NEWS OF THE WORLD PANCREATOLOGY

(according to the materials of the Joint Meeting of the International Association of Pancreatology and Korean Pancreatobiliary Association, South Korea, Seoul, September 4–7, 2013)

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Key words: pancreatology, pancreatitis, pancreatic cancer, exocrine pancreatic insufficiency, treatment

September 2013 Seoul held a joint meeting of the International Association and the Korean pancreatology pancreatobiliary associations, which were reported by the latest advances in diagnosis and treatment of diseases of the pancreas (pancreas). Our attention was drawn to the results of studies outlined below.

Su Mi Lee et al. (South Corea) reported on the effect of silibinin on cell adenocarcinoma of the pancreas. Experiment shows the cells which were incubated with adenocarcinoma of the pancreas with silibinin isolated from milk thistle has been demonstrated anti-cancer effect, which is to reduce the viability of tumor cells is directly proportional to the concentration of silibinin in the incubation medium
(Fig. 1). The authors suggest that silibinin in the future should be considered as a potential therapeutic agent in cancer of the pancreas.

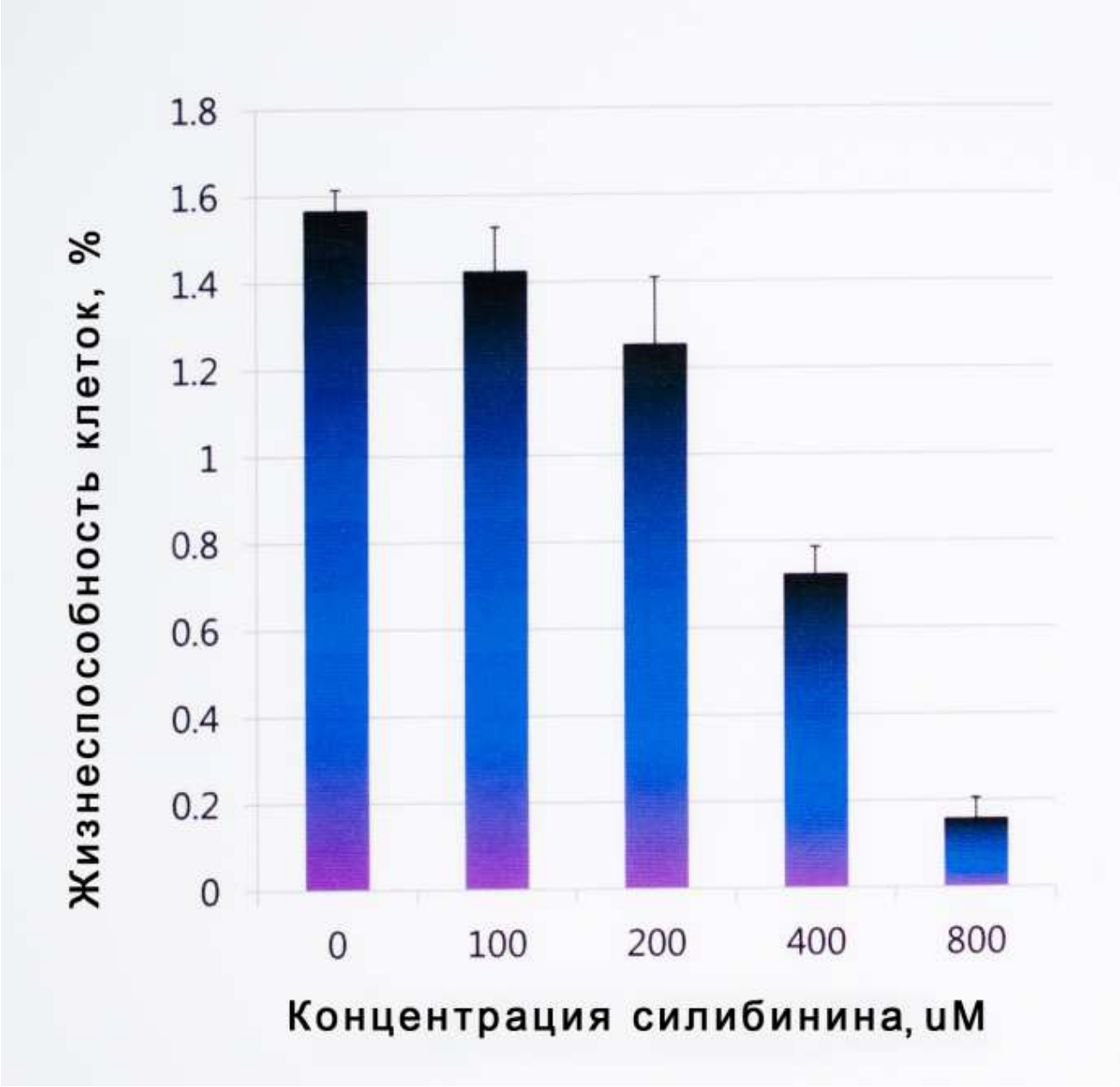

Fig. 1. Dependence of cell viability on the concentration of prostatic adenocarcinoma silibinin in the incubation medium.

Y. Kimura et al. (Japan) examined 197 patients with acute pancreatitis for 6 years. Patients underwent computed tomography (CT) with intravenous contrast. 12 (6.1%) patients in the hospital or after discharge were diagnosed with cancer of pancreas. Half of the patients with cancer of the pancreas were detected by CT extension duct at the stage of admission to hospital with a diagnosis of acute pancreatitis. The authors noted that the rate of expansion of the flow of all patients was 31.5% acute pancreatitis. Patients diagnosed with cancer of the pancreas and later extended duct of all patients

with OA and extended duct amounted to 9.7%. Localization of tumors diagnosed in the hospital — 3 (head): 1 (body): 1 (tail). Localization of tumors diagnosed during follow-up — 4 (head): 1 (body): 2 (tail). The authors concluded that the need vigilance in terms of possible cancer pancreas in patients with acute idiopathic pancreatitis especially. Such patients should be monitored and after discharge from the hospital for at least 2-3 months.

Y. Soo Lee et al. (South Korea) noted that in recent years have often encountered cases of pancreatitis due to helminthic infestation, especially ascariasis. The authors presented the clinical observation of such pancreatitis combined with acute cholangitis and noted that ascariasis in the overwhelming majority of cases, there is this combination. Treatment of these patients is usually endoscopic: it consists in removing papillosphincterotomy followed parasite of cholic and / or pancreatic duct.

M. Del Chiaro et al. (Sweden) evaluated the clinical significance of diagnostic errors in cystic tumors of the pancreas. The authors examined 141 patients, operated on for cystic pancreatic tumors. Histological examination confirmed the preoperative diagnosis in 61% of cases. 13 patients (9.2%), surgical treatment was excessive. Often clinical errors have occurred in serous cystic tumors of the pancreas, more rarely — if intraductal mucosal neoplasia (IPMN (intraductal papillary mucinous neoplasm — intraductal papillary mucinous tumor)) (Fig. 2). This study is of interest in relation to the fact that serous cystic pancreatic tumors have a very low potential for malignancy, whereas IPMN, in contrast, are prone to malignancy. In this regard, improving preoperative diagnosis is crucial.

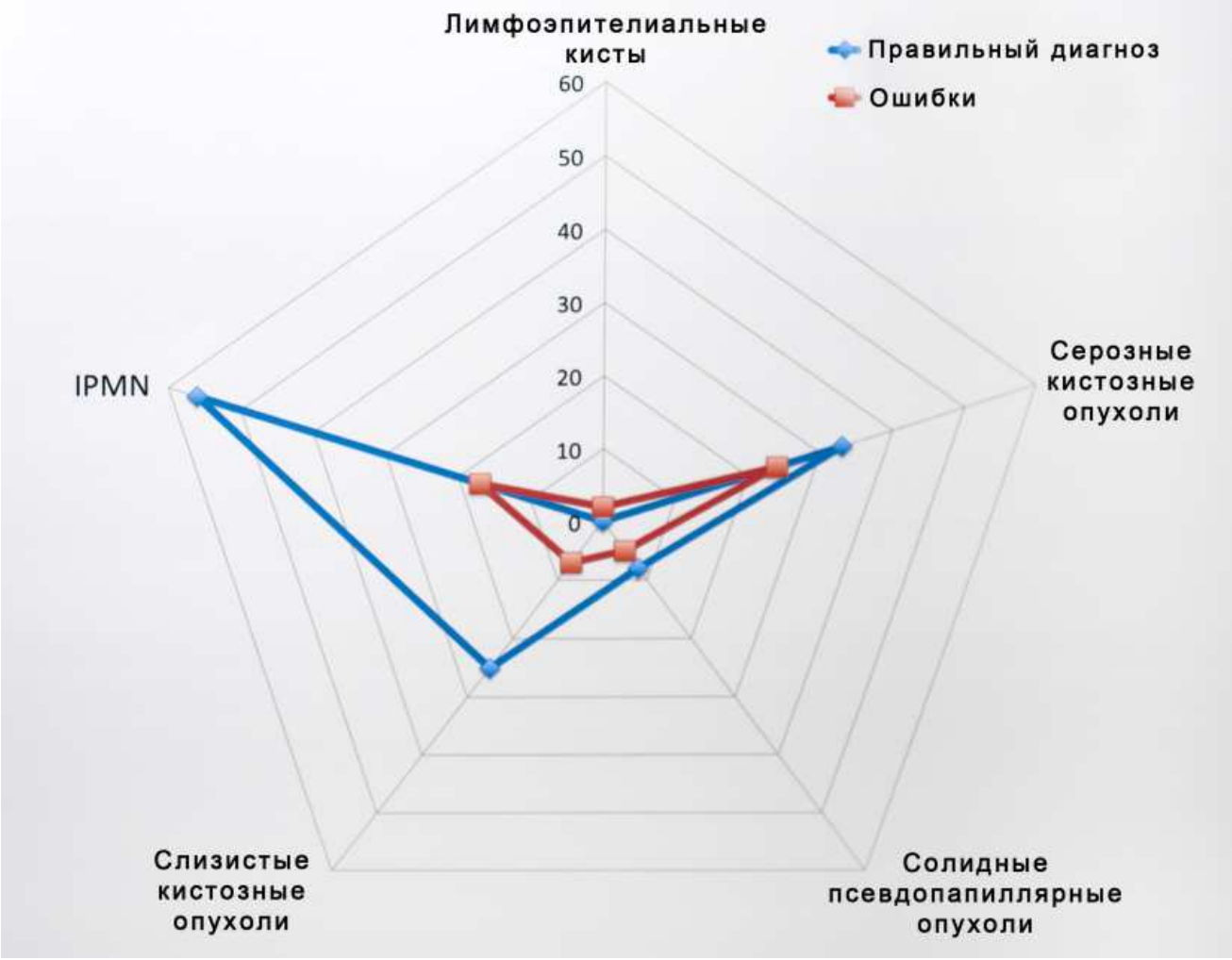

Fig. 2. The frequency of correct and incorrect diagnoses according the histology result of surgical material at cystic pancreatic tumors.

Rare clinical observation of hemangioma RV confirmed by histological examination of the resected portion of the body, presented by T. Shibata et al. (Japan). The patient for five years revealed stable size patchy education in the transition region of the head to the body of the pancreas. During selective angiography tseliakografii and upper mesenteric artery (Fig.3) suspected hemangioma. After surgery, the diagnosis was confirmed.

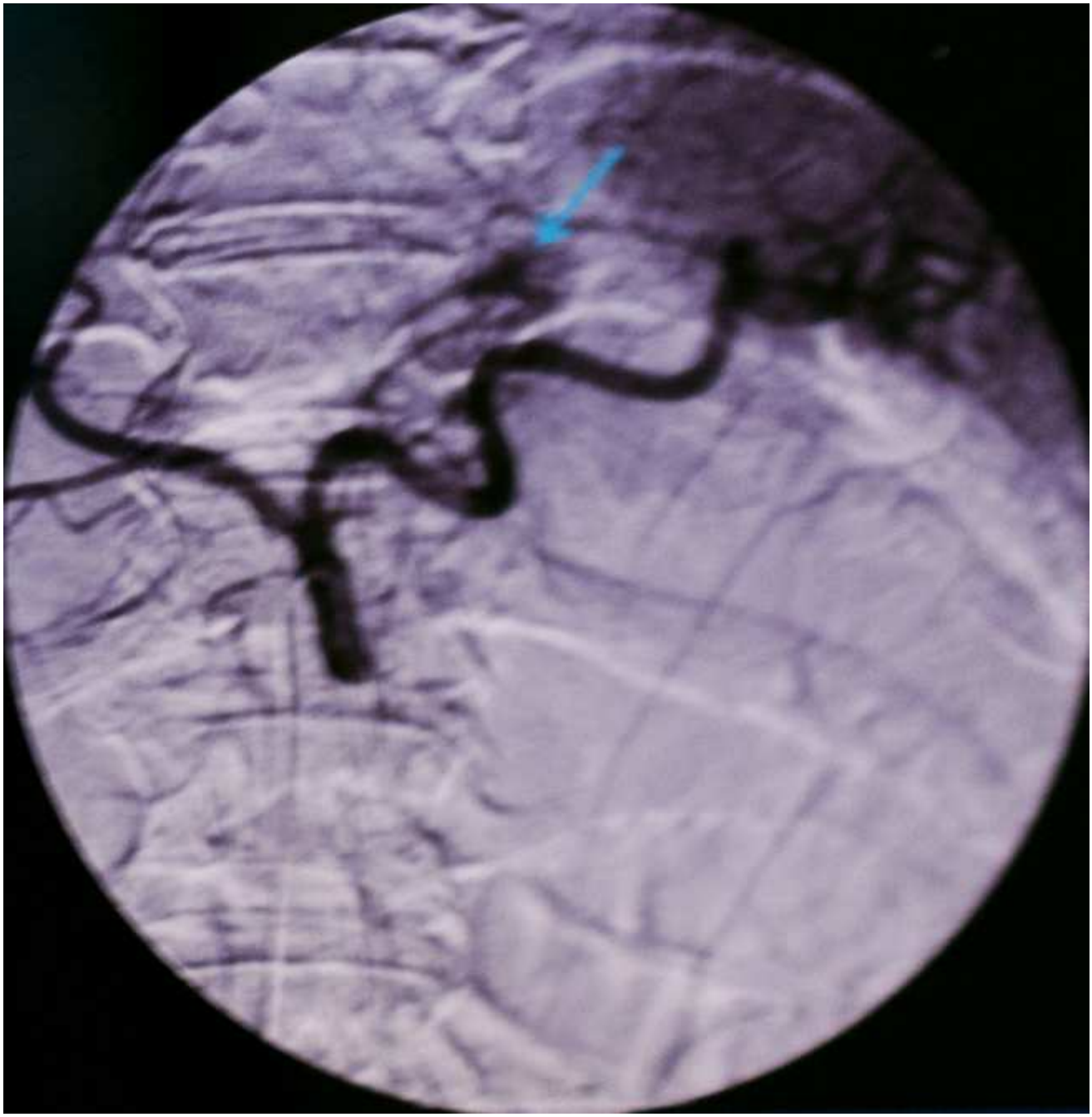

Fig. 3. Selective angiography upper mesenteric artery. The arrow shows the hemangioma of the pancreas.

Of particular interest to members of Congress called Prof. M. Tanaka (Japan) about the current approaches to the diagnosis, classification, treatment IPMN. Also discussed improving international consensus on diagnosis and treatment of IPMN, which is ductal pancreatic tumors with high columnar epithelium containing mucin with papillary growths or without affecting the main pancreatic duct (MD-IPMN) and / or its branches (BD-IPMN). As noted above, IPMN has a high risk of malignancy, especially

MD-IPMN. Deciding on the tactics of observation and treatment must be taken into account the degree of dysplasia of ductal epithelium, which may be low, high (cancer in citu), up to invasive cancer. In addition, you should consider the types of dysplasia: gastric type (light / low degree of atypia), intestinal type (moderate or severe / high degree of atypia); pancreatobiliary type (pronounced / high degree of atypia); onkotype (pronounced / high degree of atypia).

With the lecture program on the main provisions of the German consensus on chronic pancreatitis (enzyme therapy and nutrition) made Prof. M. Lerch (Germany). Lecturer highlighted the following basic positions:

- chronic pancreatitis (CP) – is a progressive chronic inflammatory disease of the pancreas characterized by irreversible structural changes that result in developing exocrine and / or endocrine RV failure. Structural changes include patchy fibrosis and diffuse or focal destruction, loss of acinar and islet cells, inflammatory infiltration and prostatic ductal changes;
- typical complications: pseudocyst, pancreatic duct stenosis and duodenal ulcers, malnutrition, chronic pain;
- abdominal pain is often the first symptom;
- CP — a risk factor for cancer of the pancreas;
- CP reduces the duration and quality of life;
- CP main symptoms:
  - pain, steatorrhea, weight loss;
  - pain — recurrent girdle, often associated with low back pain;
  - steatorrhea — excretion of more than 7 grams of fat per day as a result of malabsorption;
  - weight loss — the loss of more than 20% of body weight.

During CPs there are three stages (Fig. 4).

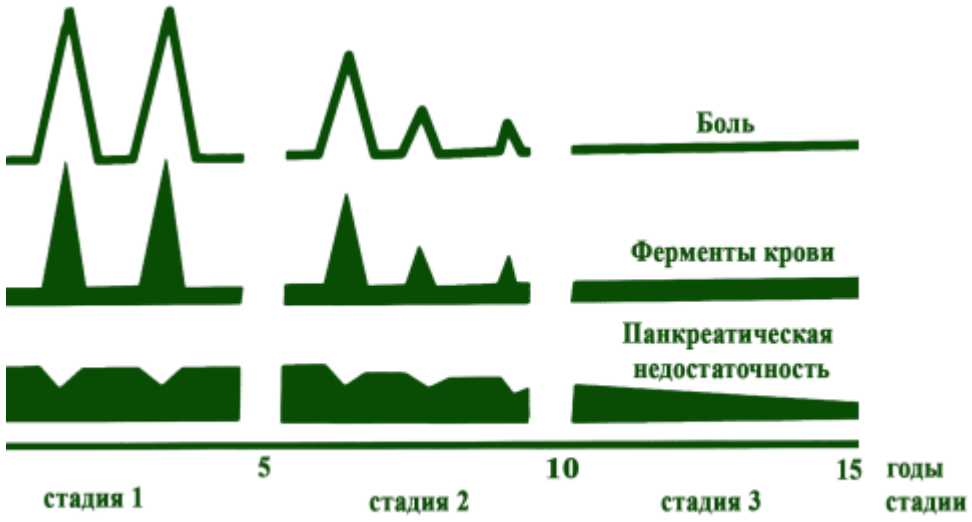

Fig. 4. CP stage flow and dynamics of the main clinical manifestations of the disease.

As a screening method of diagnosis of exocrine pancreatic insufficiency is advisable to use the fecal elastase test. It is relatively inexpensive, simple storage conditions of material, the absence of the need to abolish enzyme preparations prior to the study. It is important that at low rates of fecal elastase-1 steatorrhea occurs (i.e., a test is informative in severe pancreatic insufficiency) (Fig.5), as well as the correlation between the results of this study and the level of vitamin D metabolite in the blood (Fig.6).

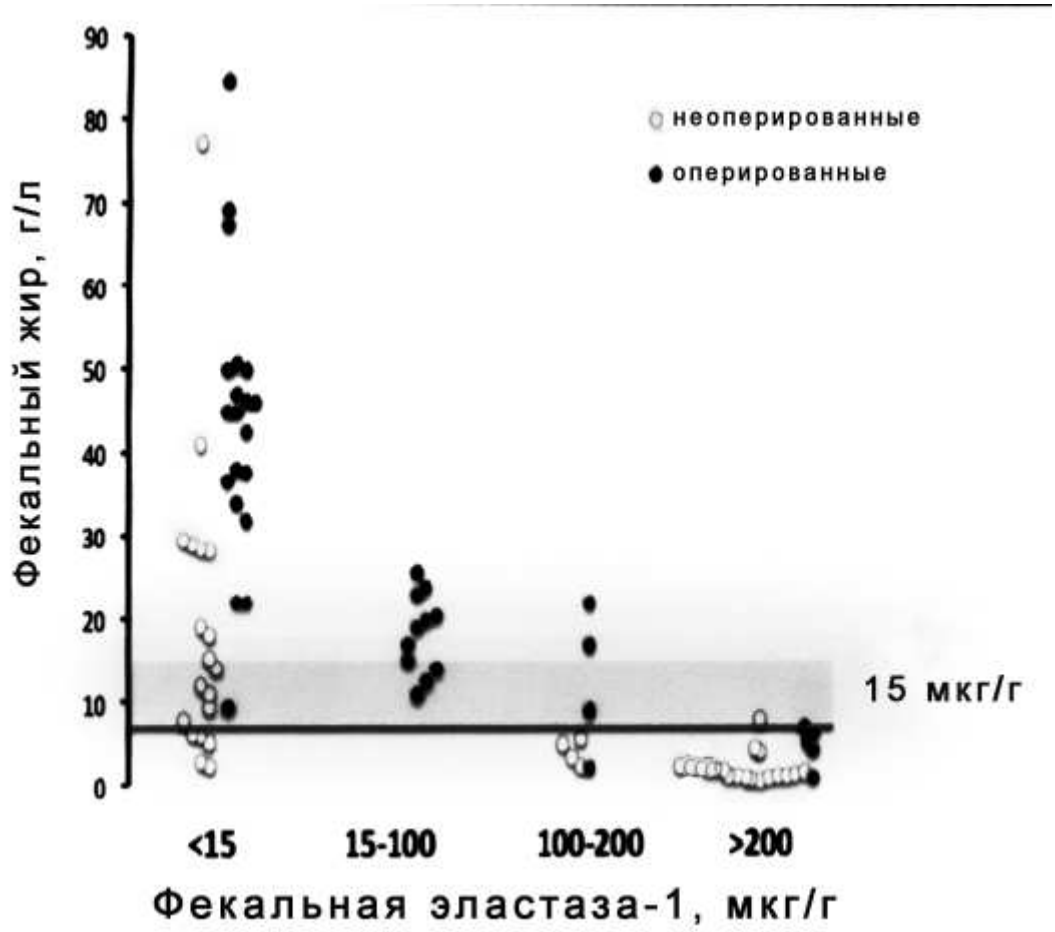

Fig. 5. Relationship between the results of fecal elastase test and steatorrhea in CP.

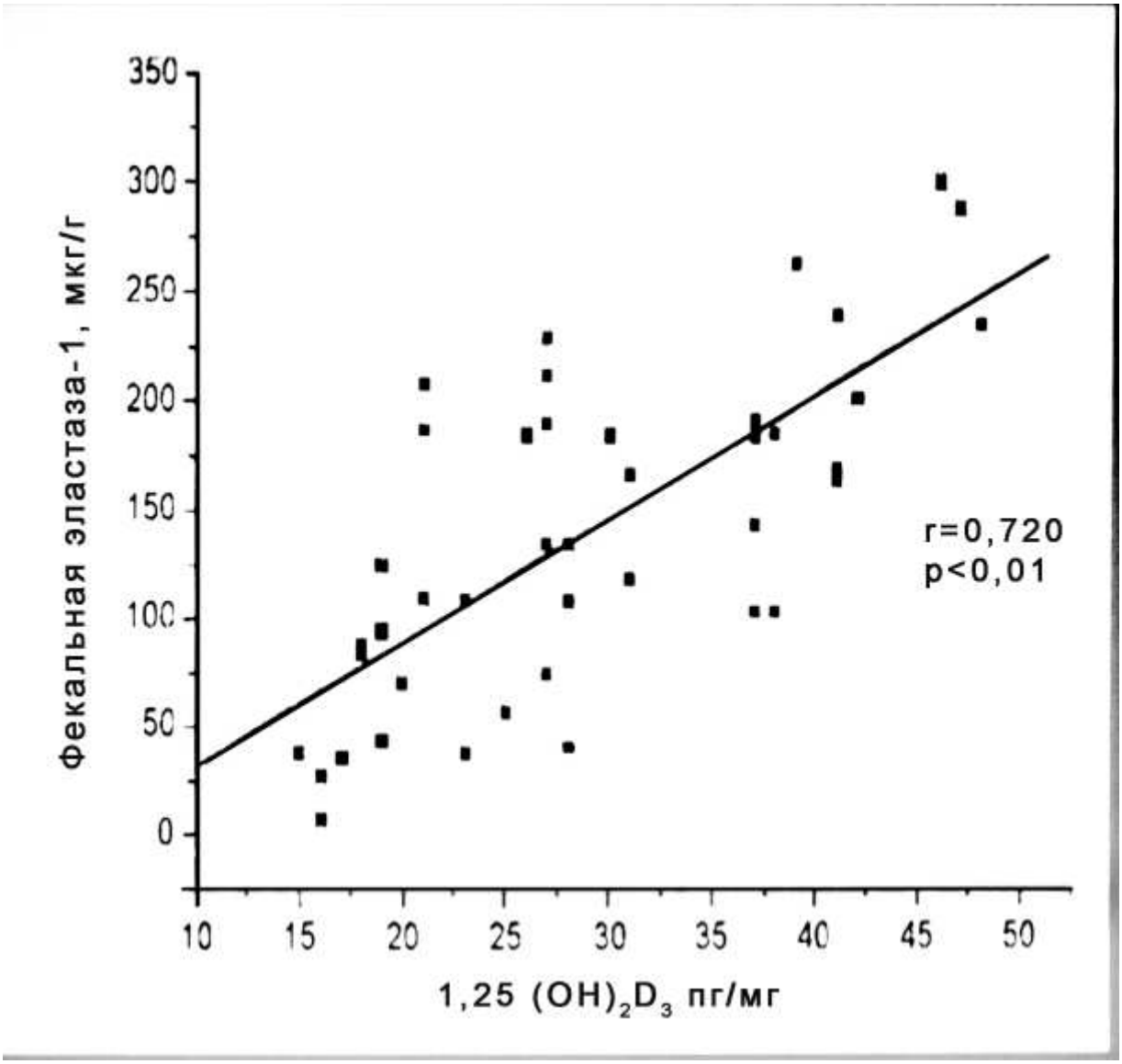

Fig. 6. Relationship between fecal elastase test results and the level of vitamin D metabolite levels in CP.

According to the German consensus, enzymes are appointed in accordance with the lipase activity: the initial dose — 20-40 thousand Ph.U. for the main meal and 10-20 thousand Ph.U. the interim meal, with little effect need to double or triple the dose, with resistance to enzyme replacement therapy should be added to the proton pump inhibitor.

Prof. M. Lerch presented algorithm enzyme replacement therapy formulated in the German Consensus (Fig. 7).

Fig. 7. Algorithm enzyme replacement therapy according to the German consensus.

Particular attention Prof. M. Lerch paid diet, which should be given to patients CP. Main positions of nutrition in CP are as follows:

- patients should receive normal diet provided adequate replacement therapy;
- necessary to compensate for a deficiency of vitamins (A, D, E, K) and micronutrients;
- it is forbidden to recommend reducing the amount of fat compared to the norm;
- it is necessary to eat 4-6 times a day in small portions;
- it is recommended to have a balanced diet with adequate caloric content to suit the tastes of the patient;
- no evidence of the need for appointing a special diet pancreatic.

P. Vijay et al. (USA) hypothesized Lipotoxicity unsaturated fatty acids, which worsens the outcome of ETA in obesity. In the pathogenesis of more severe course of acute pancreatitis in patients with obesity attaches great importance to an imbalance of adipokines, which is a source of visceral fat, as well as adipocytes localized directly into the prostate tissue (Fig. 8). Recently, particular attention is paid to visfatin. However, according to the lecturer, and a great role Lipotoxicity unsaturated fatty acids (Fig. 9).

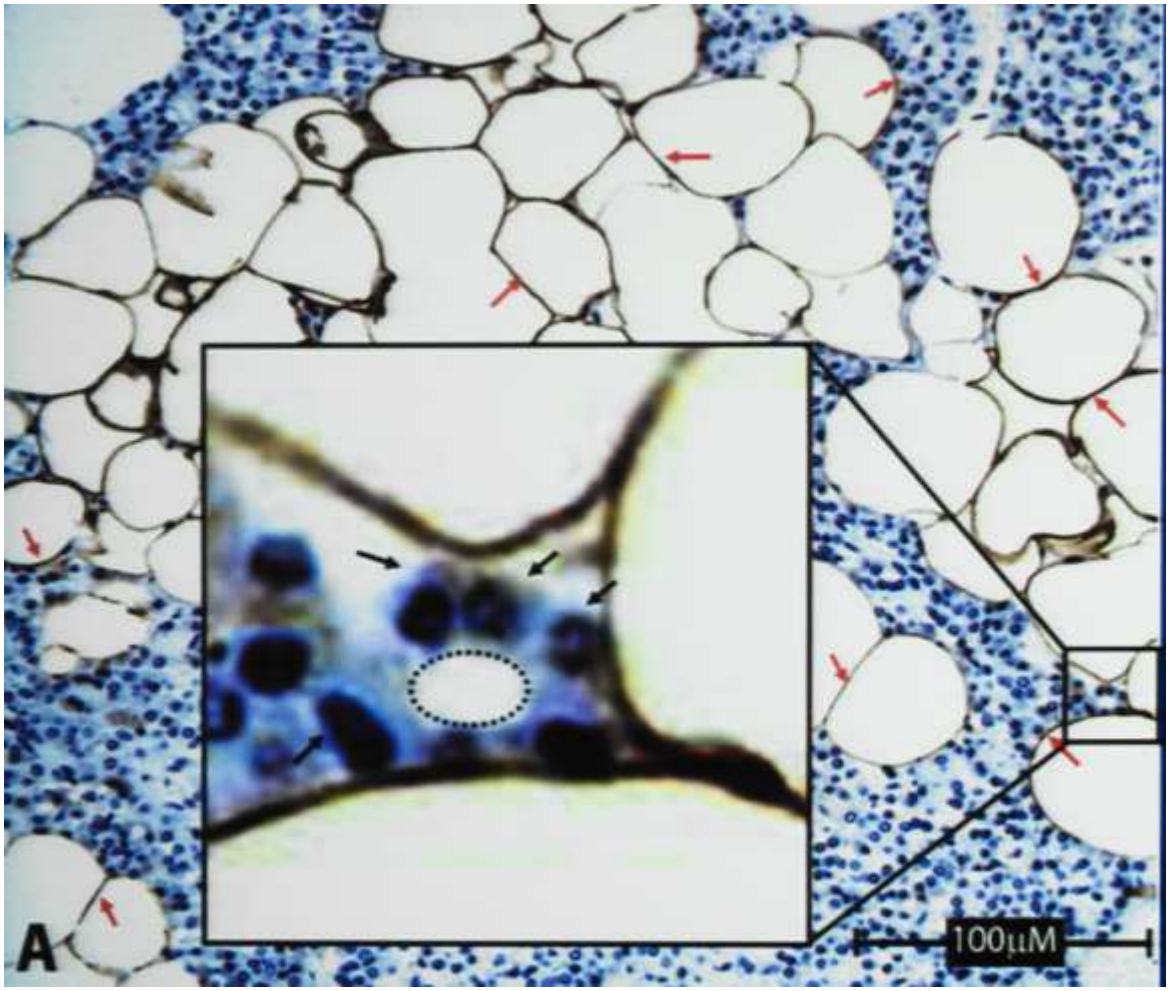

Fig. 8. Adipocytes in the pancreas (painting on adipocyte marker perilipin).

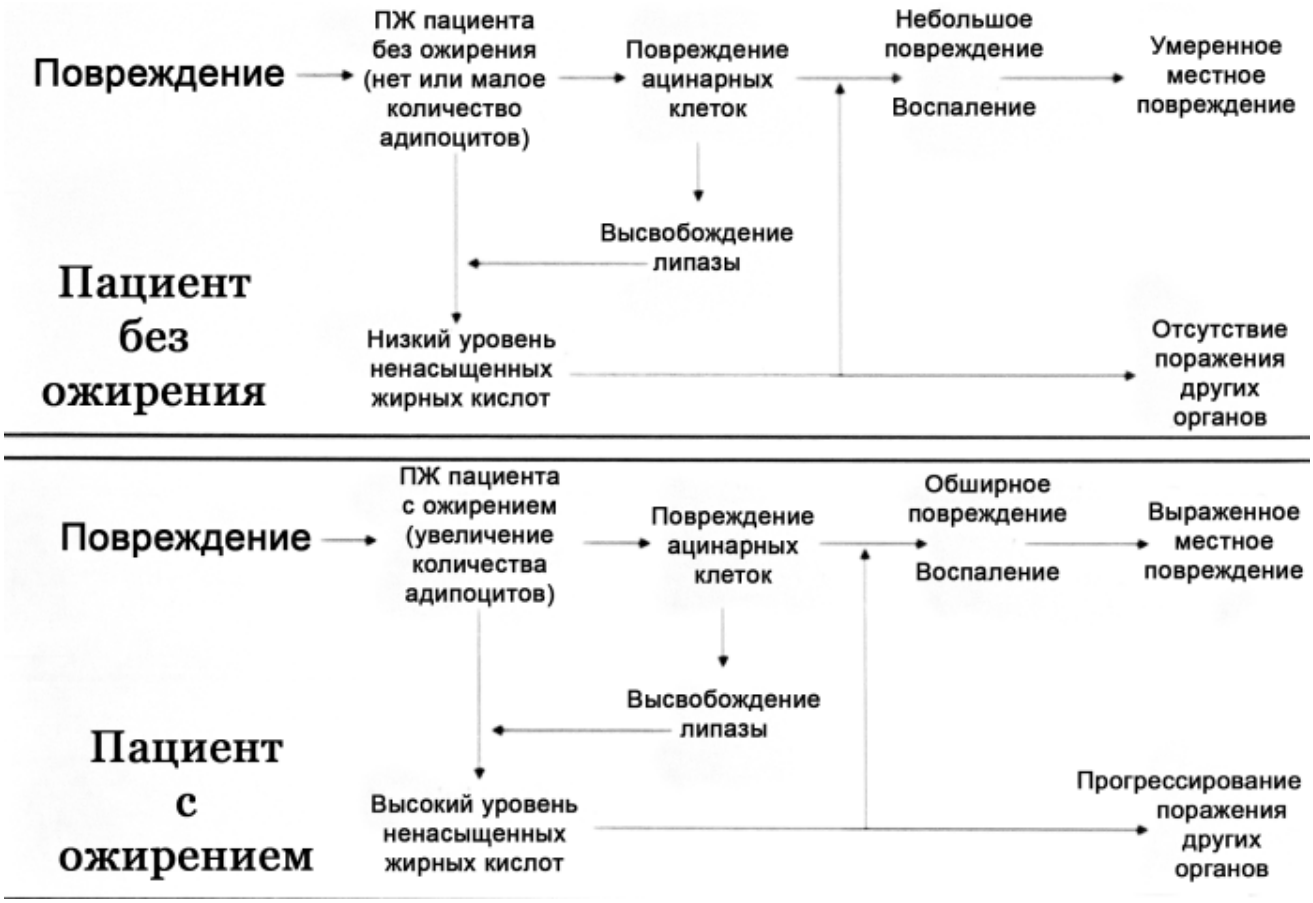

Fig. 9. Hypothesis Lipotoxicity role of unsaturated fatty acids in the deterioration of the outcome of acute pancreatitis in obesity.

N. J. Zyromski (USA) spoke about the current understanding of the significance of pancreatic fat in the development and progression of prostatic adenocarcinoma and put forward his own hypothesis (Fig. 10).

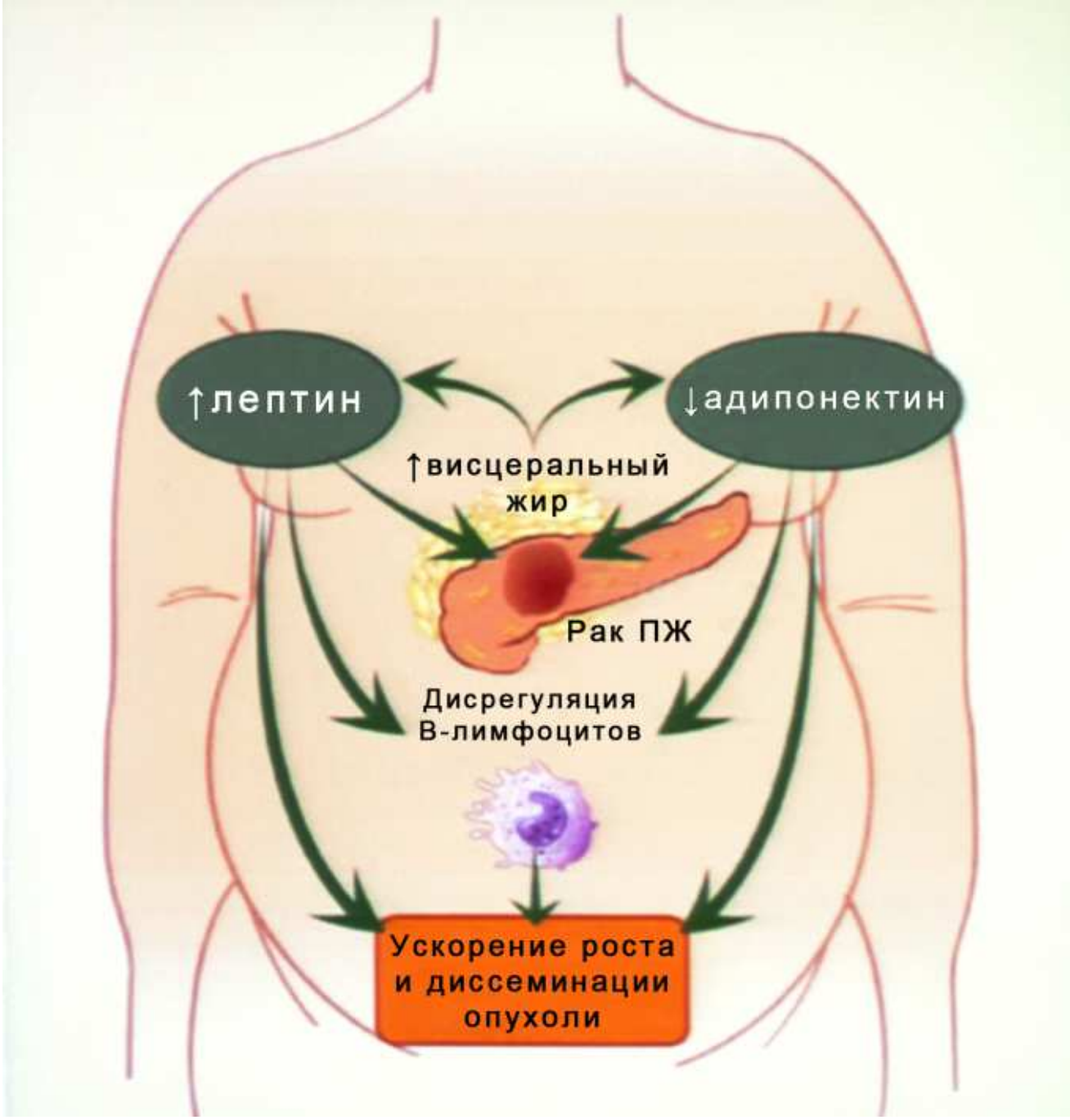

Fig. 10. Hypothesis values of pancreatic fat in the development and progression of prostatic adenocarcinoma.

Interest of the Congress was the report of K. Furukawa (Japan) on the effects of perioperative immune power after pancreato duodenektomia.

The author conducted a study of the effectiveness of a mixture of Impact, which includes: arginine (stimulation of repair and immunomodulation) RNA (purine and pyrimidine source for modulation of immunity); omega-3 fatty acids (stimulation of immune suppression of the stress response).

Following conclusions were drawn that preoperative and postoperative immune power:

- improves the results of surgical treatment;
- reduces the risk of postoperative complications and their severity;
- reduces the incidence of bacterial complications and cost of treatment;
- has immunometabolic action;
- reduces the risk of postoperative immunosuppression stressful.

I was deeply honored and charged lecture on enzyme replacement therapy in patients who had undergone surgery on the pancreas and other digestive organs. Pathophysiological changes after pancreatic resection are as follows:

- Changes in gastric physiology
  - violation of fundic relaxation due to the disappearance antrofundalnogo and duodeno-fundic reflexes;
  - disturbance of nervous stimulation of pancreatic secretion due to lack of fundic relaxation.
- Changes of duodenum physiology
  - reduction of cholecystokinin stimulation of pancreatic secretion;
  - secondary violations due to resection of the duodenum.
- Changes of RV physiology
  - pancreatectomy and its underlying disease lead to reduced secretion;
  - violations related to changes in the relationship with the stomach and duodenum.
- Eating Disorders
  - changes topographical relationships lead to asynchrony between gastric emptying and secretion of bile, pancreatic juice;
  - after gastrectomy large and indigestible particles enter into the lumen of the jejunum.

As a result of the pathophysiological mechanisms, maldigestion after pancreatic resection and / or stomach develops in 80% of cases. Much less is it formed after duodenum-preserving resection of the prostate. Noteworthy is the high risk of

pathological fractures, especially hip fractures not only after resection of the prostate, but after gastrectomy. After gastrectomy Billroth I Low risk of pancreatic insufficiency, because duodenal passage is not changed. After gastrectomy Billroth II risk of pancreatic insufficiency high — 64-70% ("blind loop", the lack of cholecystokinin stimulation).

I also reported on the outcome of the North European research "enzyme replacement therapy for exocrine pancreatic insufficiency", conducted by E. Sikkens et al. (The Netherlands). It is clear that the main treatment of exocrine pancreatic insufficiency — enzyme preparations. What complicates this treatment?

– Time dosing is different.
– Variety of patients: residual function of the pancreas, the amount received dietary fat, various doses of fermant drugs.
– No practical recommendations.

The purpose of the North European: To evaluate the adequacy of the treatment of patients with exocrine pancreatic insufficiency in the Netherlands and Germany.

Methods: anonymous survey of the Danish and the German Association of patients with pathology of the prostate.

Questions: receiving enzyme preparations, dietary counseling, dietary restrictions, clinical manifestations of pancreatic insufficiency.

Included all patients taking enzyme preparations about pancreatic insufficiency. The study included 182 patients: 137 (75%) — CP, 45 (25%) — a cancer of the prostate (before and after surgery). The following results are:

– appeal to a dietitian: CP 25%, 44% of the prostate cancer;
– appeal to a dietitian: 35% of the operated patients, 21% non-operated patients;
– dietary restrictions: CP 67%, 64% of the prostate cancer;
– dietary restrictions: 59% of the operated patients, 71% non-operated patients;
– symptoms of exocrine pancreatic insufficiency: 58% of the operated patients, 57% non-operated patients.

Summaries:

– not enough eliminated symptoms of exocrine pancreatic insufficiency;
– rare reference to a dietitian;

– nutritionist recommendations do not affect the dose of enzyme preparations and meals for patients;

– insufficient dose of enzyme preparations.

Patients do not always follow the doctor's recommendations in relation to the dose of the enzyme preparation.

Patients with postoperative maldigestion, as recommended by Prof. J. E. Domínguez-Muñoz (Spain), it is necessary to assign adequate doses of Creon: 40-50 thousand Ph.U. for the main meal and 20-25 thousand Ph.U for the interim meal.

In my lecture, I also spoke about the results of a double-blind, randomized, placebo-controlled study of S. M. Seiler et al. (Germany), on the effectiveness and safety of pancreatin minimicrospheres 25,000 with exocrine insufficiency after pancreatic resection. In the survey were included 58 patients who were randomized into 2 groups. 32 patients received Creon 25000 3 capsules on main meals (3 times a day) and 2 capsules in the interim meal (3 times a day). The main part of the study was a double-blind phase (7 days) and open phase (51 weeks, during which all patients received Creon). The study was conducted from April 2008 to July 2011 in 17 centers in Bulgaria, Germany, Hungary and Italy. There has been a considerable increase in the absorption coefficient of fat and protein in Kreon group period from the beginning to the end of the double-blind phase, whereas in the placebo group, no significant change in performance was (Fig. 11). Both coefficients remained stable during the open phase. In the open phase achieved a significant decrease in stool frequency (Fig. 12). Treatment was well tolerated, and the incidence of adverse events was low and comparable in both groups.

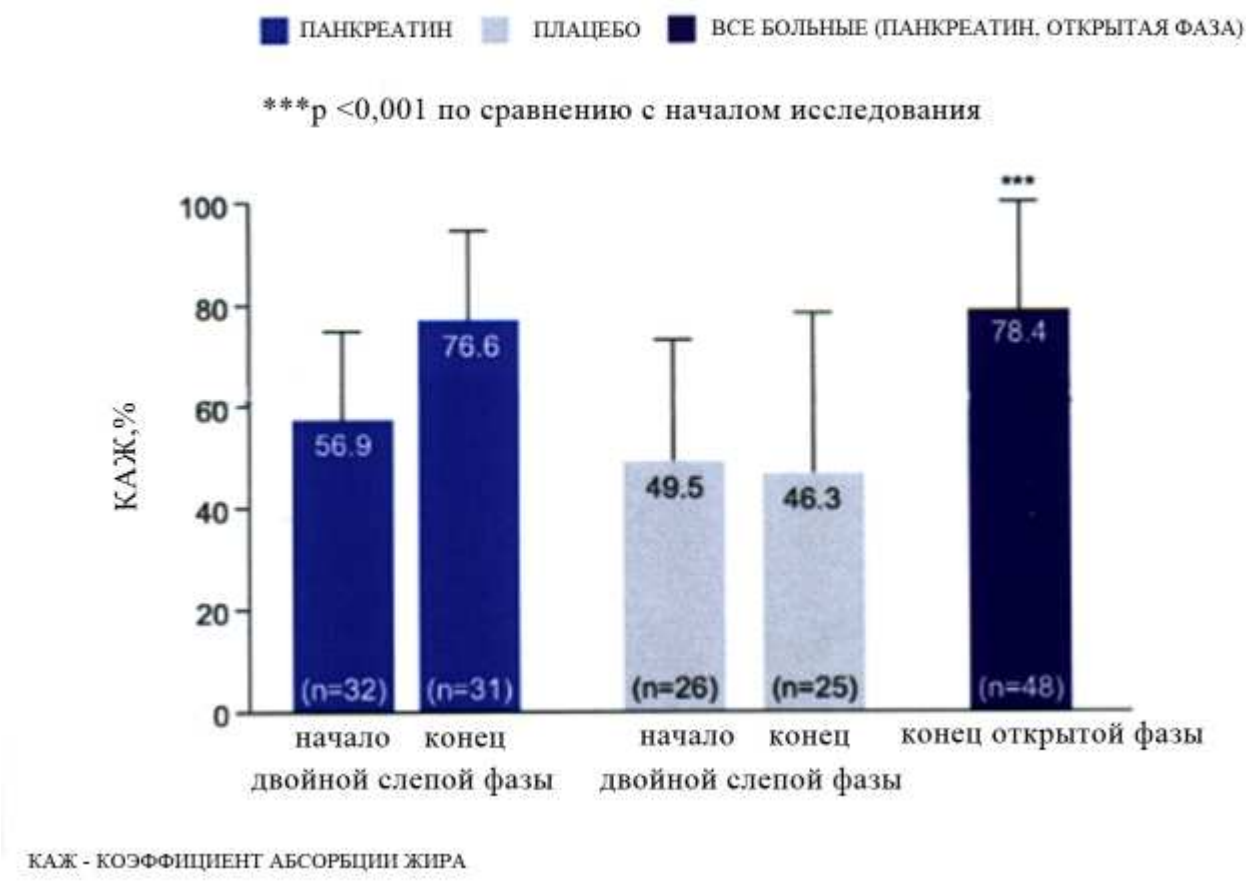

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Fig. 11. Dynamics of fat absorption coefficient.

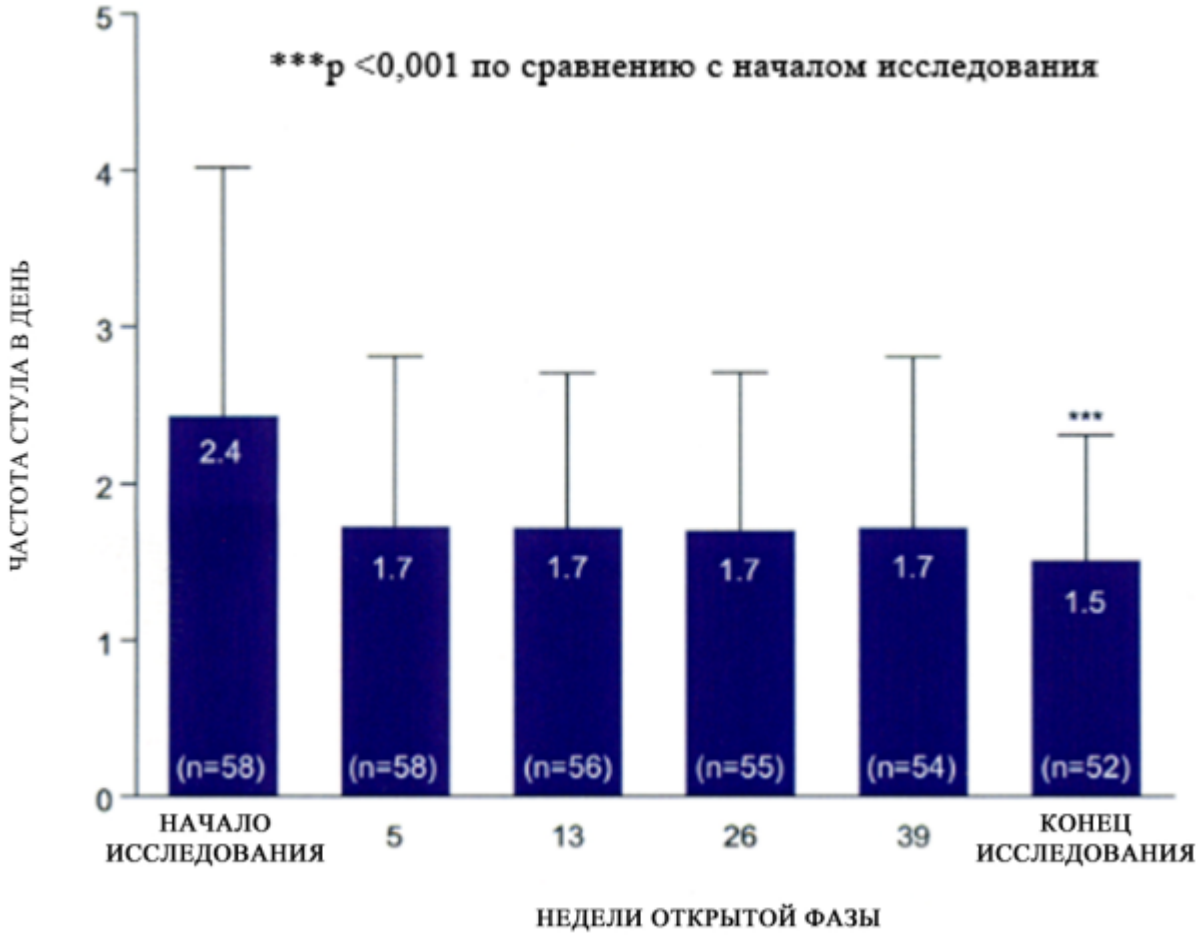

Fig. 12. Dynamics stool frequency.

I completed my lecture with algorithm treatment of exocrine pancreatic insufficiency developed in 2013 by Prof. J. E. Domínguez-Muñoz (Spain) (Fig. 13).

Fig. 13. Treatment algorithm for exocrine pancreatic insufficiency in 2013 (by J. E. Domínguez-Muñoz, 2013). BOS — bacterial overgrowth syndrome.

Of great interest was a symposium on autoimmune pancreatitis, which underwent three complex analysis of clinical cases, four professors were involved in the issue, and all the listeners.

Critical Analysis of "The international consensus on the diagnosis of autoimmune pancreatitis — is there a possibility to optimize?" held by Prof. M. Lerch. He identified the following practical problems in respect of autoimmune pancreatitis (AIP):

- AIP — rare, very rare disease, when patients among non-Asian;
- significantly more common atypical and not classic cases;
- differential diagnosis between focal changes in the prostate cancer and AIP is fuzzy, a course of steroid therapy ex juvantibus 2 weeks;
- new reliable AIP biomarkers are needed;
- relapses are a common, but a relapse does not mean that has been assigned the wrong treatment;
- no agreement on the dose of corticosteroids: in Europe — 1 mg/kg, in Japan — 0.5 mg/kg; unproven benefits of immunosuppressive drugs and biologicals;

- currently there are no reliable laboratory tests for the diagnosis of AIP: Ig G4 and auto antibodies may be normal ® on this basis do not go away from the correct diagnosis;
- for the diagnosis of type II AIP need comprehensive needle biopsy of the prostate under the control of endosonography;
- changes of pancreatic and bile duct at endoscopic retrograde cholangiopancreatography are of little value for the diagnosis; informative magnetic resonance cholangiopancreatography was not specified.

It was discussed practical value of magnetic resonance cholangiopancreatography with secretin administration for diagnosis of pancreatic insufficiency (L. Frulloni, Italy). Currently adopted the following interpretation of the results. 10 minutes after administration of secretin:

- severe pancreatic insufficiency — only filled duodenal bulb;
- moderate pancreatic insufficiency — filling up the lower bending;
- norm — filling in the lower curve.

D. I. Conwell (USA) spoke about the predictive value of functional endoscopic test for diagnosing CP: positive predictive value — 45%, negative predictive value — 97%. D. K. Lee (South Korea) spoke about the reasons for the choice of endoscopic or surgical treatment of ductal strictures and pankreolitiaze. Key summaries:

- endoscopic treatment in the beginning;
- insufficient efficacy of endoscopic treatment — Surgery;
- do not rush to surgery (strategy Step up);
- the possibility of surgical treatment depends on the patient's condition;
- surgical treatment relieves pain for a longer period than endoscopic treatment;
- if necessary, surgical treatment may be the first;
- flexible approach, taking into account all the features of the clinical situation, followed by "balancing".

Separate symposium was devoted to exocrine pancreatic insufficiency. The symposium lecture read Prof. J. E. Domínguez-Muñoz. Particular attention was drawn

to the fact that the higher the frequency of relapses malnutrition CP, as well as admission rates, as evidenced by the results of the study B. S. Sandhu et al. (Fig. 14a, б).

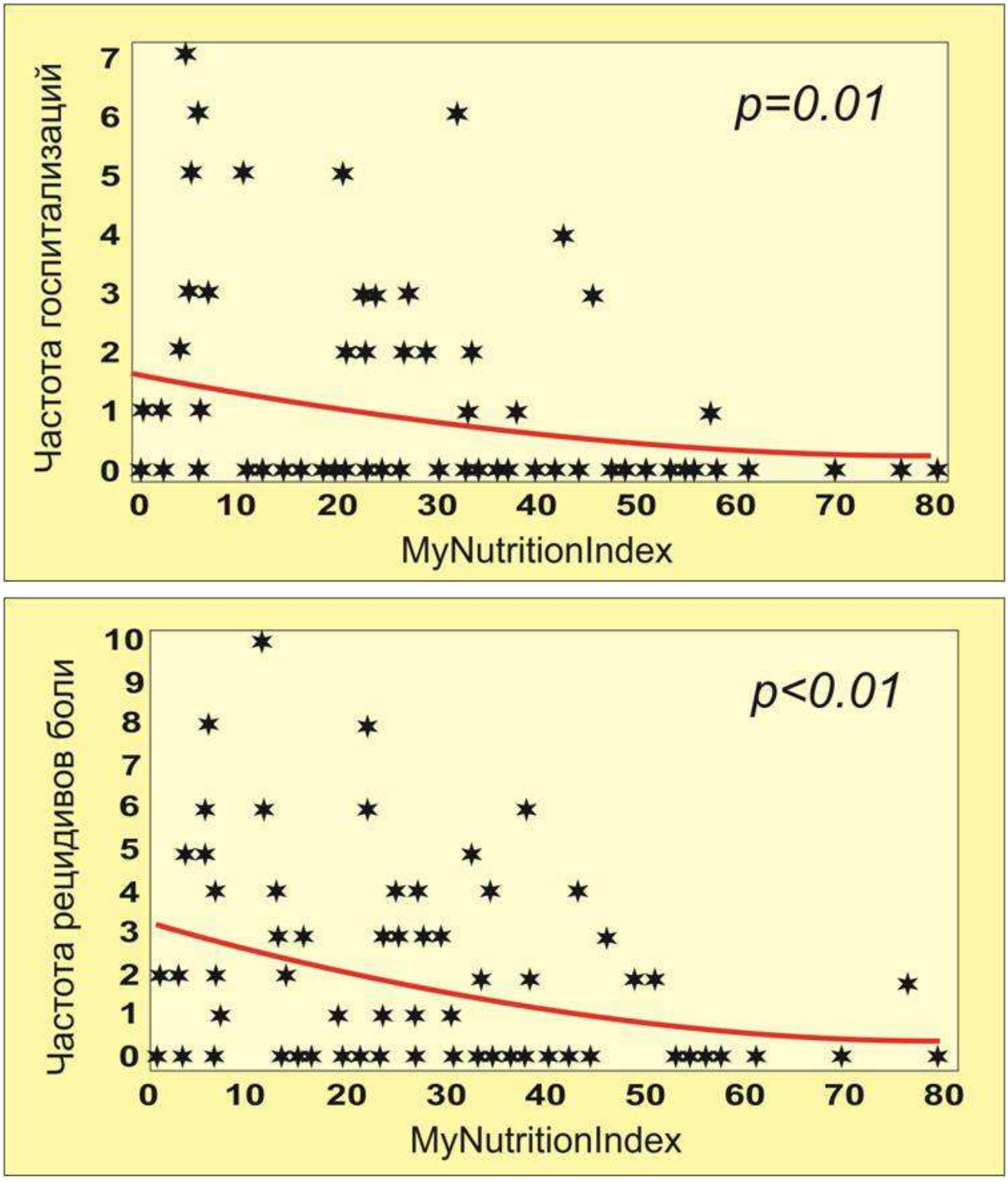

Fig. 14. Malnutrition and dependence index hospitalization (a), and malnutrition index relapse (b).

Indeed, one of the pathogenetic types of pain in patients with CP explained by pancreatic insufficiency (Fig. 15). In such patients, double-shell minimicro spherical enzyme preparations are effective in relieving pain (Creon).

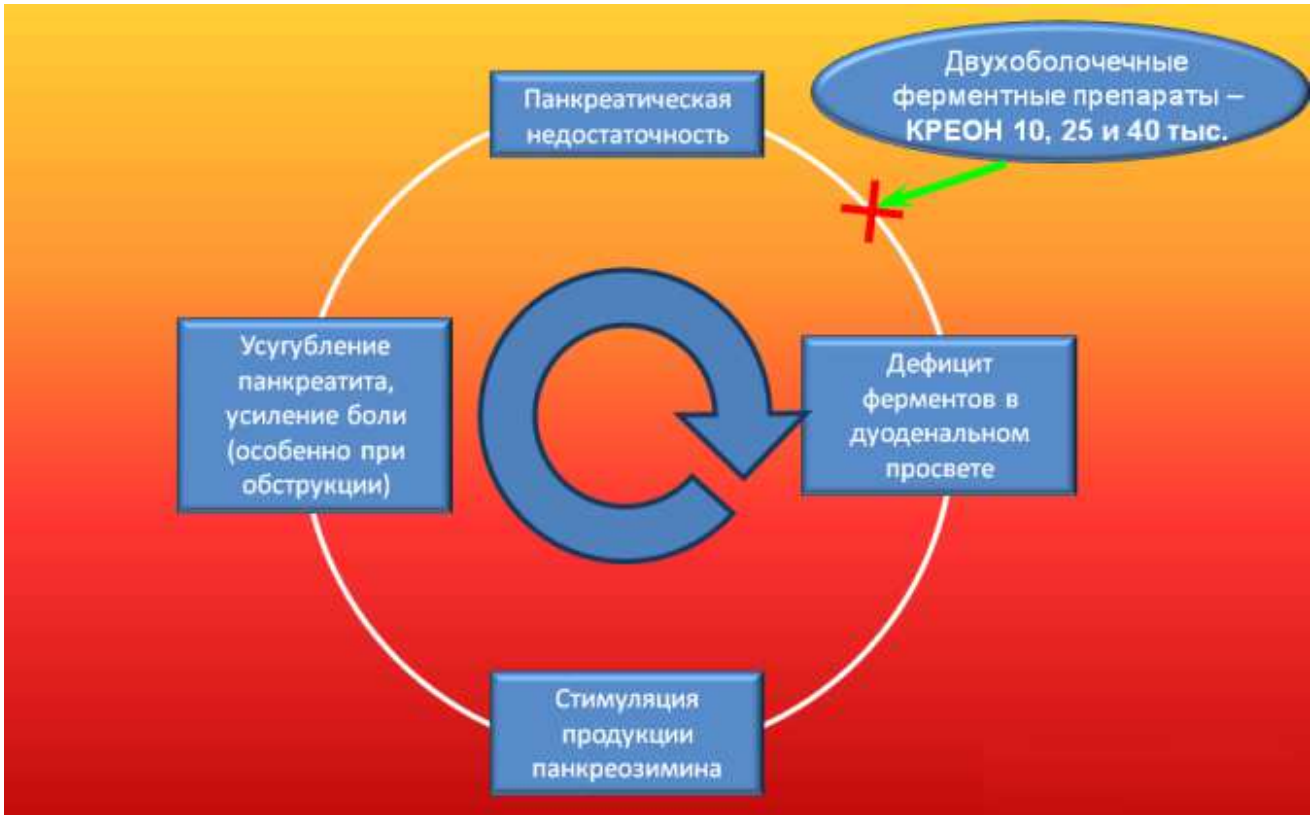

Fig. 15. Pathogenesis of pancreatic pain in CP patients with exocrine pancreatic insufficiency.

The Congress was a meeting of the Council of the International Association pancreatology to discuss the prospects of the Association, including the first steps in organizing a meeting of the European Club pancreatology in Kiev in 2016 already decorated the site of our meeting (epc2016.com), which will be gradually supplemented. We accept suggestions for site clearance with pleasure!

References

Integrated Approaches to the Pancreas: Basic Science and Cutting-edge Practice. — Joint Meeting of the International Association of Pancreatology & the Korean Pancreatobiliary Association, Seoul, Korea, September 4–7. — 2013. — 243 p.

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Article presents an overview of the results of the Joint Meeting of the International Association of Pancreatology and Korean Pancreatobiliary Association, describes the main achievements in the field of diagnosis and treatment of pancreatitis, pancreatic cancer. Particular attention is paid to the treatment of exocrine pancreatic insufficiency, diagnostics of autoimmune pancreatitis, as well as the pathogenesis of pancreatitis in patients with obesity.