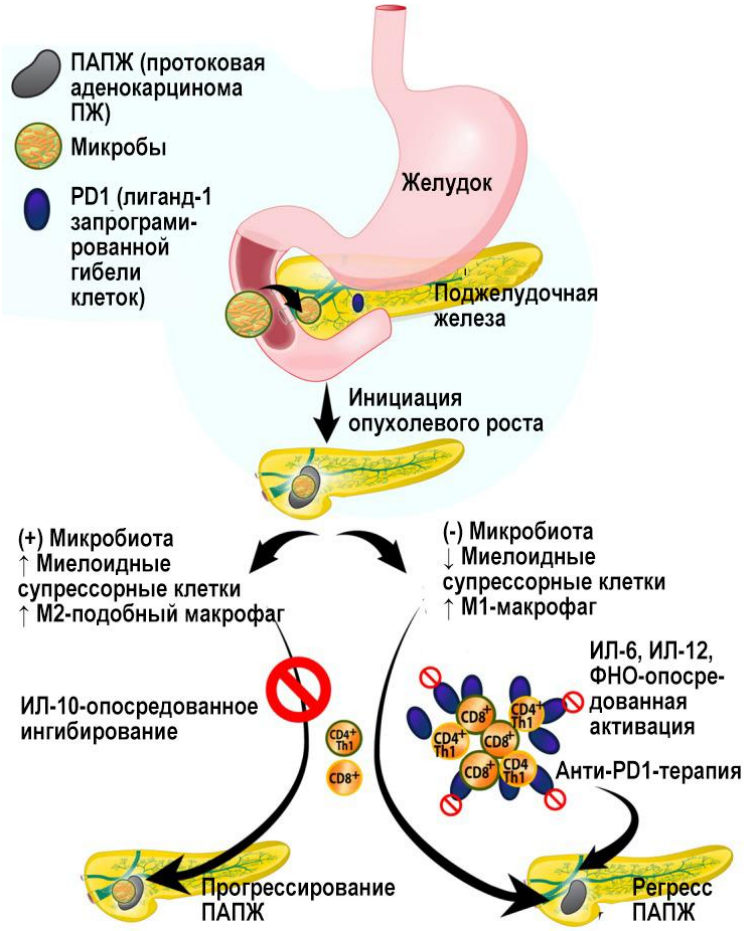


Fig. 6. Presumptive mechanisms of pancreatic carcinogenesis involving microbiota (according to R.M. Thomas et al., 2018 [6])

Diagnosis

In addition to studying the etiopathogenetic features of pancreatic damage, much attention is paid to the diagnosis of diseases of this unique organ, including the identification of signs that distinguish them from other nosologies. For example, A. Madro et al. (Poland) analyzed the feasibility of using miRNAs (MiR) in the differential diagnosis of CP and pancreatic cancer. To this end, researchers studied MiR in patients with CP (n=34), pancreatic cancer (n=26) and healthy individuals (n=14). It turned out that the determination of MiR-1290 in combination with CA 19-9 and γ-glutamyl transpeptidase can be an informative marker for the differential diagnosis of CP and pancreatic cancer, while the combination of MiR-195-5p with amylase, C-reactive protein can serve as a prognostic marker of malignancy CP.

A. Anu et al. (Finland) evaluated the diagnostic informative value of determining the soluble plasminogen activator receptor urokinase type (suPAR) for the differential diagnosis of benign and malignant pancreatic tumors. Scientists analyzed the biological material obtained from 46 patients who underwent surgery on the pancreas. In addition, the levels of suPAR and CA 19-9 were examined in the blood serum of patients. The information content of the first marker turned out to be higher than the second: the sensitivity and specificity of suPAR were 88% and 86%, respectively, while similar indicators for CA 19-9 were 69% and 71%, respectively. Serum suPAR

levels in pancreatic adenocarcinoma were significantly higher than in benign tumors and precancerous neoplasia (Fig. 7).

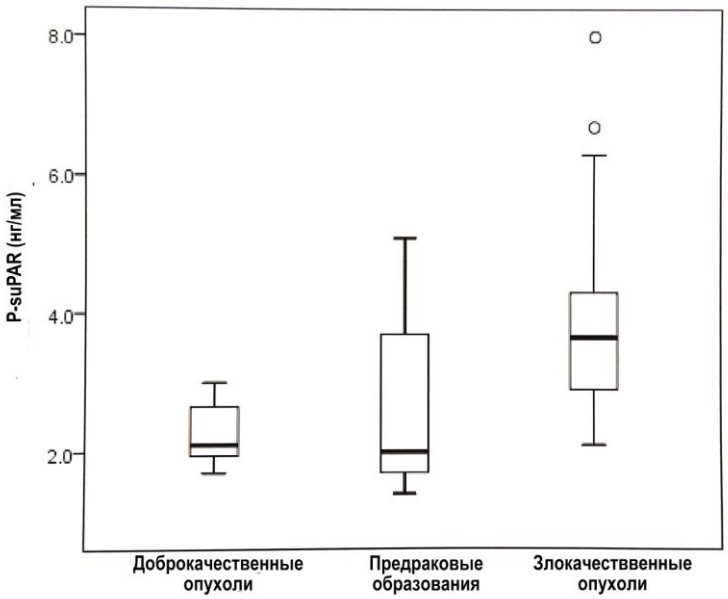


Fig. 7. Blood suPAR level for various pancreatic pathologies (according to A. Anu et al., 2019 [1])

M. Jalal et al. (Great Britain) analyzed the possibility of using nutritional markers for the diagnosis of exocrine pancreatic insufficiency (EPI). Examining 144 patients and diagnosing residence permit with fecal elastase test, the researchers found the presence of residence permit and selenium deficiency in 25.8% of patients compared with patients who did not have residence permit and signs of selenodeficiency (7.4%; p=0.28). Other significant trophological differences in patients suffering from EPI and not having this complication were absent. With a serum concentration of selenium below 0.61 μmol/L in patients with a high risk of residence permit (CP, diabetes mellitus (DM), prolonged alcohol abuse), the sensitivity, specificity, positive and negative predictive value of this indicator were 25.81% and 92.45%, 66.66% and 68.06%. The authors ascertained low sensitivity of selenium as a diagnostic marker of residence permit. Therefore, selenium can have only additional value in the diagnosis of residence permit and can be used in combination with other laboratory and instrumental studies.

Among the many works presenting new methods of instrumental diagnostics in pancreatology, the message of L. F. Cherciu et al. (Romania). The researchers evaluated the diagnostic capabilities of endoscopic fine-needle biopsy under ultrasound guidance with confocal laser endomicroscopy in determining the intraductal papillary mucosa of the pancreatic neoplasia. Based on the results of a meta-analysis of 37 studies, the authors concluded that confocal laser endomicroscopy, supplemented by histological examination, is a modern, minimally invasive informative method for the diagnosis and differentiation of pancreatic cystic formations (Fig. 8).

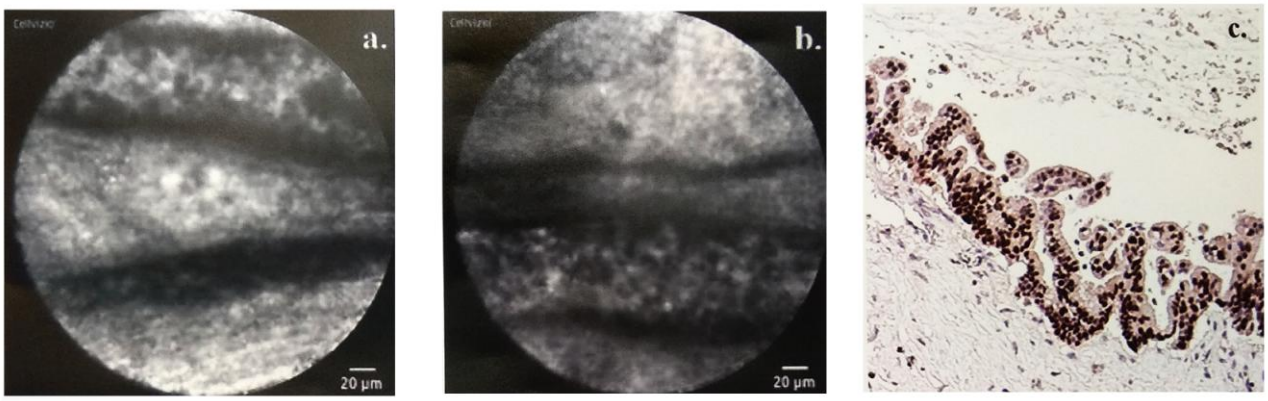


Fig. 8. Confocal laser endomicroscopy (a, b) with a fine needle biopsy (c) with intraductal mucosa of pancreatic papillary neoplasia (according to L.F. Cherciu et al., 2019 [1]). Hematoxylin-eosin, ×100

In a retrospective multicenter study conducted in patients with CP and EPI (n=265), I. Ozola-Zalite et al. (Latvia) investigated new methods for diagnosing sarcopenia. Determining the thickness and cross-sectional area of the lumbar muscles during computed tomography (CT) (Fig. 9), scientists have proved that the presence and severity of sarcopenia is associated with the degree of residence permit and the intensity of the pain syndrome.

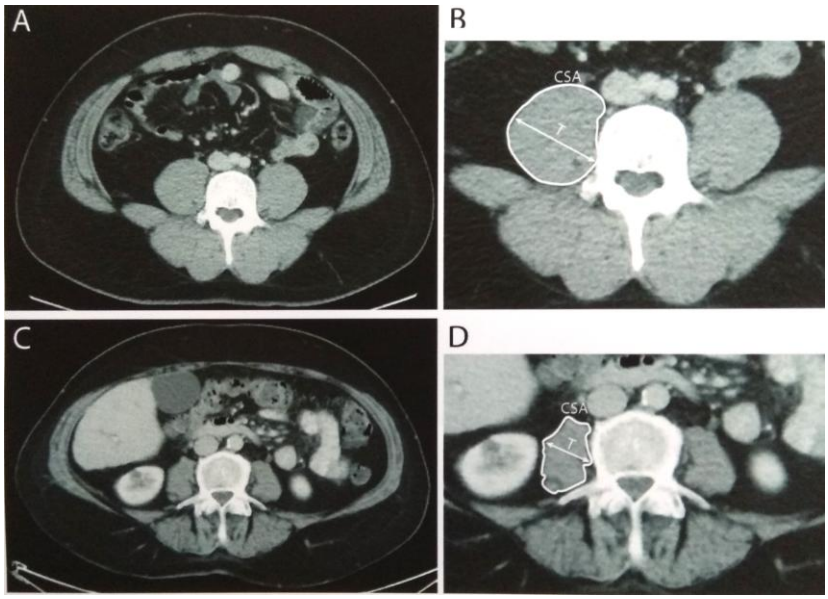


Fig. 9. Determination of thickness and cross-sectional area of the lumbar muscles (according to I. Ozola-Zalite et al., 2019 [1]). A, B — norm, C, D — sarcopenia

Of course, the presence of concomitant pathology can aggravate the course of CP. According to S. Vancsa et al. (Hungary), the presence of liver steatosis adversely affects the course of acute pancreatitis (AP). This conclusion is based on the results of a meta-analysis of 12 studies in which patients with AP took part (n=6233). Scientists have found that liver steatosis significantly increases the risk of death (relative risk, RR 3.24), severe AP (RR 2.37), the development of pancreatic necrosis (RR 2.27) and the formation of multiple organ failure (RR 1.94), and also lengthens the duration of inpatient treatment ($p<0.001$). Therefore, the diagnosis of liver steatosis along with other factors can be used to determine the prognosis of AP.

H. Niimi et al. (Japan) studied the relationship between the development of liver steatosis after surgery on the pancreas with the type of operation and the residual volume of pancreatic tissue. 295 patients who underwent various operations on the pancreas were examined. The results obtained indicate that a fundamentally important factor leading to liver steatosis is a decrease in the

volume of the pancreatic parenchyma (Fig. 10).

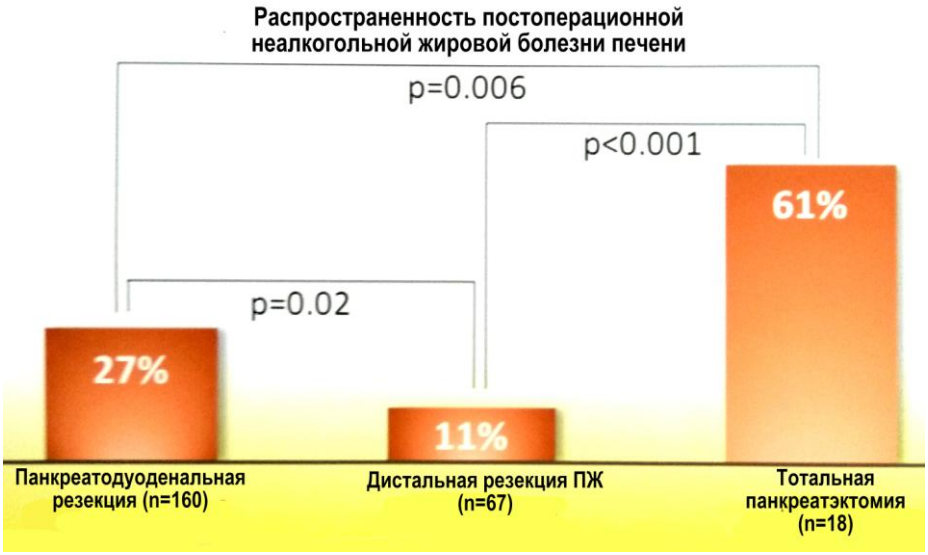


Fig. 10. Frequency of liver steatosis after various surgical interventions (according to H. Niimi et al., 2019 [1])

A new method for analyzing pancreatic pain was proposed by S. S. Olesen et al. (Denmark). According to the design of their multicenter study, which was attended by practically healthy individuals (n=122), an algesimeter (point pressure technique) and a cold pressor test were used to assess the threshold of pain sensitivity. Sensitivity studies were performed in "pancreatic dermatomes": on the upper abdomen and back, as well as in three control zones. Subsequently, the ratio between pain thresholds measured in the pancreatic and control zones was calculated. The degree of segmental hyperalgesia was evaluated by calculating special indices different for constant and repeated pressure. It turned out that the pain threshold in women is significantly lower than men ($p<0.05$). Researchers have developed criteria for differential diagnosis to determine the level of sensitization (segmental, central, common hyperalgesia — Fig. 11). The application of the proposed standardized protocol, according to the authors, will allow to determine the mechanisms of pain in patients and choose treatment tactics.

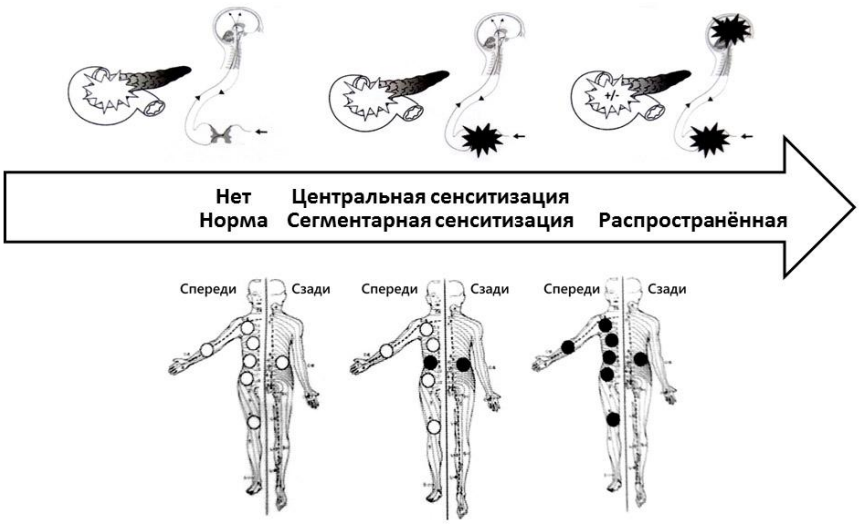


Fig. 11. Various options for sensitization in pancreatic pathology (according to S. S. Olesen et al., 2019 [1])

Peculiarities of CP course

Many works presented during the EPC 2019, analyzed the features of the course of AP and

CP, depending on the presence of a variety of concomitant pathologies, genetic characteristics, bad habits, and drugs taken. For example, S. S. Olesen et al. (Denmark) studied the relationship between the intensity, nature of abdominal pain in CP and alcohol abuse, nicotine. In the framework of a multicenter cross-sectional study, in which patients with CP took part (n=1384; of them 801 experienced severe pain, 583 did not complain of pain), multivariate logistic regression models were constructed (Fig. 12, 13).

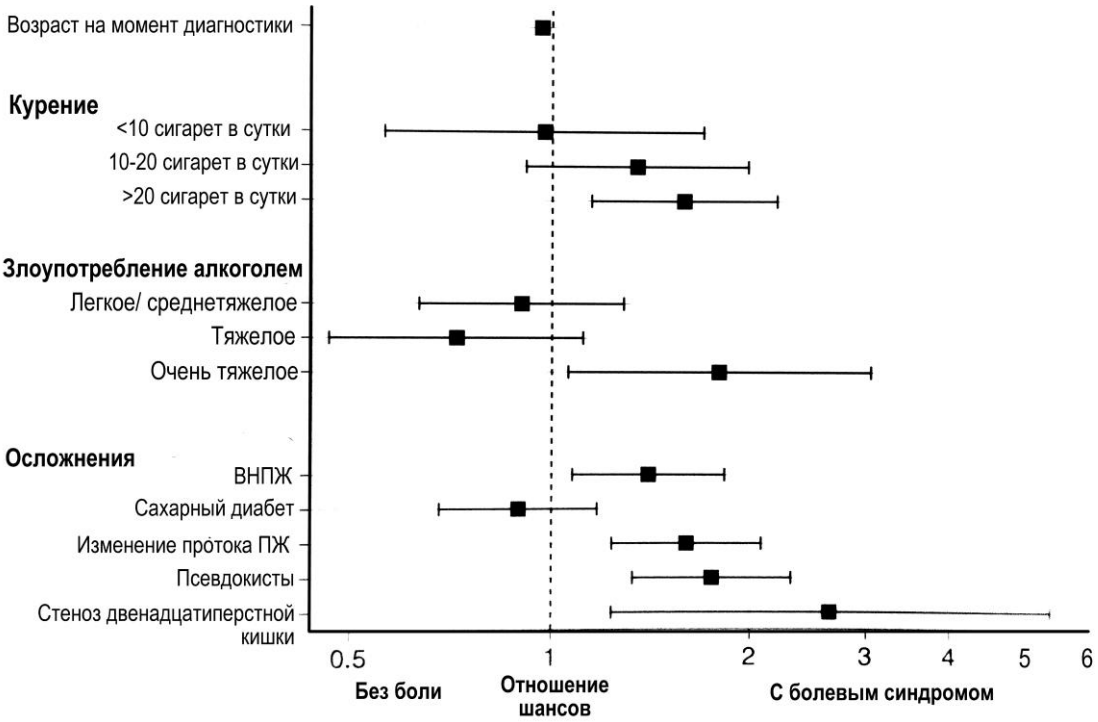


Fig. 12. Diagram reflecting a multivariate regression logistic model of the ratio of factors of absence and presence of pain in CP (according to S. S. Olesen et al., 2019 [1])

The authors found that the appearance of severe abdominal pain in patients with CP should be expected with active smoking of patients (odds ratio, OS 1.6; 95% confidence interval, CI 1.1-2.2; p=0.005), alcohol abuse (OS 1,8; 95% CI 1.1-3.0; p=0.03).

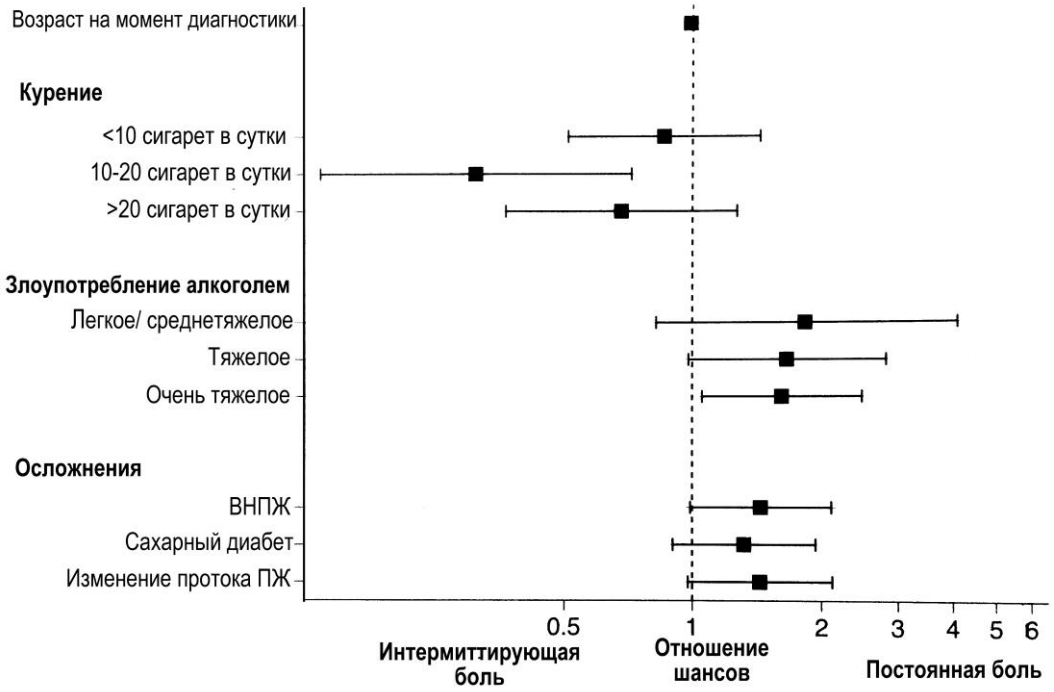


Fig. 13. Diagram reflecting a multivariate regression logistic model of the ratio of the factors of the presence of periodic and constant pain in CP (according to S. S. Olesen et al., 2019 [1])

In addition, a variety of CP complications (duodenal stenosis, pseudocysts, and EPI) were also significant risk factors for pain (in all cases $p \leq 0.01$) (Fig. 12). Interestingly, in most cases smokers experienced periodic pain ($p=0.03$), and alcohol abusers experienced constant pain ($p=0.006$) (Fig. 13).

A number of works was an analysis of the course of CP depending on the presence of concomitant pathology; much attention was paid to the effect of bacterial overgrowth syndrome (BOS) on the course of CP. For example, C. N. Paik et al. (South Korea) studied the incidence of BOS in the small intestine with CP, as well as the effect of BOS on the clinical manifestations of the disease. The design of the one-center prospective study involved the involvement of patients with CP (n=46) and healthy subjects (n=49) who underwent a glucose breath test. The obtained results allowed the authors to name the risk factors for the development of BOS for chronic heart failure: these were residence permit, diabetic neuropathy, the use of opioids or proton pump inhibitors, alcohol abuse, and a history of surgical intervention on the pancreas. A significant difference was found ($p<0.05$) in the incidence of BOS in patients with CP compared with the control group (60.9% vs 26.5%) (Fig. 14).

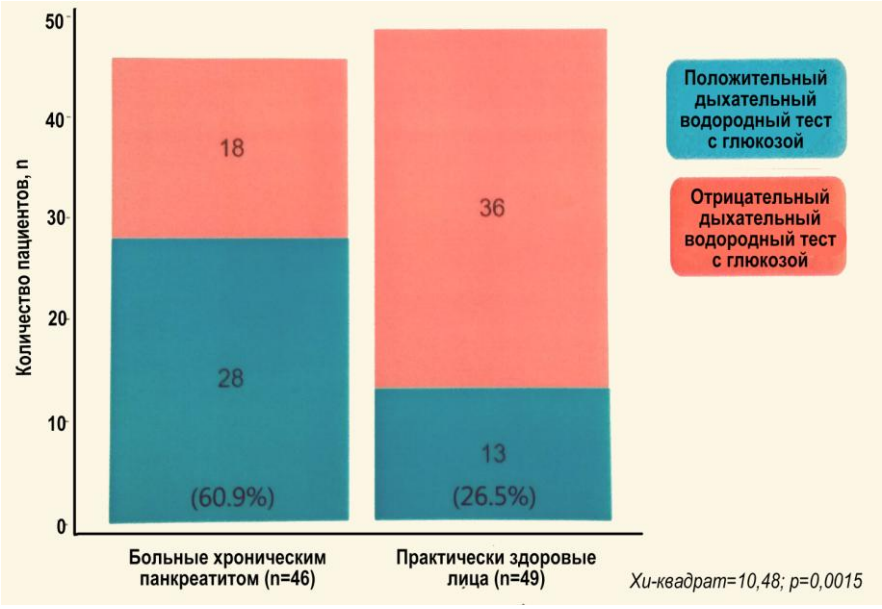


Fig. 14. Frequency of BOS in the small intestine in patients with CP and healthy (according to C. N. Paik et al., 2019 [1])

Researchers noted a tendency toward greater intensity of nausea in patients with BOS (p=0.07) (Fig. 15). Having ascertained the high incidence of BOS during CP, C. N. Paik et al. insist on the need for drug correction of this concomitant pathology, because BOS worsens the effectiveness of enzyme replacement therapy (ERT) and exacerbates (although unreliably) the severity of the clinical manifestations of CP.

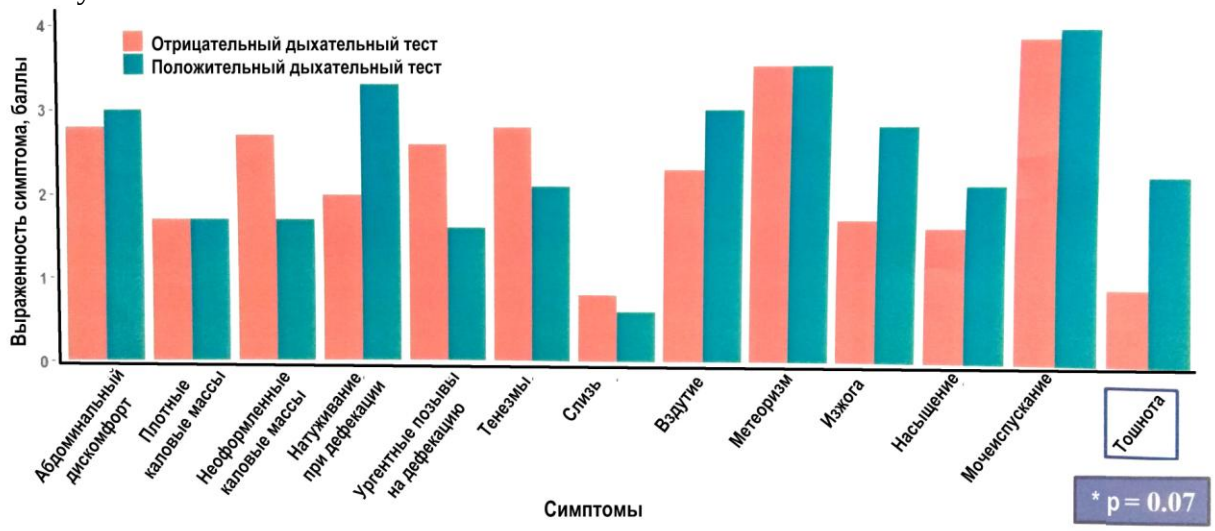
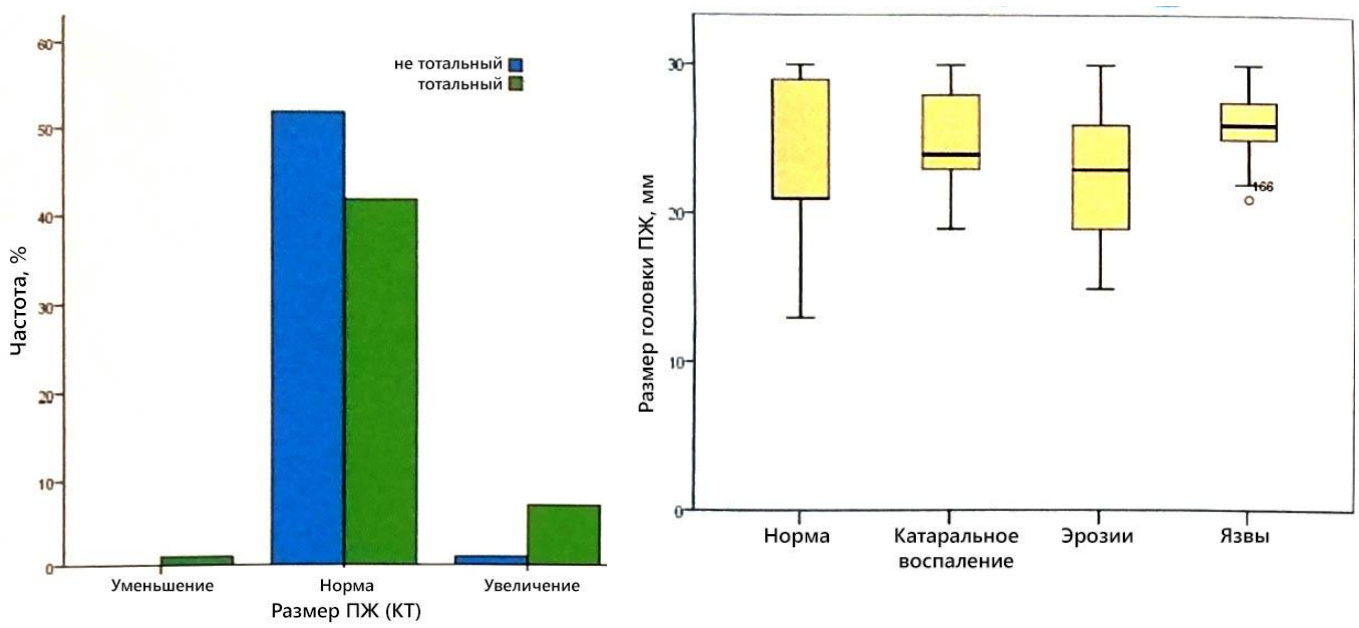


Fig. 15. Severity of clinical manifestations in patients with CP depending on the results of a respiratory test with glucose (according to C. N. Paik et al., 2019 [1])

An interesting retrospective study was conducted by A.V. Okhlobystin et al. (Russia), who analyzed the results of abdominal CT scans in 146 patients with non-ulcerative colitis (NUC). In some patients (n=21; 10.6%), primary sclerosing cholangitis (PSC) was also diagnosed. According to CT results, the presence of concomitant PSC negatively affects the state of the pancreas, causing a change in its size: an increase (n=8; 5.5%) or a decrease (n=7; 4.8%) (Fig. 27). Two patients were diagnosed with pancreatic pseudocysts, while calcifications in the pancreatic tissue were not detected in any patient. Also, CT signs of autoimmune pancreatitis were not detected (characteristic data of imaging research methods, as well as an increase in the level of IgG4 in the blood), including in patients with PSC. The researchers analyzed the frequency of pancreatic size changes depending on the volume (Fig. 16A) and the degree (Fig. 16B) of colon damage.



A B

Fig. 16. Features of pancreatic lesions in NUC (according to A. Okhlobystin et al., 2019 [1]). A – dependence of the size of the pancreas on the extent of the lesion of the colon with NUC; B – pancreatic head size with varying degrees of damage in patients with NUC.

It turned out that a severe course of UC is associated with a significant increase in the level of blood amylase (94.22±28.03 U/l) and urine (616.12±156.88 U/l) compared with the control (respectively, 64.05±2.59 U/l, p=0.027; 313.10±1.06 U/l, p<0.001). Monotherapy with azatiprine or its combination with corticosteroids has been associated with pancreatic edema (increased head size). When taking corticosteroids, an increase in urine amylase activity (but not blood) was more often recorded. Examples of changes in the pancreas and colon mucosa are shown in Fig. 17.

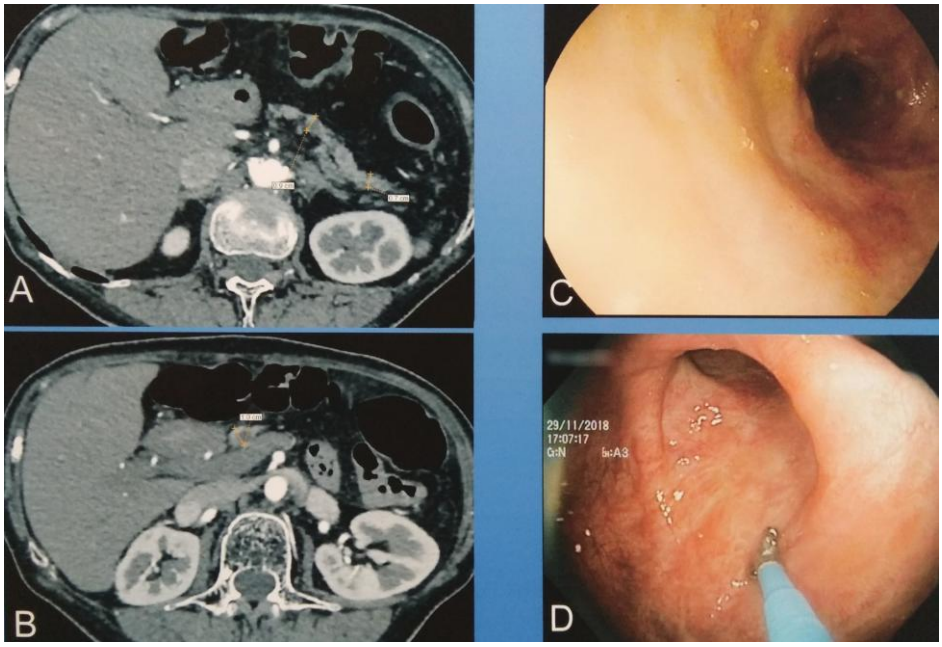


Fig. 17. Examples of pancreatic lesions and the results of colonoscopy in the examined patients with NUC (according to A. Okhlobystin et al., 2019 [1]). A – pancreatic atrophy; B – pseudocyst of the pancreatic head; C – decreased haustration, edema; D – hyperemia, fibrin-coated erosion.

EPI and ERT

The likelihood of EPI was analyzed by scientists from different countries. D. A. Sangnes et al. (Norway) studied the incidence of autonomic diabetic neuropathy in the presence of exocrine pancreatic insufficiency (Fig. 18).

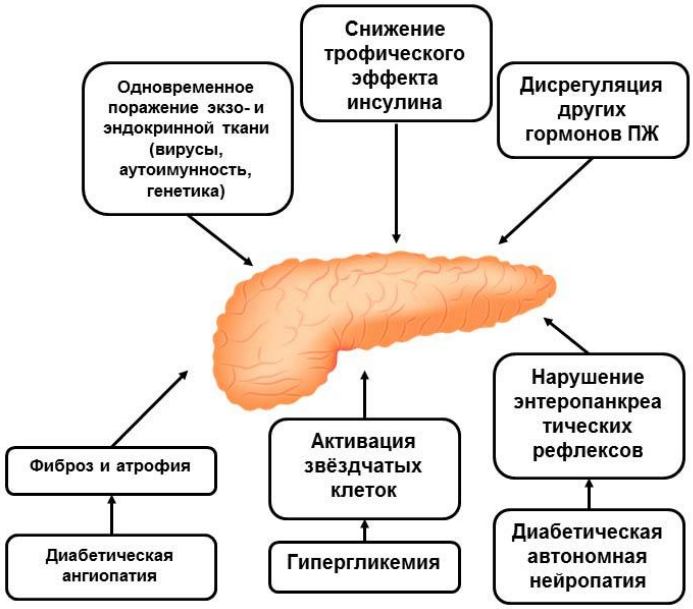


Fig. 18. EPI pathogenesis in diabetes (according to D.A. Sangnes et al., 2019 [1])

Scientists examined 59 patients with CP, 12 (20.3%) of whom were diagnosed with EPI based on the results of fecal elastase test. Assessing the heart rate variability and sensitivity of baroreflexes, the researchers recorded significant changes in these parameters in patients with EPI compared with patients with diabetes and unchanged level of fecal elastase. Based on the data obtained, the authors suggested that the development of residence permit is associated with autonomous diabetic neuropathy.

I. Laitinen et al. (Finland) studied the state of pancreatic exo- and endocrine function in patients undergoing pancreatoduodenectomy (n=21), 2-5 years after surgery. All participants in the study underwent magnetic resonance cholangiopancreatography (MRCP) with secretin, fecal elastase test, glucose, glycosylated hemoglobin level were determined, and quality of life was assessed. After 2-5 years after surgery, MRCP, signs of pancreatic atrophy were determined in 71% of cases, dilatation and/or strictures of the pancreatic duct were recorded with the same frequency. The functional state of the pancreas in the examined patients, whose quality of life remained satisfactory, is shown in Fig. 19.

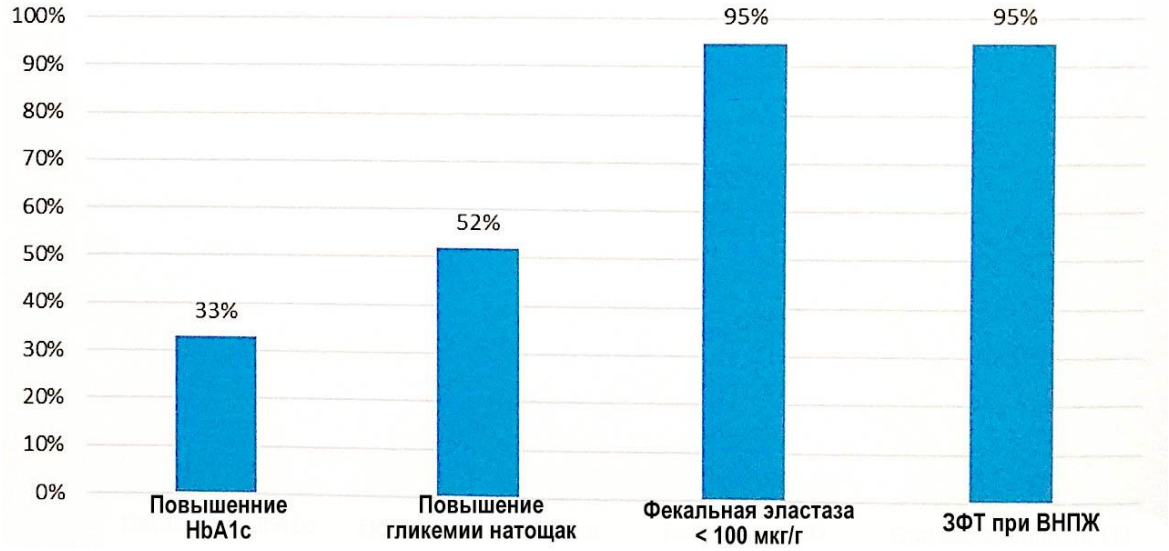


Fig. 19. Indicators of the functional state of the pancreas in patients after pancreatoduodenectomy, 2-5 years after surgery (according to I. Laitinen et al., 2019 [1])

The vast majority of reports delivered at EPC 2019 highlighted the features of drug, surgical and genetic correction of various pancreatic diseases. A. Waage et al. (Norway) analyzed the decision of the multidisciplinary commission of the Oslo hospital on the choice of tactics for treating 169 patients with CP (Fig. 20).

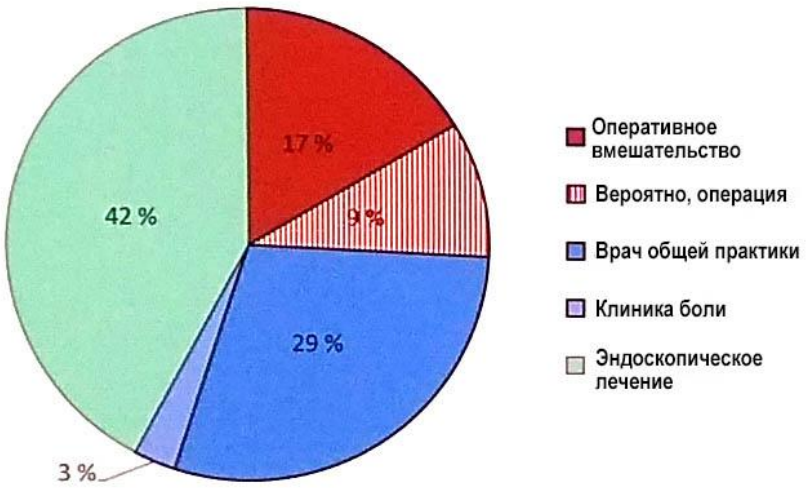


Fig. 20. CP treatment tactics in accordance with the decision of the multidisciplinary commission (Oslo, Norway) (according to A. Waage et al., 2019 [1])

Some patients (42%) recommended endoscopic treatment, 29% received conservative therapy, 17% of patients underwent surgery. After treatment, a significant decrease in intensity or complete leveling of pain was noted in 89% of patients; recorded an improvement in their quality of life.

According to T. Xie et al. (China), which analyzed the characteristics of the course of idiopathic CP (n=1633), the natural evolution of the disease is accompanied by the development of severe steatorrhea (Fig. 21). Therefore, the authors emphasize the need for dynamic monitoring of patients with idiopathic CP and the timely appointment of ERT in order to avoid the occurrence of steatorrhea.

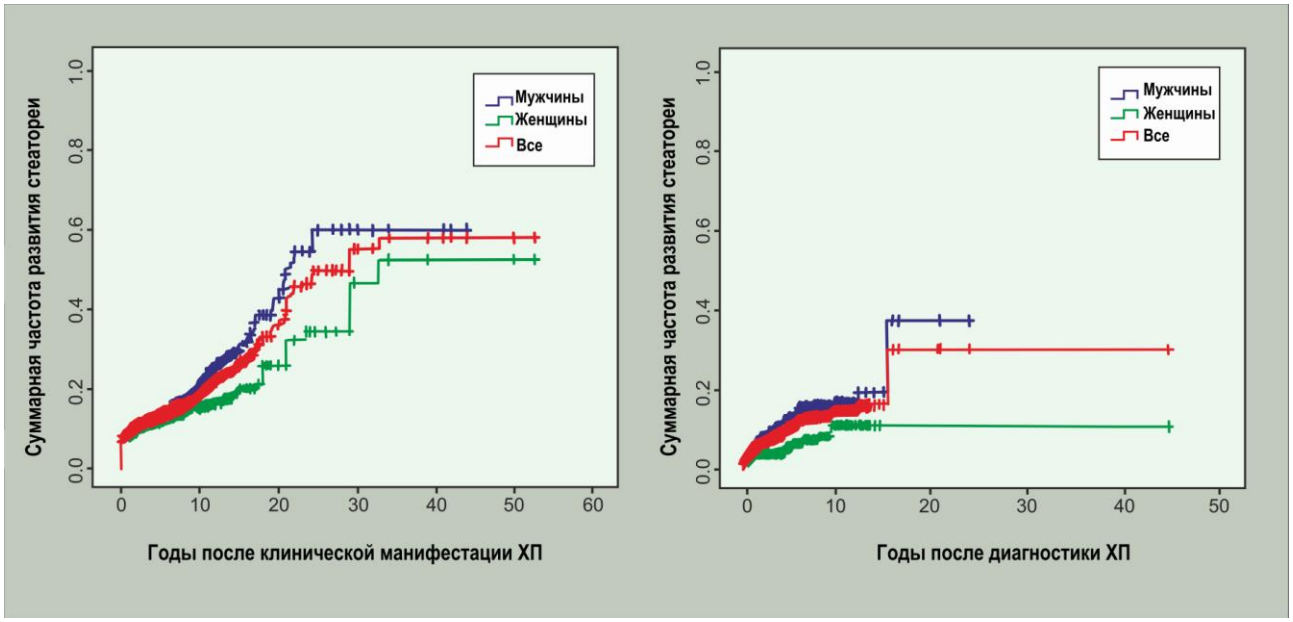


Fig. 21. Total incidence of steatorrhea in idiopathic CP (according to T. Xie et al., 2019 [1])

The need for the appointment of ERT is emphasized by B. D. Vasile et al. (Romania), who examined patients with pancreatic steatosis (n=44) diagnosed during endosonography. A decrease in fecal elastase-1 was recorded in 27.2% of cases, the most characteristic clinical manifestations of the disease were an increase in body mass index, hyperlipidemia. Interestingly, concomitant liver damage in the form of non-alcoholic fatty liver disease was observed in 41.7% of patients with signs of permanent residence, and in 34.4% of patients without permanent residence. The incidence of diabetes and metabolic syndrome with pancreatic steatosis is shown in Fig. 22. Noting that pancreatic steatosis in one third of cases leads to the emergence of EPI, the researchers emphasized the need for the timely appointment of ERT.

Fig. 22. Incidence of diabetes and metabolic syndrome in patients with pancreatic steatosis (according to B. D. Vasile et al., 2019 [1])

Fundamental principles of ERT were revealed in his lecture by prof. J. E. Domingues-Munoz.

First of all, the speaker drew the attention of the participants of EPC 2019 to a high mortality rate of patients with CP, which significantly exceeds that in the general population due to the mortality of patients suffering from CP and EPI (Fig. 23). This fact determines the need for the timely appointment of ERT using the optimal drug in adequate doses.

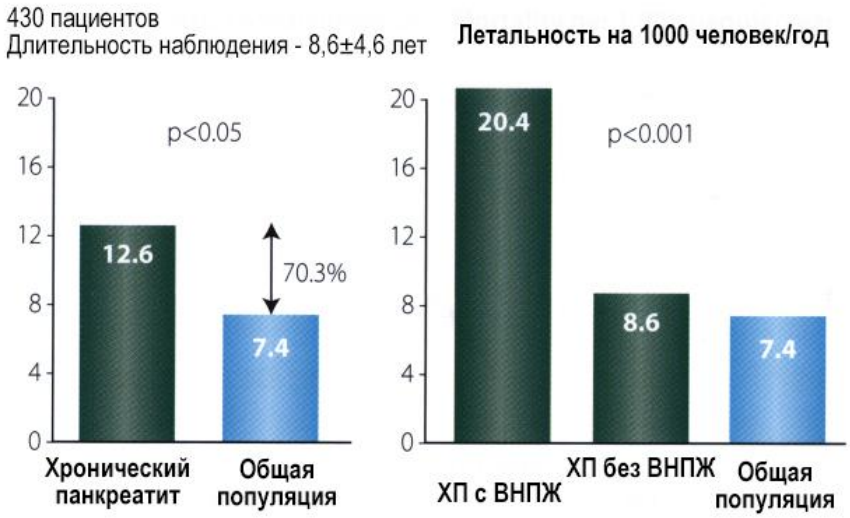


Fig. 23. Mortality of patients with CP with and without residence permit compared with mortality in the general population (according to D. de la Iglesia-Garcia et al., 2018 [3])

Professor J. E. Domingues-Munoz presented the results of a double-blind, randomized, placebo-controlled, multicenter study [4]. As part of this trail, patients with CP (n=62) were prescribed a minimicrospherical enzyme preparation at a dose of 80 thousand FIP with a main meal and 40 thousand FIP with a bite for 51 weeks (Fig. 24, 25).

Fig. 24. Results of a double-blind, randomized, placebo-controlled, multicenter study of the efficacy and safety of a minimicrospherical enzyme preparation for CP: clinical symptoms, body weight, fat and nitrogen absorption coefficients (according to H. Ramesh et al., 2013 [4])

In addition to the results indicated in Fig. 24 and 25, there was a significant decrease in the severity of clinical symptoms, an improvement in overall well-being and quality of life ($p \leq 0.001$).

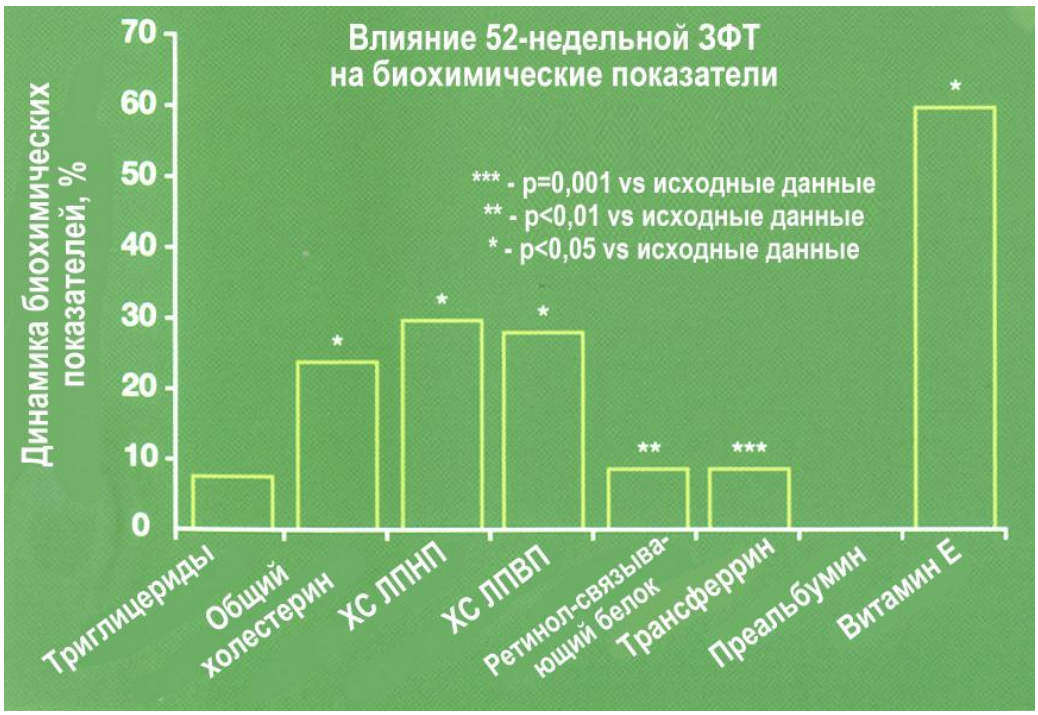


Fig. 25. The results of a double-blind, randomized, placebo-controlled, multicenter study of the efficacy and safety of a minimicrospherical enzyme preparation in CP: biochemical parameters (according to H. Ramesh et al., 2013 [4]). LDL cholesterol — low density lipoprotein cholesterol, HDL cholesterol — high density lipoprotein cholesterol.

Substitution therapy is necessary not only for CP, but also for patients undergoing resection surgery on the pancreas (Fig. 26). As an example, the results of a double-blind, randomized, placebo-controlled multicenter study in parallel groups are presented [5]. Patients who underwent surgery on the pancreas received a minimicrospherical enzyme preparation at a dose of 75 thousand FIP with a main meal and 50 thousand FIP with a bite for 1 week, an open period of 1 year. Good tolerability of the drug, the absence of side effects.

Fig. 26. Results of a parallel double-blind, randomized, placebo-controlled multicenter study of the efficacy and safety of a minimicrospherical enzyme preparation in patients undergoing pancreatic surgery (according to C. M. Seiler et al., 2013 [5])

Another multicenter, randomized, double-blind, placebo-controlled study examined the effectiveness of ERT: H. Kim et al. (South Korea) analyzed the effectiveness of high-dose CTF after pancreatoduodenectomy. The study involved patients (n=304) who underwent the indicated surgical intervention. Patients were randomized to the main (n=151) and control groups (n=153). Patients included in the main group received microtableted pancreatin at 36 thousand FIP 3 times/day for 3 months. Representatives of the control group took a placebo for the indicated time. The researchers analyzed the effect of ERT on body weight, the severity of clinical manifestations, the dynamics of nutritional parameters, quality of life before surgery, in the early postoperative period, and also 3 months after surgery. Scientists have recorded a significant increase in body weight and an increase in the level of prealbumin in the blood in patients receiving ERT (Fig. 27, 28).

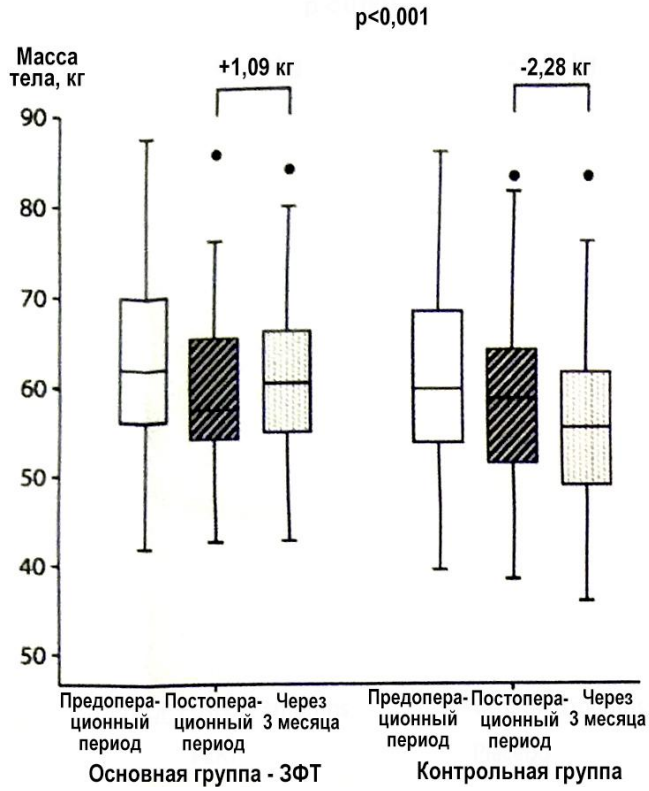
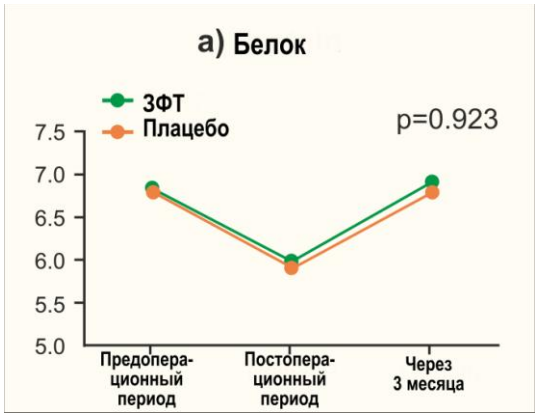
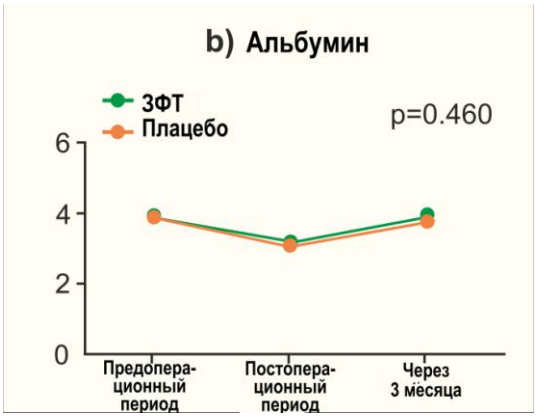
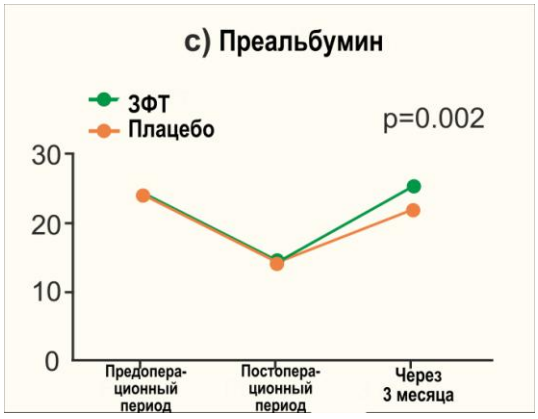


Fig. 27. Dynamics of body weight in patients undergoing pancreatoduodenectomy (according to H. Kim et al., 2019 [1])







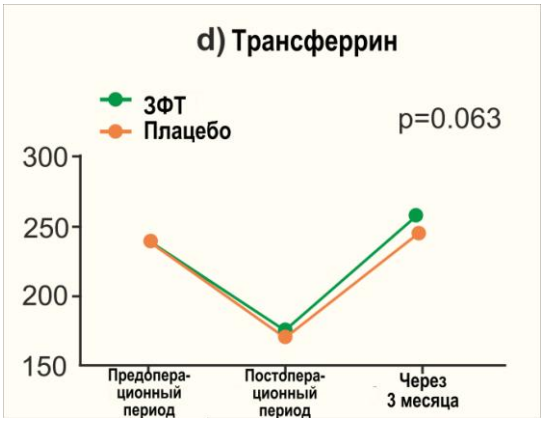
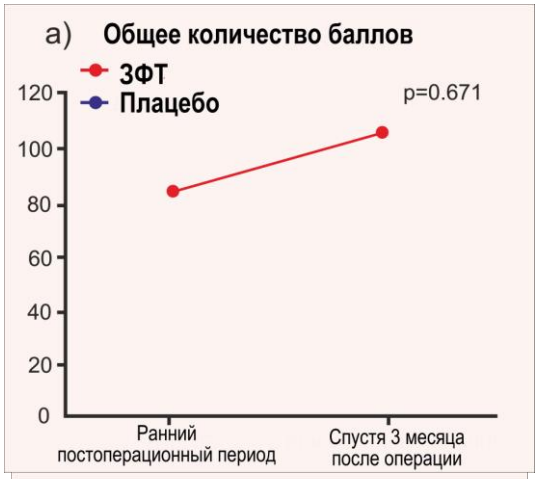
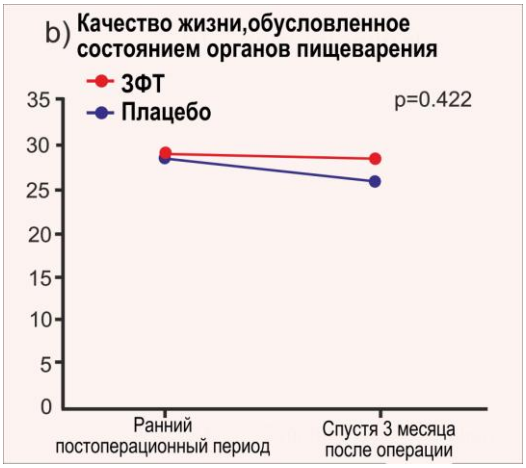
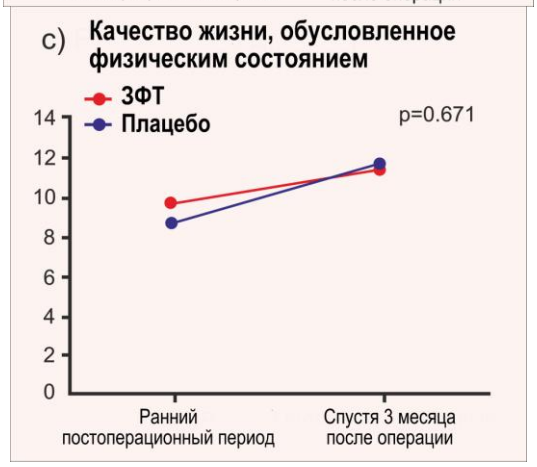


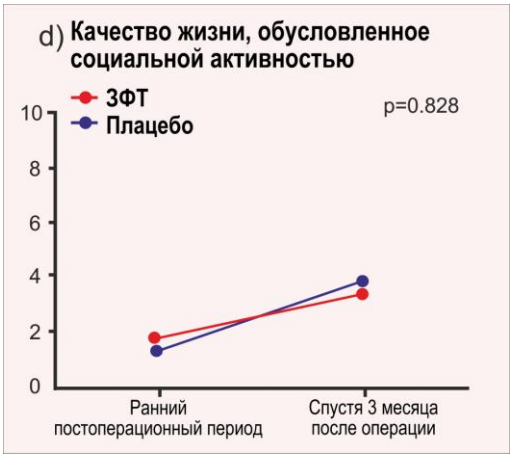
Fig. 28. Dynamics of nutritional parameters in patients after pancreatoduodenectomy (according to H. Kim et al., 2019 [1])

A tendency toward an improvement in the quality of life in patients receiving a microtableted drug was also identified (Fig. 29). Thus, the work carried out under the direction of H. Kim is the first highly proven study to evaluate the effectiveness of ERT in patients after pancreatoduodenectomy. The authors convincingly proved the need for this type of treatment and emphasized the desirability of monitoring nutritional status, improving the education of patients with EPI.









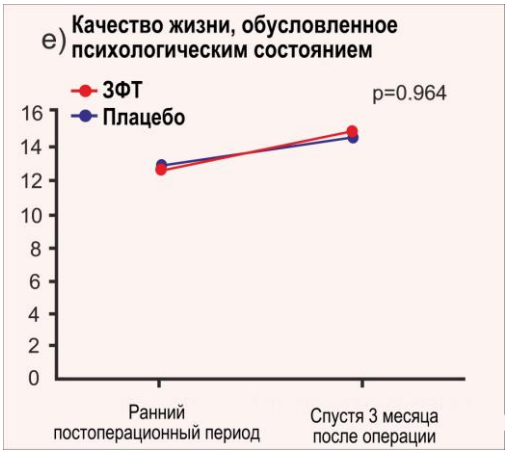


Fig. 29. Dynamics of quality of life in patients undergoing pancreatoduodenectomy on the background of ERT (according to H. Kim et al., 2019 [1])

The presented results of theoretical and experimental scientific research will serve as the basis for expanding conceptual ideas about the formation and progression of pancreatic diseases, the occurrence and course of a wide variety of complications, in particular, EPI, as well as the development and improvement of methods for correcting pancreatic pathology.

Members of the Ukrainian delegation received a lot of new information and adequately presented their achievements. Ahead is a great opportunity to apply the information received. And most importantly — the dates of the European Congress of Pancreatologists in Kyiv have already been determined: June 22–25, 2022. Organization starts now.

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News of European pancreatology
(by materials of the 51st Meeting of the European Pancreatic Club)

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Key words: European Pancreatic Club, Ukrainian Pancreatic Club, progress of pancreatology, diagnostics and treatment of chronic pancreatitis, pancreatic insufficiency

This article presents an overview of the results of practical and basic research in the field of pancreatology, which were presented during the 51st Meeting of the European Pancreatic Club (2019). Achievements of leading European pancreatologists in the study of the etiology, pathogenesis, diagnosis, treatment of pancreatitis, pancreatic tumors are briefly described. The article presents clinical features of acute and chronic pancreatitis, depending on the variety of concomitant pathology, genetic characteristics, bad habits, drugs taken. New opportunities for the differential diagnosis of chronic pancreatitis and pancreatic cancer using miRNA are considered, as well as the feasibility of determining the soluble urokinase-type plasminogen activator receptor (suPAR) in order to differentiate benign and malignant pancreatic tumors. Approaches to the diagnosis of abdominal pain, use of computed tomography for the diagnosis of sarcopenia are described. Results of basic research analyzing the mechanisms of pancreatic cancer development are presented. Modern theory on the role of microbiota and syndrome of bacterial overgrowth in the pancreatic oncogenesis processes is revealed. Pathogenetic features of the formation of exocrine pancreatic insufficiency and effectiveness of its correction via enzyme replacement therapy with the use of modern drugs are emphasized. Results of randomized controlled studies that proved effectiveness and safety of microtablet preparation in correction of exocrine pancreatic insufficiency in patients undergoing pancreatoduodenectomy are presented.