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3D MODELING CAPABILITIES IN ASSESSING RESECTABILITY OF PANCREATIC HEAD TUMORS

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INTRODUCTION

Relevance and degree of development of the dissertation research topic

Pancreatic head cancer ranks 6th-7th among oncologic diseases and 4th-5th among causes of mortality, with only 5% of patients achieving a five-year survival rate [3, 15, 173, 177]. The reasons for unsatisfactory treatment results include, first of all, late diagnosis of the disease. According to pathologoanatomic autopsy data, 10% of patients with an unidentified lifetime source of peritoneal carcinomatosis suffered from pancreatic cancer [174].

Surgical treatment is possible in only 20% of patients in whom the tumor is preoperatively recognized as resectable (T1-2 N0-1 M0). According to the literature, surgical treatment is recommended at the first stage; more than 80% of patients relapse within the first year after surgery, and the median survival rate is 8.9-19 months [6, 16, 181, 192]. In palliative chemotherapy, the clinical response to treatment reaches 20-36.7%, with a median survival of 5.1-10.1 months [24, 192].

The initial detection as well as the determination of resectability in pancreatic head cancer depends on radiation methods, including ultrasound, computed tomography and magnetic resonance imaging. The diagnostic value of these methods in recognizing pancreaticoduodenal masses is: MRI sensitivity 90.2%, accuracy 87.8%; MSCT sensitivity 89.4%, accuracy 91.8%; Endo ultrasound sensitivity 76.4%, accuracy 86.1%. When methods are combined, the accuracy of pancreatic cancer detection reaches 98.4% [28, 38, 44]. The main criteria of resectability of non-metastatic pancreatic cancer (PC) include the absence of tumor spreading to the main vessels. Only in 15-18% of patients the tumor is recognized resectable. In 40% of patients who are planned to undergo radical surgical intervention, palliative surgery is eventually performed due to the local spread of the process during intraoperative revision [6]. Along with early recognition of the PG cancer, determination of tumor resectability is an urgent task facing preoperative diagnostics.

Late diagnosis of PG cancer is explained by extremely poor clinical symptomatology at the early stage of the disease. Instrumental methods of investigation, including radiation diagnostics, often state the fact of presence of a mass without clear characterization of its invasion into adjacent structures. Introduction of such modern methods as MRI, CT, EUS into the mandatory list of examination does not always allow to obtain a comprehensive objective picture of the oncologic process [19].

Thus, given the ambiguity of early diagnosis and determination of resectability of PG cancer, improving the methods of radial diagnosis, anamnesis, analysis of specific information, including 3D modeling, is important for clinical practice and patient outcomes [18, 20].

Purpose of the study

To improve the accuracy of diagnosis and assessment of resectability of pancreatic head cancer on the basis of complex use of radiation methods with 3D-reconstructions of the pancreaticoduodenal zone.

Key Objectives:

1. To clarify the possibilities of multimodal radiation diagnostics using endoscopic ultrasonography, computed tomography and magnetic resonance imaging in the preoperative assessment of the prevalence of pancreatic head cancer.

2. To evaluate the results of a hybrid 3D model (MRI-EUS) in determining the preoperative stage of the pancreatoduodenal tumor process.

3. To conduct a comparative analysis of the results of MRI and CT 3D modeling of the pancreatoduodenal zone.

4. To compare the radiation and intraoperative patterns in assessing the resectability of pancreatic head cancer.

Scientific novelty of the study

1. Based on multimodal data of magnetic resonance imaging and endoscopic ultrasonography, a three-dimensional reconstruction of the

biliopancreaticoduodenal zone of patients suffering from pancreatic cancer was performed.

2. Optimized assessment of preoperative staging of pancreatic cancer on the basis of three-dimensional reconstruction with improvement of visual determination of tumor invasion into the main vessels and metastasis to the regional lymph nodes.

3. The criteria of resectability of pancreatic cancer were optimized and expanded, which allowed to improve the immediate and long-term results of surgical intervention.

Practical relevance

The performed work allowed us to clarify and expand the indications for surgical treatment of the pancreatic head cancer. It was established that three-dimensional reconstruction of the pancreaticoduodenal zone is a highly informative method for tumor process assessment with sensitivity 92% and specificity 67,8% in the pancreatic head cancer in conditions of altered anatomo-topographical relationships of normal and pathological structures. Magnetic resonance tomography and endoscopic ultrasonography of the abdominal cavity, used to assess the degree of tumor spread to the adjacent main vessels and to clarify the stage of regional lymphadenopathy, are especially important for surgical treatment of patients. Establishing the stage of the disease and the degree of spread of the tumor process is of great practical importance for assessing the operability of the patient and choosing the nature of surgery.

Propositions for defense:

1. Application of 3D-visualization allows to perform an objective assessment of resectability of the pancreatic head tumor and determine the scope of surgical intervention.

2. 3D-modeling of the pancreaticoduodenal zone based on MRI and EUS is a highly informative technique for assessment of regional invasion of pancreatic head carcinoma with sensitivity up to 92.0% and specificity up to 67.8%.

3. The use of 3D model based on CT improves topical diagnosis of

pancreatic tumors in the conditions of altered anatomo-topographic location, presenting a picture as close as possible to the intraoperative one, which allows planning both the volume and the course of surgical intervention.

Main scientific results

1. The article "The role of 3D modeling in pancreatic surgery" (pp. 23-36, 80-85, [19] in the list of references) describes the possibilities of various methods of radiation diagnosis, as well as a multimodal approach to building three-dimensional models in assessing the prevalence of pancreatic head cancer based on modern literature data, as well as comparing the results of a study of various methods in daily practice in a multidisciplinary hospital.

2. The article "The role of 3D modeling in assessing the prevalence of pancreatic head cancer" (pp. 5, 35, [18] in the list of references demonstrates the results of a study of the possibilities of three-dimensional modeling in assessing the infiltration of pancreatic head tumor of adjacent great vessels with an assessment of the accuracy of preoperative staging of the oncological process.

3. The article "The importance of 3D modeling in assessing the resectability of pancreatic head cancer" (pp. 5, 35, [20] in the list of references demonstrates its own statistical data on the possibilities of three-dimensional modeling in assessing the invasion of pancreatic head cancer, preoperative staging of the oncological process based on various methods of radiation diagnosis, as well as on the basis of multimodal 3D models.

4. The patent "Method for diagnosing tumor invasion in pancreatic head cancer" (pp. 47, 53) is based on a comparison of 3D models of the pancreatoduodenal zone based on magnetic resonance imaging before and after the introduction of a synthetic vasopressin analog. The method is based on the assessment of spasm of the main venous vessels after administration of a vasopressin analogue, and, as a result, a more accurate diagnosis of invasion of venous structures in the common oncological process of the pancreatic head.

Compliance of the thesis with the passport of specialty

Topics, methods of research presented in the thesis correspond to the passport of scientific specialty 3.1.25 - Radiation diagnostics.

Degree of reliability, approbation of the work and realization of the research results

The main results of the thesis research and approbation of the work were presented in the form of reports at the meetings at the Nevsky Radiological Forum (07-08.04.2023г), at the meeting of the Department of Oncology with a course of radiation diagnostics and radiation therapy of the St. Petersburg State University (14.06.2022г).

Personal contribution of the thesis candidate

The author independently obtained scientific results summarized in the dissertation work. The author was directly involved in the examination of patients, analyzing the results of research, determining the diagnostic efficiency of research methods, statistical processing of the obtained data.

Publications

On the subject of the dissertation work published 6 works, including 5 articles in journals included in the list of scientific publications recommended by the Higher Attestation Commission of the Russian Federation.

Structure and volume of the dissertation

The dissertation is outlined on 100 pages of computer text, consists of an introduction, three chapters, conclusion, deductions, practical recommendations and a list of literature, which includes 37 domestic and 166 foreign sources. The presented material is illustrated with 24 figures and 11 tables.

CHAPTER 1. CURRENT STATE OF EPIDEMIOLOGY, MULTIPARAMETRIC DIAGNOSTICS AND TREATMENT OF PANCREATIC HEAD CANCER

In recent decades, despite diagnostic successes, the incidence of adenocarcinoma of the head of the PG has been steadily increasing, and the problem of early detection, accurate diagnosis and staging remains relevant. The criteria of resectability of PG cancer developed several years ago, based on the degree of involvement of large vessels in the tumor, are not unified and have several versions.

1.1 Epidemiology of pancreatic head cancer

In early 2021, new global statistics on the incidence and mortality of 36 types of cancer in 185 countries were published. According to the data, cancer is the leading cause of death and a severe barrier to extending the life expectancy of the population in most countries of the world [179].

To date, pancreatic cancer (PaCa) ranks fourth in Western countries among the causes of death associated with malignant neoplasms. Resectability in PaCa remains low (10-20%), and 5-year survival rate does not exceed 5% [5, 22, 125, 132, 150].

If we analyze the statistics obtained for the most common types of cancer (breast, lung, prostate, colorectal, liver, rectum, cervix, esophagus, thyroid, bladder), the number of new diagnoses significantly prevails over the number of deaths. In the case of PaCa, 495,773 new cases of cancer of this localization (2.6% of all cancers of various localizations) and 466,003 deaths due to it (4.7% of all deaths due to cancer) were recorded worldwide in 2020.

PaCa develops more frequently in men than in women with an incidence rate of 4.9 and 3.6 per 100,000 population, respectively. Older age is a significant risk factor for the development of PaCa. The age-specific incidence rate of PaCa is 10.4 per 100,000 population in the age group 55-59 years, 24.0 and 55.7 per 100,000 population in the age groups 65-69 and ≥75 years, respectively [175].

A large number of new patients were reported in Asia (233,701) and Europe (140,116) [179]. Projections by the American Association for Cancer Research (AACR) have shown that by 2030, PaCa and liver cancer will rank second and third in cancer mortality, and ahead of breast, prostate, and colorectal cancer, respectively. New advances in cancer screening, prevention, and treatment can affect cancer incidence and/or mortality, but close collaboration between scientists and health care workers is necessary to realize this goal [160].

According to IARC data, our country is a region characterized by high incidence and mortality rates of PaCa [7, 8]. In 2019, the incidence rates of PaCa were 9.31 for men and 5.68 for women. In a number of regions of the Russian Federation, the incidence of PaCa is higher than the national average (Fig. 1).

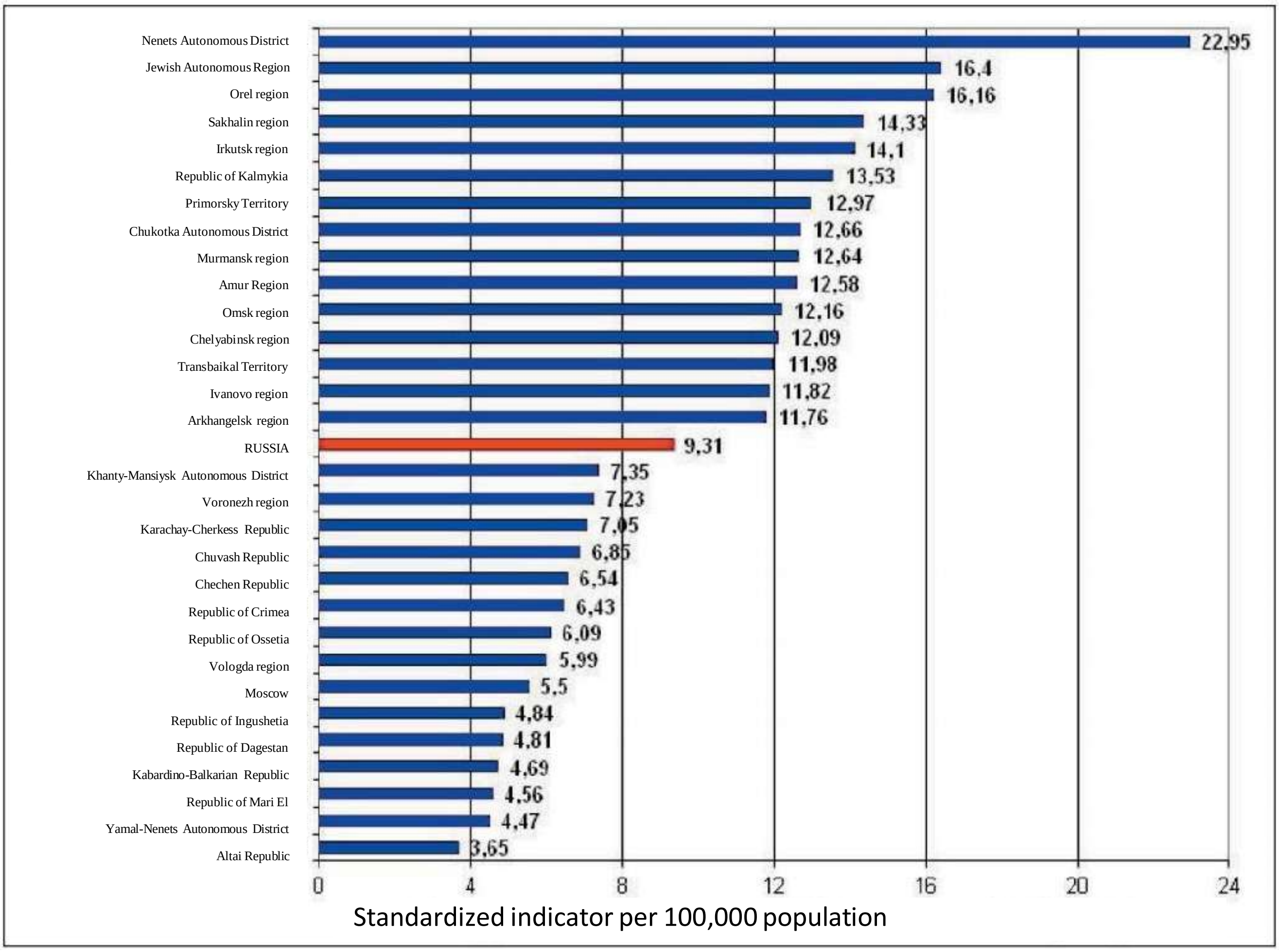


Figure 1 - Regions of the Russian Federation with the highest and lowest incidence rates of PaCa, 2019 (per 100 thousand population)

As can be seen from Figure 1, the highest incidence rates were observed in the Nenets Autonomous District (22.95), the Jewish Autonomous Region (16.4), and the Orel Region (16.16), while the lowest incidence rates of PaCa were registered in the Altai Republic (3.65) [7, 8].

The mortality rates from PaCa in Russia are also high [3, 6, 13, 174]. The mortality rate from PaCa in 2019 was 9.26 in men and 5.27 in women. In Russia, as in other countries, the mortality from cancer correlates with the incidence, i.e., it is high in regions with high incidence and low where the incidence is low. For example, the highest mortality rate from cancer in men in the Jewish Autonomous Region was 20.88, in the Nenets Autonomous District - 17.27, and the lowest - in the Chechen Republic (2.15). In Russia, the mortality rates from PaCa in women also vary considerably: the Nenets Autonomous Okrug is the leader (9.94), followed by the Sakhalin Oblast (8.64), the Amur Oblast (8.6), and the lowest mortality rate is in the Republic of Ingushetia (0.96) [7, 8].

The morbidity and mortality rates of PaCa are practically not different from each other. The five-year survival rate of PaCa patients in Russia does not exceed 1%. In some years, mortality was higher than morbidity, indicating undercounting in the lifetime of PaCa patients [7, 8]. Figure 2 shows the dynamics of morbidity and mortality from PaCa in Russia among men and women for 10 years, starting from 1990.

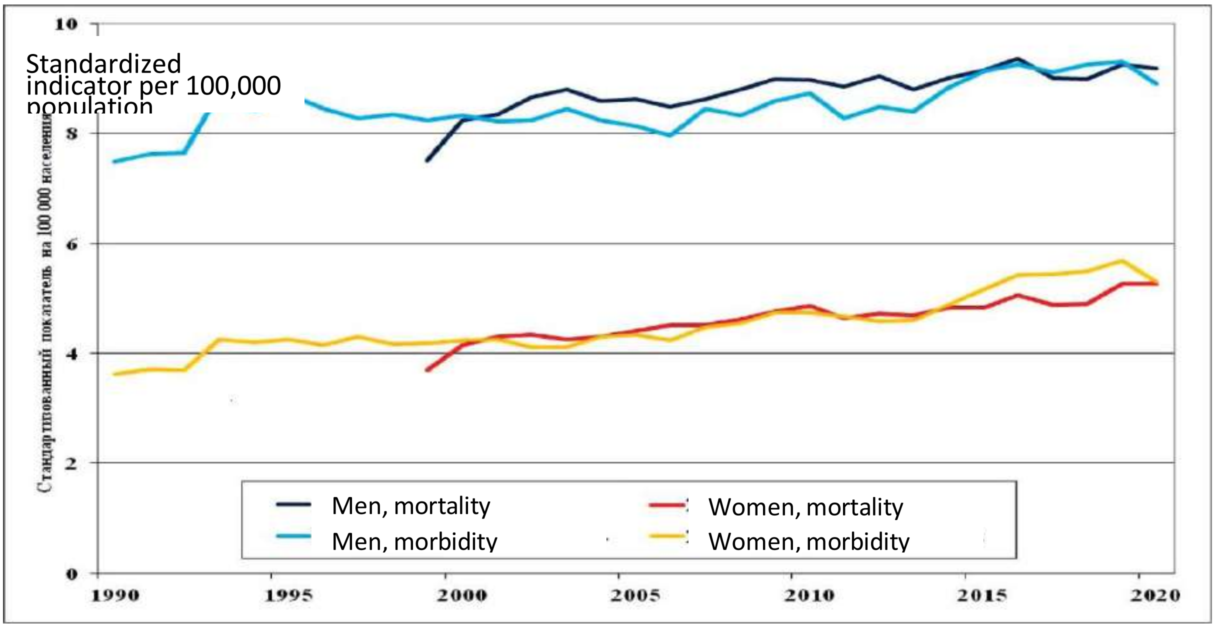


Figure 2 - Dynamics of pancreatic cancer incidence and mortality in Russia

As can be seen in Figure 2, over the last decade in Russia there has been an increase in the incidence and mortality of cancer in both men and women. Since 1990, the morbidity and mortality from PaCa in men has increased by about 50%. The most pronounced increase in morbidity and mortality from PaCa is observed in women: morbidity and mortality from PaCa has increased 2-fold. Apparently, this gender difference in the dynamics of indicators is associated with a higher prevalence of risk factors of PaCa among women. For example, the prevalence of obesity is significantly higher among Russian women compared to men [1]. As a rule, PaCa is a disease of the elderly, since 90% of newly diagnosed patients are older than 55 years [78]. Analysis of mortality by age groups showed an increase in mortality in older age groups (60-64, 65-69, 70-74, 75-79) in both men and women. No growth trends were observed in younger age groups (35-39, 40-44, 45-49, 50-54, 55-60).

Thus, most often the tumor of the studied localization occurs in elderly patients with a mean age at disease debut of 71 years in men and 75 years in women.

Modern classification of malignant neoplasms is based on their cellular differentiation (ductal, acinar or neuroendocrine) and their macroscopic characteristics (solid or cystic). Intraductal adenocarcinoma of the PG accounts for 90% of all malignant neoplasms of this localization. Among other malignant tumors of the PG (pancreatic neuroendocrine tumors, solid-pseudopapillary tumors, acinar cell carcinoma, and pancreatoblastoma), neuroendocrine tumors are the most common, accounting for 5% of malignant pancreatic tumors [26, 42, 152, 187].

Infiltrating ductal adenocarcinoma of the PG develops from various noninvasive pre-tumor lesions, which include intraductal papillary mucinous neoplasia, mucinous cystic neoplasia, and pancreatic intraductal neoplasia (PanIn).

Intraductal papillary mucinous neoplasia are non-invasive mucin-producing epithelial tumors that form long finger-like papillary growths.

Mucinous cystic neoplasia are mucin-producing epithelial tumors that form cysts, with distinctive stromal tissue.

PanIn are non-invasive epithelial tumors of small size that are located in the small ducts of the pancreas and are characterized by cytologic and architectural atypia. There are several stages of PanIn depending on the histologic changes of the ductal epithelium [26, 42, 152, 187].

The evolution of PanIn1 into PanIn3 is defined by an increase in cellular and nuclear atypia. PanIn3 often manifests in association with invasive ductal adenocarcinoma of the pancreas. Importantly, a typical feature of pancreatic cancer is the formation of a dense stroma that is composed of cellular and fibrillar elements-a desmoplastic reaction. A key role in the desmoplastic reaction belongs to stellate cells, which are activated by transforming growth factor 1 (TGF-1), fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF). This leads to their differentiation into myofibroblasts, which actively secrete collagen and other components of the extracellular matrix [15, 25, 48, 62, 185].

Desmoplastic reaction plays a major role in tumor formation, progression, invasiveness and metastasis. A peculiarity of pancreatic cancer stroma is its ability to cause immunosuppression, which leads to suppression of antitumor immunity. In addition, stellate cells have been shown to contribute to the modification of tumor metabolism by secreting essential amino acids, particularly alanine, which promotes the use of glucose and carbon supplied by glutamine as an energy source in the tricarboxylic acid cycle. These metabolic changes reduce the tumor's dependence on serum glucose and nutrients [152].

Genetic abnormalities in PaCa are quite diverse. A point mutation of the KRAS oncogene is detected already at early stages, which is observed in various precancerous lesions as well as in PaCa. Further mutations that lead to non-neoplastic changes in PanIn are observed in tumor suppressor genes (CDKN2A, TP53 and SMAD4). Further accumulation of genetic and epigenetic lesions lead to transformation of pre-tumor lesions into invasive carcinoma of the PG. Mutations in MLL3, TGFBR2, ATM, ARID1A, ROBO2 and KDM6A genes are observed less frequently in intraductal adenocarcinoma of PG. It should be noted that mutations in chromatin-regulated genes (MLL, MLL2, MLL3, and ARID1A) are associated with increased survival, while loss of SMAD4 is associated with a worse prognosis [1, 23, 77, 126, 143].

Most mutations are observed in a small percentage of tumors, so they are considered "passengers" of carcinogenesis. However, a recently proposed theory suggests that several "passenger" genes with weak carcinogenic effects, when combined, may play a significant role in carcinogenesis. It is important to note that, despite the wide variety of genetic mutations in PaCa, damage to specific signaling pathways, particularly Wnt/Notch and TGF-β, as well as impaired DNA damage control are of primary importance. Therefore, targeted therapies targeting signaling pathways should be more effective compared to targeting damage to specific genes [85].

Post-transcriptional regulation or silencing of gene expression occurs mainly through non-coding RNAs. The most studied of these are microRNAs (miR). Disruption of miR regulation can provide information about transcriptional regulation and also serve as a biomarker of survival and early tumor detection.

Current studies have shown upregulation of miR-21, 23a, 31, 100, 143, 155, and 221, and downregulation of miR-148a, 217, and 375 in intraductal adenocarcinoma of the PG. In addition, high expression of miR-21, miR - 31 and low expression of miR-375 have been shown to be markers of unfavorable prognosis and poor survival in intraductal pancreatic adenocarcinoma [85, 91, 150].

The main acquired risk factors for the development of PaCa are smoking (overall relative risk 1.74) and increased alcohol consumption (overall relative risk 1.45) [54, 65, 93,178].

Obesity is a significant risk factor for the development of PaCa. Carcinogenesis is enhanced in excess adipose tissue, probably through the mechanism of atypical glucose metabolism. Obesity with a body mass index> 30 kg/m2 corresponds to a 20-40% higher mortality rate from PaCa [43, 57, 61, 116, 135, 173].

Several studies have demonstrated associations between type 1 and type 2 diabetes mellitus and PaCa, with risk ratios as high as 2.0 and 1.8, respectively. The results of several meta-analyses confirm that diabetes mellitus is associated with an increased risk of developing PaCa. Diabetes mellitus is both an early manifestation and an etiologic factor of PaCa [56, 159, 169, 200].

Chronic pancreatitis has long been identified as a risk factor for the development of PaCa [169]. However, only 1.8% of these patients have PaCa within 10 years of diagnosis and 4% after 20 years [87]. A significant proportion of pancreatitis cases are thought to result from pancreatic hypertension [49], indicating that this condition may be either a risk factor or a sign of early disease.

Dietary factors influence up to 30-50% on the occurrence of PaCa and there is evidence that some foods are associated with a higher risk, while others are even protective [133, 137, 202]. Regardless of their role in the occurrence of obesity: butter, saturated fats, red meat and processed foods are clearly associated with PaCa [84, 139, 149]. While high intake of fruits and food components containing folic acid may reduce the risk of developing PaCa [45, 73, 130, 155].

Various chemicals have been reported to increase the relative risk of developing PaCa, including chlorobenzene, chlorinated hydrocarbon, nickel, chromium and their compounds, silica dust and others [40, 107, 120, 172].

To summarize, it should be noted that from 5% to 10% of cases of PaCa are associated with genetic changes. In the remaining 90%, the main risk factors are smoking, Helicobacter pylori infection and factors related to dietary habits (meat consumption, low fruit and vegetable intake, diabetes, alcohol consumption). Some factors are difficult to interpret, such as chronic pancreatitis, which is known as a risk factor but may be associated with alcohol consumption, which is a risk factor in itself. Diabetes is also known as a risk factor, but this may be the initial manifestation of PaCa and may also be a symptom of chronic pancreatitis.

1.2 Clinical and radiation diagnostics of pancreatic head cancer at the present stage

In most patients with PaCa, the process develops in an asymptomatic stage to a metastatic or locally advanced state, when invasion of neighboring vessels is already present. Surgery is a radical treatment option even for selected patients with invasion of the main vessels, with a 5-year survival rate after resection of ≈20%, but this is only possible in 15-20% of patients [153, 171, 185]. Therefore, accurate determination of tumor resectability when adjacent vessels, such as the superior mesenteric vein, portal vein, may be affected represents a critical diagnostic and treatment issue. Currently, decisions regarding the resectability of PaCa are based on radial imaging techniques, the objectives of which are:

1. Identify and characterize the tumor mass of the PG with signs of malignancy.

2. Identify or exclude the connection of the mass with duodenum, jejunum and its mesentery, with the main arteries and veins in the area of tumor location.

3. Identify distant metastases, metastases to regional lymph nodes, as well as lesions of the liver and peritoneum, excluding surgical intervention.

Consequently, the main purpose of clinical and radiation diagnostics in PaCa along with tumor detection and assessment of its parameters is to determine the signs indicating the extent of the process, allowing surgeons to make a decision on the resectability of the mass.

1.2.1 Current capabilities of ultrasound and X-ray computed tomography in assessing the prevalence of pancreatic head cancer

Ultrasound is widely used in the diagnosis of pancreaticoduodenal neoplasms. In the predominant number of examinations of patients diagnosed with mechanical jaundice ultrasound is the first method of investigation. Ultrasound is highly informative, safe for the patient and has no contraindications. According to the results of recent studies, the diagnostic accuracy of ultrasound in the primary detection of pancreatic head tumors is comparable to the data of computed tomography and reaches 87-90%, and when using color Doppler mapping - 94% [111, 118, 144].

Ultrasound allows us to assess the extent of the cancer process in the pancreas, secondary changes in lymph nodes, liver, and in some cases to determine dissemination through the peritoneum. The pancreas is a retroperitoneal organ with complex topographic-anatomic relationships, and therefore the sensitivity of transabdominal ultrasound is relatively low for assessing the resectability of pancreatic cancer [59, 91, 166]. Sensitivity according to the literature ranges from 48% to 89% with lower specificity and accuracy, with the variation in these values depending on tumor size and diagnostician experience [53, 74]. The use of color Doppler mapping (CDI) allows a more accurate description of the vascular architectonics of the peripancreatic region and assessment of the degree of tumor involvement of the vascular wall.

Planning of radical surgical treatment in oncopathology of the head of the pancreas requires information about invasion of carcinoma into the main vessels. Previously, portal and superior mesenteric veins involved in the tumor process stopped surgeons from radical treatment; today, only tumor invasion into the wall of the superior mesenteric artery, hepatic artery, and jejunal trunk prevents surgery

[51, 105, 109]. Assessment of vascular invasion in the CDI mode of ultrasound is characterized by a sensitivity of 87-93% [47, 124, 190, 199].

The criteria of vascular involvement in the tumor process according to ECHO-picture in the CDI mode include: absent border between the tumor and the vessel wall, visualization of the vessel in the tumor, narrowing of the vessel lumen, stenosis and thrombosis of the vessel [41, 69, 70].

Thus, ultrasound is the most accessible method at the initial stage of patient's examination, allowing to detect the fact of tumor presence, signs of local and distant metastasis and occupies the first place in the algorithm of patients' examination.

Computed tomography (CT) is the "gold standard" for the evaluation of pancreatic head tumors with a sensitivity of 76% to 92% in the diagnosis of pancreatic cancer [72, 183]. CT has been shown to have an accuracy of 85-95% for tumor detection, a positive predictive value of 89-100% for nonresectability, and a negative predictive value of 45-79% for resectability [154].

It is optimal to perform CT before biliary stenting because the stent causes artifacts in the pancreatic head that can mask the lesion, in addition, the trauma of stent insertion can cause inflammatory changes that are sometimes indistinguishable from tumor [38, 95].

The protocol for pancreatic CT with bolus contrast should be at least a two-phase study with imaging during the pancreatic and hepatic phases.

A direct CT sign of PaCa is a hypodense focus (≥10 NU) in relation to the surrounding parenchyma, which is most often characterized by indistinct irregular contours, it is located against the background of unchanged organ parenchyma. Indirect CT signs of PaCa include bulging of the organ contour with local increase in size, pancreatic and biliary hypertension (Virsung's duct dilated >5 mm and common bile duct >8 mm) with block at the level of the mass, metastatic liver involvement, ascites [88, 89, 90].

In addition, the pancreas distal to the tumor usually appears atrophic, which is visualized on CT as a fairly uniform diffuse thinning of the organ parenchyma.

In most cases, an increase in regional lymph nodes (upper, lower, anterior pancreaticoduodenal, lymph nodes around the common bile duct, proximal mesenteric lymph nodes, splenic and ventral lymph nodes) of more than 1 cm when measured along the short axis of the node, with an increase in their number and, in some cases, an increase in densitometric indices is detected. As the tumor grows, it usually infiltrates peripancreatic structures and may lead to occlusion of adjacent vessels and, in some cases, adjacent organs [14, 32, 156, 170, 184].

In the current literature, there are very contradictory data on the accuracy of CT data in the assessment of tumor invasion. The main reason for the differences in CT signs of vascular invasion of arteries and veins is that vein walls are thinner and more pliable than arterial walls. When a tumor surrounds a vein, its walls become irregular leading to narrowing of the vein lumen. The velocity of blood flow through the veins is low. Often the tumor grows through the wall of the vessel, which leads to venous thrombosis, causing occlusion of the vein. Arterial vessels, on the contrary, are characterized by thicker walls, greater elasticity, and smaller caliber; therefore, even when arteries are located in the tumor structure, their lumen is often unchanged and uniform during contrast enhancement [27, 36, 88, 89, 90].

Various criteria of resectability of the head of the PG cancer have been described in the literature. These criteria include: absence of distant metastases, absence of tumor invasion of large arteries and extensive venous invasion. In recent years, the NCCN principles (version 1.2017) have been favored, in which resectability is represented by 3 forms: resectable cancer, borderline resectable cancer, and unresectable pancreatic head cancer (Fig. 3).

Categories	Arterial invasion	Venous invasion
Resectable	✓ No arterial invasion of the TC, SMA, OPA	✓ No invasion into the SMV and PV and vessel contact ≤ 180 °of circumference without compromising contour integrity
Borderline resectable	✓ Tumor is in contact with the OPA without spreading to the TC ✓ Tumor contacts SMA <180v variant anatomy (supplementary or replacement right hepatic artery, etc.) and tumor contact with these vessels	✓ Tumor contacts the SMV or PV more than 180e, with vein irregularity or thrombosis, but with intact vessel above and below the involved segment and the possibility of resection and reconstruction ✓ The tumor is in contact with the VCI
Non-resectable	✓ Tumor contact with SMA >180° ✓ Tumor contact with TC 2180 ✓ Contact with the first branch of the SMA	✓ Unable to reconstruct the portal mesenteric venous axis due to massive tumor invasion or extensive thrombosis ✓ Tumor in contact with the first branch of the SMV

Figure 3 - Criteria for arterial and venous invasion in cancer of the head of the PG:

TC - celiac artery, SMA - superior mesenteric artery, OPA - common hepatic artery, SMV - superior mesenteric vein, VV - portal vein, VCI - vena cava inferior

If the tumor surrounds the vessel more than 180 degrees and occludes the superior mesenteric vein (SMV)/ portal vein (PV) without surgical options for reconstruction, it is considered T4 disease and is unresectable [12, 35, 161, 162]. Recent studies have shown that the sensitivity of CT for unresectable disease ranges from 52% to 91% and specificity from 92% to 100% [127, 151, 180].

The use of CT angiography is also of key importance in assessing the venous anatomy. Multiple jejunal branches flowing into the superior mesenteric vein complicate venous reconstruction, often making it impossible. Also exclude the possibility of intervention are such unfavorable variants of arterial anatomy as low branching of the common hepatic artery from the hepatic trunk with location under the portal vein, as well as branching of the common hepatic artery from the superior mesenteric artery and its spread through the retroperitoneal edge of soft tissue resection. However, changes in angioarchitectonics may contribute to the resection. For example, when the common hepatic artery branches directly from the aorta (the jejunal trunk supplies blood only to the splenic and gastroduodenal arteries) or the accessory right and left hepatic arteries branch off the superior mesenteric artery or the left gastric artery [13, 33, 55, 79, 98, 115], this only confirms the importance of knowing the vascular architectonics of the operation.

The most valuable advantage of CT is the possible multiplanar reconstruction (MPR) of images, as well as the creation of three-dimensional models. MPR allows to achieve high-resolution images, with the possibility of studying areas of interest in all planes, making images more visual and familiar to surgeons. In three-dimensional modeling on the basis of CT with bolus contrast enhancement it is possible to create volumetric images of anatomical zones with demonstration of correlations of pathological focus, vessels, surrounding organs [9, 11, 34, 114, 193]. Such processed images allow to significantly expand diagnostic capabilities of CT, improve visualization of pancreatic vessels and ducts of PG. There are data that MPR images have significantly increased diagnostic capabilities of CT in detection of PG tumors, especially in small sizes [11, 21, 96, 108, 122, 186].

Nevertheless, the computed tomographic method has certain disadvantages. The main one is preoperative characterization of secondary affected abdominal lymph nodes and the presence of distant metastases of small size (<2cm). While generally a safe, noninvasive, and relatively inexpensive imaging modality, contrast CT is accompanied by the risk of nephrotoxicity from iodine-containing contrast agent as well as radiation exposure. Despite this, most centers still support the use of CT as the first-line modality of choice for the diagnosis of pancreatic cancer [9, 10, 37, 114, 193].

As for the N-criterion, using a short axis size of 10 mm, CT has a sensitivity of only 15% for detecting nodal metastases [17, 80, 129]. Using a threshold of 5 mm, the sensitivity of CT increases to ~ 70% and the specificity decreases to 65%. At the same time, according to the literature, histological examination revealed benign hyperplasia in 40-60% of lymph nodes recognized as metastatically affected by CT. In addition, metastatically affected lymph nodes are not always enlarged in size [63, 128, 147].

Regarding the application of 3D models in the assessment of the cancer process prevalence and preoperative staging in PG cancer, such techniques are actively used to construct 3D images of the main vessels and assess the degree of their lesion.

Thus, triphasic, contrast-enhanced, thin-section, multidetector, spiral computed tomography with 3D reconstruction serves as the preferred way to visualize the relationship between the tumor and the nearby vasculature and thereby determine resectability. However, given that the only direct indication of the presence of a mass has been identified so far, the CT method cannot be recognized as universal. Therefore, CT should be improved or the method should be used in combination with other imaging methods. In this case, the strengths of CT can be utilized by other tomographic methods.

1.2.2 The role of endoscopic ultrasonography in the staging of pancreatic head cancer

Endoscopic ultrasonography (EUS) is a modern method of detecting pancreatic tumors, staging and determining resectability, which has proven effective in assessing the degree of tumor invasion, as well as in detecting regional metastatic lymphadenopathy. EUS involves endoscopic examination of the upper gastrointestinal tract using an echoendoscope. The transducer of the echoendoscope is located in the stomach, in close proximity to the pancreas, which allows high-resolution detailed images of the pancreas and surrounding vessels, lymph nodes, and the left lobe of the liver. The role of EUS is especially important for the evaluation of masses smaller than 2 cm, as well as the possibility to biopsy the tumor [31, 75, 131].

Pancreatic adenocarcinoma most often arises in the head of the pancreas (65%) and usually presents as a hypoechogenic solid mass with poorly defined margins [58]. Tumor in the head of the pancreas causes ductal obstruction with secondary dilatation of both common bile and pancreatic ducts [30, 148, 157]. In Doppler studies, ductal adenocarcinoma of the pancreas is characterized by poor vascularization and consequently poor enhancement in all phases of contrast. This may also be due to marked desmoplasia, low mean vessel density or the possible presence of necrosis and mucin [8, 62, 81, 189, 196]. It was shown that the diagnostic accuracy of EUS in the absence of tumor detection on spiral CT was 92% [68, 112, 113, 176]. Fibrotic paracancerous and inflammatory changes play a certain role, reducing the reliability of the data. In some cases, this may lead to erroneous interpretation of the performed EUS study, namely, to failure to recognize the tumor nature of the mass and the depth of its invasion. In large meta-analyses of EUS with fine needle aspiration (EUS-FNA) a high accuracy of the method in the diagnosis of pancreatic tumors with sensitivity of more than 85% and specificity of 96% was proved [119, 168]. EUS has also proven to be a reliable method for assessing process staging with sensitivity and specificity of 72% and 90%, respectively, for stage T1-T2, 90% and 72%, respectively, for stage T3-T4, and 87% and 92%, respectively, for vascular invasion [119]. However, it has been noted that the accuracy of the method decreases in the presence of stents placed in the bile ducts. At the same time, the results of the study depend on the experience of the specialist performing the study.

EUS has also been shown to be a reliable imaging modality for detecting vascular, especially venous, invasion, with an accuracy of 82%, with an overall complication rate of up to 0.85% (including infection, acute postmanipulative pancreatitis) [82, 83, 104, 191].

Endoscopic diagnosis is particularly informative in the presence of masses that may mimic pancreatic cancer, such as autoimmune pancreatitis or lymphoma [76, 145, 146] and is a reliable method for the definitive histological diagnosis of a tumor mass by EUS-FNA [56, 81, 189, 196].

Determination and assessment of the degree of metastatic lymphoadenopathy causes rather great difficulties in preoperative staging of pancreatic cancer. When diagnosing different groups of lymph nodes, only their size and densitometric density indices are determined. The resolving ability of

EUS, besides the size of lymph nodes, can characterize their shape, sharpness of contours, structure, echogenicity indices and accurately differentiate the cortical and cerebral layers of lymph nodes, which cannot be assessed by CT. On this basis, compared with other known methods, the reliability of endo-US in staging N-criterion pancreatic cancer is higher [67, 141, 163, 198].

Thus, EUS is a safe, well tolerated procedure and has the added advantage of allowing fine-needle aspiration to obtain material for cytopathologic diagnosis. This is particularly important in tumors smaller than 2 cm, in cases of clinical suspicion of pancreatic cancer, when other modalities have failed to identify the tumor mass and perform biopsy.

At the same time, in the conditions of multimodal multiparametric study, the issues of cancer staging may remain unresolved at the preoperative stage due to complex topographic-anatomical relationships that complicate biopsy.

1.2.3 The role of magnetic resonance imaging in the staging of pancreatic head cancer

Magnetic resonance imaging in pancreatic tumors in contrast to CT, ultrasound and EUS has a higher tissue sensitivity. The use of different sequences, diffusion-weighted images allows to recognize the presence and nature of volumetric masses, to characterize their structures, including differentiation of solid and cystic components, necrosis zones and hemorrhages. Thus, it is possible to determine the organ affiliation, size, connection with adjacent structures and vessels, presence of metastases in lymph nodes, liver, peritoneum, etc. To diagnose ductal adenocarcinoma of the pancreas it is recommended to perform MRI of abdominal cavity organs with dynamic intravenous contrasting. The optimal protocol should provide obvious contrast between the normal pancreatic parenchyma and the affected organ structure [29, 142, 178].

The minimum acceptable MR imaging protocol for the pancreas should include T1-weighted images, T2-weighted images, magnetic resonance cholangiopancreatography (MRCPG), diffusion-weighted imaging (DWI), and dynamic enhancement with arterial phase, portal vein phase, and breath-hold phase, using a fast gradient echo sequence.

The MR signal from the area of malignant lesion of the pancreatic head is characterized by hypointense signal on T1-VI, with moderately hyperintense signal on T2-VI, DWI relative to healthy glandular tissue. At dynamic contrast enhancement with gadolinium a slower accumulation of EF and slower washout than in unchanged pancreatic tissue is determined [64, 158, 197].

It is also necessary to perform magnetic resonance cholangiopancreatography for visualization of pancreatic duct, nature and extent of common bile duct stenosis in cancer of the head of the pancreas, pathological inclusions, detection of retention cysts, besides, MRCPG is informative to determine the presence of stones as an alternative cause of bile ducts or pancreatic ducts dilatation [161, 162].

Given the greater soft tissue contrast on MRI compared with CT, there are several specific clinical situations in which MRI is superior to CT. These include small tumor size, hypertrophied pancreatic head, and focal fatty infiltration of the organ parenchyma (39, 110, 188). Although CT currently plays an important role in the evaluation of pancreatic masses, MRI with MRCPG allows for more successful early tumor detection, allowing for a comprehensive analysis of morphological changes in the pancreatic parenchyma as well as the pancreatic duct.

Diffusion-weighted images are also used to characterize pancreatic lesions in the case of various pathological entities: cystic lesions, pancreatitis and malignant tumors. MRI has the advantage of superior soft tissue contrast, which is important for the detection of small tumors or tumors not deforming the duct, which can be detected with the standard MRI protocol. The use of diffusion-weighted imaging may allow earlier detection of pancreatic adenocarcinoma, as these neoplasms are characterized by increased signal intensity on diffusion-weighted images and high weighting ratios (b > 500 C/mm> 2), with relatively low ICD values due to limited diffusion caused by fibrosis [48, 92, 94].

The Incoherent Motion Model (IVIM), considering these sources of signal decay, provides a theoretical basis for deriving diffusion and perfusion parameters from DWI. Recently, the IVIM approach with multiple B-values has been incorporated into the diagnostic protocol for pancreatic tumors, and several papers have shown promising results regarding the differentiation of pancreatic cancer from unaltered pancreatic tissue [71, 117, 165, 203]. DWI facilitates the visualization of small metastases that have high signal intensity, unlike other sequences.

Current MRI technology allows 3D reconstructions to be obtained for the study of peri-pancreatic vessels. The optimal time for imaging of the peripancreatic vascular network has been demonstrated: biphasic visualization 15 s and 45 s after the contrast agent (gadolinium) enters the abdominal aorta [71, 117, 165, 203].

The accuracy of MRI for vascular imaging is very close to that of CT [165, 203]. MR signs of large vessel lesions include: tumor adhesion to the vessel in the presence of tumor infiltration of perivascular tissue. Visualization of circular contact of the tumor with the vessel for more than ½ of the circumference may indicate invasion into the vessel wall; if the vessel passes through the tumor thickness, or in the presence of deformation of the vessel along one of the walls with a length of more than 2 cm or occlusion of the vessel with the presence or absence of collaterals, tumor sprouting of the vessel is likely.

Currently, MRI is used in the initial stage of diagnosis in pancreatic head cancer complicated by biliary hypertension and jaundice to clarify the cause and assess the extent of the tumor. The accuracy of MRI assessment of vascular invasion is comparable to CT and, therefore, due to its imaging advantages, can be recommended as a primary diagnostic procedure for patients with contraindications to CT (allergy to iodine-containing contrast agents, renal failure, pregnancy) or with insufficient informative CT data.

1.2.4 The role of three-dimensional modeling in assessing the prevalence of pancreatic head tumors

Due to the special anatomical relationship between the pancreas and the adjacent trunk vessels, three-dimensional reconstructions help to obtain additional information about this relationship, which is currently the most valuable advantage of CT - the possibility of multiplanar reconstruction (MPR). With MPR, good image quality with high resolution is achieved, which allows to analyze the areas of interest in all planes. 3D modeling on the basis of CT with bolus contrast enhancement allows to create volumetric images of anatomical zones, with clarification of relations of pathological focus, vessels and surrounding organs. 3D reconstructions are based on fusion of phases of each object under study into its maximum (peak) contrast phase. At the same time, axial slices, which are raw data, are more informative, and phase superimposition by postprocessing methods plays an important role in assessing the relationships of organs, vascular structures, and formations only in case of accurate comparison with axial slices [60, 90, 106].

Invasion of portal vein or superior mesenteric vein in PG surgery today is not considered as a contraindication to intervention, while the possibility of prosthesis may be difficult in case of a large extent lesion. 3D images are better able to fully depict the level of invasion and its extent, which helps to shape the surgeon's tactics [105, 136].

It is important for the surgeon to be able to see the tumor, both in itself and in the context of the surrounding structures, in three dimensions from all sides, with particular interest obviously being given to the presence and degree of contact with relevant vessels or surrounding organs. It is also possible to confidently assess the tumor volume in relation to healthy PG parenchyma. Free-rotating 3D imaging allows the surgeon to visualize the extent of venous invasion more clearly.

3D visualization of primary data requires semi-automatic segmentation of structures of interest: pancreas, tumor, stomach, liver, spleen, kidney, and any cysts. PG tumors are the most time consuming and problematic segmentation process, as it is difficult to recognize the boundaries between the organ tissue and tumor, and surrounding structures due to growth outside the organ boundaries. Data preparation includes all important organs and vascular structures of the abdominal cavity, to provide the surgeon with maximum information, allowing possible problems in the exposure of the PG to be included in the surgical planning [97, 121, 172, 194].

Thus, the reconstruction procedure for visualization of the PaCa today is still characterized by the need for a large amount of effort, primarily of a technical nature and time-consuming. Also, objective and accurate localization of the tumor remains impossible, due to segmentation performed according to the subjective interpretation of the radiologist. Tumor segmentation is impossible with the use of automatic image processing procedures, which is due to the often insignificant differences in the thickness of the organ tissue and the tumor, which cannot be recognized by the computer program. However, there are very promising approaches to organ segmentation that make the automatic procedure tangible. Statistical shape models learn the average shape of an organ with its variants from training data. Using even state-of-the-art models, it can be shown that segmentation work can be significantly reduced for the liver [20, 97, 121, 194].

It can be said that three-dimensional visualization of pancreatic carcinomas with surrounding vessels and organs is currently constrained by the large amount of effort involved, but it primarily provides the surgeon with valuable additional information. Post-processing images significantly expand the diagnostic capabilities of CT, allowing to assess the prevalence of the cancer process and to perform preoperative staging in PaCa, improving visualization of pancreatic vessels and ducts of the pancreas [123, 160, 164].

Thus, clinical and radiation diagnostic methods play a crucial role in the diagnosis and management of patients with pancreatic adenocarcinoma. CT is the most widely available and proven method for visualization of pancreatic adenocarcinoma. To maximize the diagnostic performance of CT, the use of a PG protocol is mandatory. The sensitivity of CT for the diagnosis of pancreatic adenocarcinoma (89-97%) and its positive predictive value for predicting non-resectability (89-100%) are high. The positive predictive value of CT for predicting resectability (45-79%) is low because diagnostic criteria for recognizing tumor vascular invasion favor specificity over sensitivity to avoid denying surgery to patients with potentially resectable tumor [19, 97, 121, 194).

In addition, the sensitivity of CT for small metastases to the liver and peritoneum is limited. Magnetic resonance imaging has not shown better performance than CT for the diagnosis and staging of pancreatic adenocarcinoma, but may be useful as an adjunct to CT, especially for the evaluation of small liver lesions that cannot be fully characterized by CT. Ultrasound is often the first study obtained in patients with obstructive jaundice or unexplained abdominal pain, but its usefulness in the diagnosis of pancreatic adenocarcinoma is limited. Endoscopic ultrasound is generally considered superior to CT for the diagnosis and local staging of pancreatic cancer, but its stand-alone use is limited by its inability to evaluate distant metastases [18, 20].

1.3 Classification of pancreatic head cancer

Positive long-term outcome of pancreatic cancer treatment is based on the most accurate clinical staging of the disease. The modern clinical classification of pancreatic cancer according to TNM system is proposed in the 7th edition of the American Joint Committee on Cancer (AJCC). The staging system for pancreatic cancer was revised according to the resectability of the tumor and is based on the relationship between the tumor and vascular structures, as well as the possibility of achieving a negative resection margin during surgery.

According to this provision, patients with stages I and II, as well as the majority of stage III patients, were categorized as resectable. Invasion into the abdominal trunk, or the superior mesenteric artery less than 180º in circumference, or the common hepatic artery without spreading to the abdominal trunk (usually at the mouth of the gastroduodenal artery) is defined as marginal resectability (Table 1).

Table 1 - Staging of pancreatic cancer proposed by the American Joint Community from Cancer Research (7th edition)

Stage	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1 T2 T3	N1 N1 N1	M0 M0 M0
III	T4	Any N	M0
IV	Any T	Any N	M1

However, according to the NCCN (National Comprehensive Cancer Network), extremely resectable pancreatic cancer is defined as tumor invasion of veins, including the superior mesenteric or portal veins, and arteries: gastroduodenal, superior mesenteric, common hepatic, or abdominal trunk.

Thus, there is a clear distinction between extremely resectable and locally advanced pancreatic cancer. In both cases, invasion of adjacent tissues and mesenteric vessels is noted. However, in the former, invasion is minimal, allowing a macroscopically clean resection margin to be achieved. At the same time, it should be remembered that their prevalence is much greater than that of potentially resectable tumors, so a microscopically positive resection margin (R1) is significantly more common when surgery is performed as the first stage of treatment [171].

The A021501 study showed that R0 resections are possible in 64% of patients, but vascular resections have to be performed in 80% of cases.

In the 8th edition of the American Joint Cancer Research Community classification (2017), the staging of exocrine and endocrine pancreatic cancer is different from the 7th edition (2010). The T category from descriptive characteristics is revised in favor of size-based definition. In addition, tumors corresponding to the T4 category cannot be considered resectable because the definition of resectability is not agreed upon among different treatment facilities and evolves with advances in surgical technique [56].

In addition, the N category in the 8-view classification takes into account not only the presence of metastases to regional lymph nodes but also the number of affected lymph nodes [50]. The staging of exocrine pancreatic cancer proposed in the 8th edition of the American Joint Community for Cancer Research are summarized in Table 2.

Table 2 - Staging of pancreatic cancer proposed by the American Joint Community from Cancer Research (8th edition)

Стадия	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1-T3	N1	M0
III	any T T4	N2 any N	M0 M0
IV	any T	any N	M1

Computed tomography, the first-line imaging method for suspected pancreatic cancer, is considered the best method for primary diagnosis of pancreatic cancer because it provides reasonably high image quality. Magnetic resonance imaging is the second-line method for suspected pancreatic cancer and is usually used for doubtful cases. Both CT and MRI are highly sensitive for detection and T-criteria staging of pancreatic cancer, with sensitivities of up to 96% and 93.5%, respectively. Computed tomography is superior to MR in assessing tumor resectability with accuracy rates of up to 86.8% and 78.9%, respectively [50].

1.4 Treatment methods for pancreatic cancer depending on stage

Traditionally, surgical, radiation and chemotherapeutic methods of treatment are used in the treatment of PG cancer. In most cases, combined or complex treatment of the tumor is resorted to, but they can also be used independently.

Pancreaticoduodenal resection is the only method that allows to count on achieving a radical result of treatment in pancreatic cancer. At the same time, different variants of neoadjuvant treatment have been proposed to increase resectability.

It should be noted that variants of economical pancreaticoduodenal resection, such as, for example, V.A. Mikhailichenko's operation (1964) are currently performed only in exceptional cases and are of more historical interest, as they do not meet oncologic standards. Neoadjuvant polychemotherapy and radiation therapy play a significant role in improving the results of treatment of patients with extremely resectable pancreatic cancer [102, 103].

At present, the role of different variants of neoadjuvant polychemotherapy in pancreatic cancer continues to be studied worldwide. Clinics in America, Europe and Asia are investigating the possibility of using different chemopreparations and their combinations in extremely resectable pancreatic cancer.

Gemcitabine, capecitabine, 5-fluorouracil and docetaxel are considered as monotherapy. Among polychemotherapeutic regimens for neoadjuvant treatment of pancreatic cancer, combinations based on gemcitabine and 5-fluorouracil are most often considered.

Gemcitabine-based polychemotherapy regimens are as follows: gemcitabine + oxaliplatin; gemcitabine + S1 (tegafur); gemcitabine + cisplatin; gemcitabine + 5-fluorouracil + cisplatin; gemcitabine + docetaxel; gemcitabine + capecitabine; gemcitabine + capecitabine + docetaxel; gemcitabine + bevacizumab; gemcitabine + cetuximab; gemcitabine + 5-fluorouracil + cetuximab.

Among the polychemotherapy regimens based on 5-fluorouracil, the following are encountered: 5-fluorouracil + cisplatin ± cytarabine; 5-fluorouracil + irinotecan + oxaliplatin.

Thus, in the work based on the analysis of 39 studies on the results of neoadjuvant chemotherapy in pancreatic cancer in 145 patients, it was shown that complete tumor response (according to radiological examination) was achieved in 3.8% of observations, which was noted in 8 of the analyzed studies (20.51%). Partial tumor response was achieved in 20.9% of cases. Stabilization of the tumor process was noted in 54.3% of patients, and cancer progression - in 16% of observations. At the same time, the authors pay attention to the fact that gemcitabine-based regimens showed better results compared to 5-fluorouracil-based regimens. In addition, administration of the combination of drugs showed an advantage compared to monotherapy with chemopreventive agents. Also, partial tumor response and process stabilization were more pronounced in the group of patients with marginally resectable cancer compared to resectable tumor. The use of radiochemotherapy was found to show better results compared to chemotherapy [200].

Among 1458 patients, 1131 were operated on, with resections performed in 897 patients. The overall resectability was 57.7%, with resectable patients undergoing resection in 73.0% of cases and extremely resectable patients in 40.2% of cases.

The pure resection margin (R0) was achieved in 84.2% of cases: 88.2% and 79.4% in resectable and marginally resectable patients with locally advanced pancreatic cancer, respectively.

At the same time, the most promising neoadjuvant polychemotherapy regimens for pancreatic cancer are: FOLFIRINOX (5-fluorouracil / leucovorin + irinotecan + oxaliplatin) and gemcitabine + nab (nanoparticle albumin-bound) - paclitaxel. The FOLFIRINOX regimen is the first line of polychemotherapy in the treatment of patients with metastatic pancreatic cancer according to the results of the PRODIGY 4/ACCORD 11 trials [195].

Studies conducted in America and Japan indicate that neoadjuvant polychemotherapy regimens FOLFIRINOX and gemcitabine + nab-paclitaxel are promising, but it is noted that further clinical trials are required to establish their efficacy. In addition, according to the researchers, correction of neoadjuvant polychemotherapy regimens is possible.

At the same time, according to S. Heinrich et al. (2017), despite the lack of evidence regarding the effectiveness of neoadjuvant polychemotherapy for pancreatic cancer, increasing the probability of R-0 resections in patients with marginally resectable pancreatic tumors. Among the preoperative treatment modalities that are predictive of improved pancreatic cancer outcomes are various options for radiation treatment of the tumor. These include: 3D conformal radiotherapy, intensity modulated radiotherapy, image-guided radiotherapy, stereotactic radiotherapy (ablation), radioactive particle therapy (photons, protons, heavy ions) [86].

Assessing the possibilities of using these methods of preoperative radiotherapy, F. Roeder (2016) concludes that it is possible to expand the therapeutic window in the treatment of pancreatic cancer by reducing the toxicity of chemopreparations, damaging effect of radiation therapy, and increasing the biological effect of neoadjuvant treatment. In addition, the author notes that the use of a combination of intraoperative radiotherapy together with postoperative distant radiotherapy can significantly reduce the probability of locoregional recurrence [163].

The use of neoadjuvant chemoradiotherapy can also improve the results of treatment of patients with extremely resectable pancreatic cancer. In the studies conducted by S.-H. Zhan et al. (2018), it was shown that the use of radiochemotherapy allowed to achieve both complete and partial tumor response in more observations compared to chemotherapy. At the same time, tumor process stabilization was significantly higher in patients who received only chemotherapy [201].

In addition, the use of chemoradiotherapy does not allow to achieve an increased resection rate in patients with extremely resectable pancreatic tumors, while the rate of R0-resection was significantly higher in the radiochemotherapy group compared to the group receiving chemotherapy treatment alone (86.5% vs. 75.3%, respectively). At the same time, J. B. Rose et al. (2014), note that the use of chemoradiotherapy treatment can increase resectability in case of ineffectiveness of preoperative chemotherapy [167].

It should be noted that gemcitabine has radiosensitizing properties and its use as the basis of the radiochemotherapeutic treatment regimen allows to achieve better treatment results and survival.

Various postoperative treatment options are being considered to improve survival and outcomes in pancreatic cancer patients. These can include: adjuvant chemotherapy and radiation therapy, immunotherapy and gene therapy. It should be noted that in Europe, the chemotherapeutic approach is favored (Conko-001 study), while in the USA, chemoradiation is preferred [99].

The same drugs are used for adjuvant chemotherapy as for neoadjuvant chemotherapy for pancreatic cancer. As mentioned, the main regimens are FOLFIRINOX and gemcitabine-paclitaxel. Studies are currently underway to prioritize chemotherapy regimens. Most researchers are leaning towards the possibility of using the regimen. FOLFIRINOX as the first line of chemotherapeutic treatment allowing to achieve either stabilization of tumor process or disease control. At the same time, the high toxicity of such a regimen makes it necessary to choose patients carefully.

At the same time, ongoing studies show that the results of the FOLFIRINOX regimen in patients with R0-resections have already been obtained and are quite encouraging, which may lead to the development of a new treatment strategy for pancreatic cancer [115]. However, M. Krishnan et al. (2017) point out that all the benefits of adjuvant chemotherapy in patients with extremely resectable pancreatic cancer (stage III disease) are noted only in the early stages of treatment [110].

Various radiation therapy options are used after radical surgical treatment, however, according to N. Ma et al. (2017), the use of radiochemotherapy method can achieve better survival compared to radiation therapy. According to L.M. Miller-Ocuin et al. (2017), the use of radiochemotherapy in the postoperative period can improve treatment outcomes, overall survival in patients in whom the distance from the tumor to the resection margin was $\leq$ 1 mm [138].

Immunotherapy for pancreatic cancer is based on a combination of drugs aimed at blocking immune checkpoints. Immune therapy options can be divided into 3 categories:

1. Therapy aimed at increasing antigenic properties of tumor cells to activate antitumor activity of T cells;

2. Modulation of the microenvironment surrounding the tumor to attenuate immunosuppression;

3. Therapy aimed at breaking down the desmoplastic barrier surrounding the tumor, leading to its infiltration by T-cells.

It should be noted that despite the theoretical promise of immunotherapy in pancreatic cancer, all studies devoted to the use of any immunopreparations in monotherapy have shown their ineffectiveness; therefore, the search for variants of combined immunotherapy is currently underway.

Another promising avenue in the treatment of pancreatic cancer is gene therapy. Currently, gene therapy is at the starting stage of clinical trials and its introduction into the therapeutic program of pancreatic cancer treatment will not be rapid [168].

To date, the main directions of gene therapy are the use of tumor suppressor genes (TR53, p21WAF1, p16INK4A or DPC); genes that prevent angiogenesis and proapoptotic genes; the use of small non-coding mRNAs, interfering RNA, and antisense therapy; the use of oncolytic virotherapy (Oncorine H101, Onyx-15, T-VEC, Talimogen laherparepvec, Imlygic, etc.) [168].) [168].

Different methods of gene therapy are proposed: intravenous, subcutaneous administration of drugs, as well as injection directly into the tumor under the control of endosonography. Despite a large number of studies and encouraging results at the first stage, the results of the second stage of clinical trials did not show a significant difference between standard methods of treatment and gene therapy; therefore, new variants of gene therapy are currently being searched for.

CHAPTER 2. RESEARCH MATERIALS AND METHODS

2.1. Clinical characteristics of patients

Our study included 93 patients treated from 2019 to 2022 in the surgical department of the City Marian Hospital with pancreaticoduodenal masses. There were 44 males (47.31%) and 49 females (52.69%). The age ranged between 44-90 years, the average age of the patients was determined as 67 ± 0.74 years.

As the results of pathohistologic examination, presented in Figure 6, have shown, in the majority of the examined - 68 (73,12%) pathohistologically revealed adenocarcinoma of various degrees of differentiation, in 5 people (5,38%) cystadenoma. There were also revealed the formations of duodenum in 7 (7,53%) patients, of terminal choledochus in 12 (12,90%) patients, of duodenum in 1 (1,08%) patient.

The distribution of patients according to the results of histology, treatment methods and types of palliative interventions is shown in Figures 4-6.

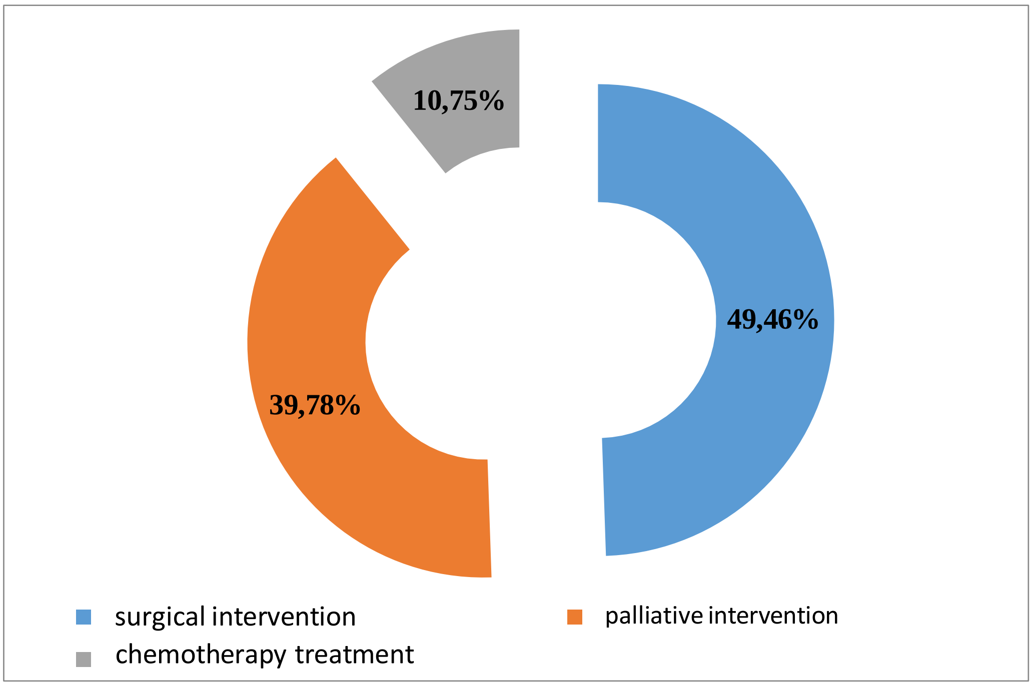


Figure 4 - Distribution of patients by treatment method

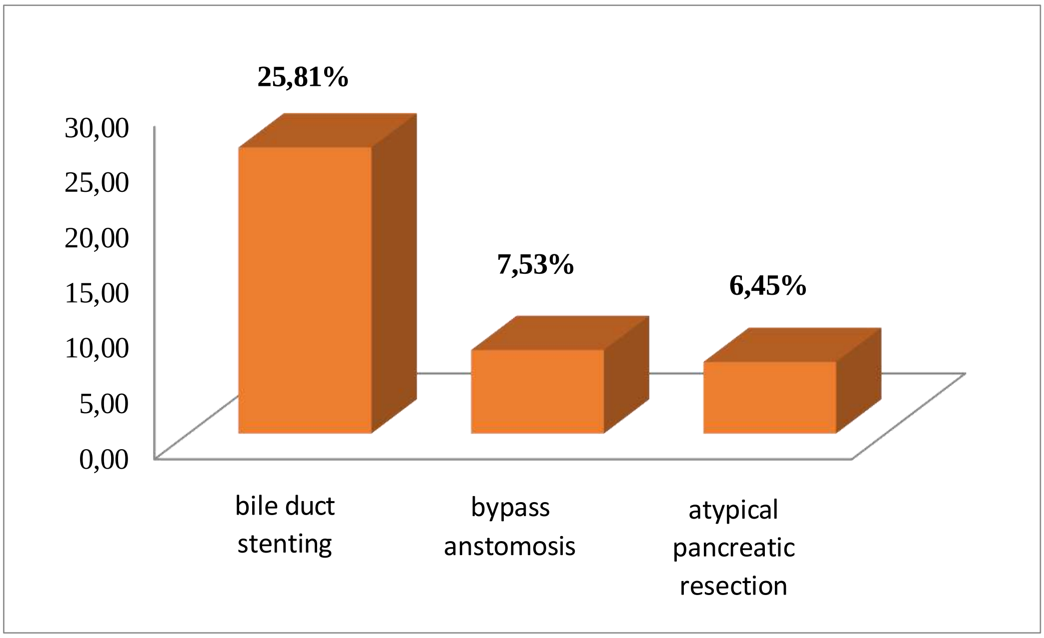


Figure 5 - Types of palliative interventions performed

As shown in Figure 4, out of the total number of patients 46 (49.46%) underwent surgical intervention - pancreaticoduodenal resection with variants of lymphodissection.

In 37 patients (39,78%) palliative interventions were performed (Fig. 5), in the form of the following manipulations:

- 24 patients (25,81%) - stenting of bile ducts,
- 13 patients (13,98%) - bypass anastomosis,

The remaining 10 (10.75%) patients were treated with chemotherapy due to concomitant pathology.

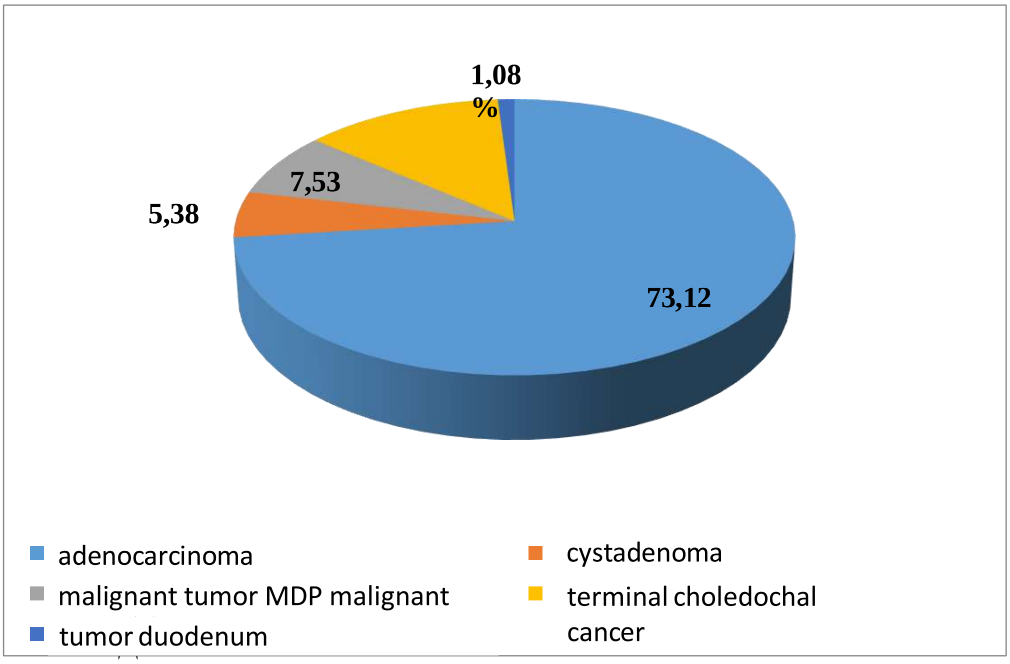


Figure 6 - Results of pathohistologic examination

The cancer process was staged according to the TNM classification (the 8th revision of 2017). The distribution of patients by stage is shown in Figure 7.

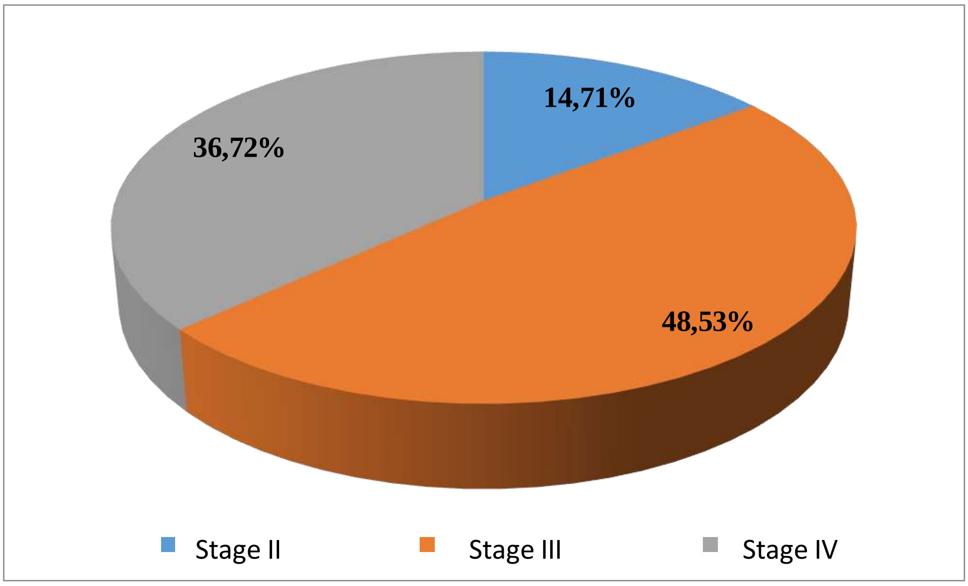


Figure 7 - Staging results

As can be seen from the diagram of Figure 7, adenocarcinoma corresponding to stage II was detected in 10 (14.71%) patients, stage III - in 33 (48.53%) patients, stage IV was determined in 25 (36.72%) patients.

Magnetic resonance tomographic study of abdominal cavity organs was performed in all 93 patients. Endoscopic ultrasonographic study (EUS) of the pancreaticoduodenal zone was performed in 59 (63.44%) patients, computed tomography examination of 39 patients.

Three-dimensional model was constructed in 58 (62.37%) patients, including 43 (46.24%) patients with integration of MRI+EUS data.

Also, 26 (44.83%) patients out of 58 patients had three-dimensional models built both on the basis of MRI and CT, which allowed comparative analysis.

2.2 Methods of investigation of patients

2.2.1 Magnetic resonance imaging in the evaluation of pancreaticoduodenal masses

All studies were performed on an Ingenia MR tomograph (Philips Medical Systems, the Netherlands) with a magnetic field induction of 3 Tesla. All patients underwent native abdominal and retroperitoneal examination supplemented with magnetic resonance cholangiopancreatography (MRCPG) protocol, as well as dynamic contrast enhancement with data collection in arterial, portal, and delayed phases.

Twenty minutes before the study, patients received an intramuscular injection of a peristalsis inhibitor. The study was performed in the supine position to maximize patient comfort. The patient's arms were placed along the torso to ensure adequate venous access.

The coil for radiofrequency signal reception was placed directly over the area of interest, for proper orientation of the coil, its center was placed at the level of the lower border of the ribs. The coil was tightly fixed to the patient's body using fixation straps.

For synchronization with respiration we used modifications of the ROPE technique, which reduces motor artifacts on MR images. For this purpose, an external respiration sensor in the form of a respiratory cushion was fixed on the diaphragm area.

During the examination, auditory contact with the patient was maintained to ensure psychological comfort and motivation for adequate execution of commands.

Scanning protocol

At the time of the study, all patients underwent ultrasound of the abdominal cavity organs, as well as clinical and biochemical blood analysis, which allowed to diagnose "mechanical jaundice" and to identify the presumed block at the level of the head of the pancreas.

The pancreas, is a lobular parenchymatous organ with alveolar-tubular structure, located retroperitoneally and having a rather complex anatomo-topographical location.

To form the most informative protocol, we initially planned to obtain T2-VI weighted images with partial filling of K-space on breath-hold to obtain an overview image of the abdominal cavity. This allowed to quickly separate patients with complications of cholelithiasis (e.g., Mirizzi syndrome) from the patients of interest.

Then, T2-VI images were performed using the turbospin-echo technology, including fat-suppressed images, to evaluate structural changes and the presence of fluid in the fascial spaces.

Further, diffusion-weighted images with ADC-mapping were obtained in the same plane to evaluate cellularity and areas of necrosis in the structure of the mass, differential diagnosis with pseudotumor pancreatitis, and evaluation of reactive pancreatitis associated with a Vrsung's duct block. B-factor was used so as to reduce the effect of IVIM-type capillary blood flow. Sequencing parameters are summarized in Table 3.

Table 3 - Information on sequences and MRI study parameters of patients with suspected pancreatic head cancer

Sequence name	**Projection**	**Type**	**fat suppression**	**TR. мс**	**TE. мс**	**FOV, мм**	**Cut thick-ness, mm**	**Gap between cuts, mm**	**Voxel size. mm**	**Number of cuts**
T2_VI with half filling of K-space	coronal	2D	no	1100	50	450x400	5	-0,3	1,2x1,36	>42
T2_VI with half filling of K-space	axial	2D	no	1400	94	450x450	5	-0,3	1,2x1,36	>42
T2_VI with half filling of K-spaces	sagittal	2D	no	1200	92	400x400	5	-0,3	1,2x1,36	>42

T2_VI SPIR RT	axial	2D	yes, spin suppres sion	878	50	300	5	0,5	1=4x1,7	>42
Diffusion-weighted image with b=0;800;1200	axial	2D	yes= spin suppres sion	305?	90	380	5	20	3x3	50
mDIXON>~ T1-VI	axial	3D	no	3,65	1,3/2,6	450x395	3=5	-1,7	1,8x1,8	60

Abbreviations used in the table: TR - Repetition time; TE - Echo time; HR - High resolution (HR-HR-MRI) images, TSE - turbospin-echo sequences, 2D - two-dimensional sequences, 3D - three-dimensional sequences allowing multiplanar reconstruction; FOV - Field of View - field of view or field of scanning, representing the area of the image in one or another plane.

On sequentially performed slices in T2-VI mode it was possible to trace the course of ducts, pancreatic tissue, as well as altered areas in the region of the organ head, having a pronounced hypointense MR-signal. The obtained images are presented in Figures 8 and 9.

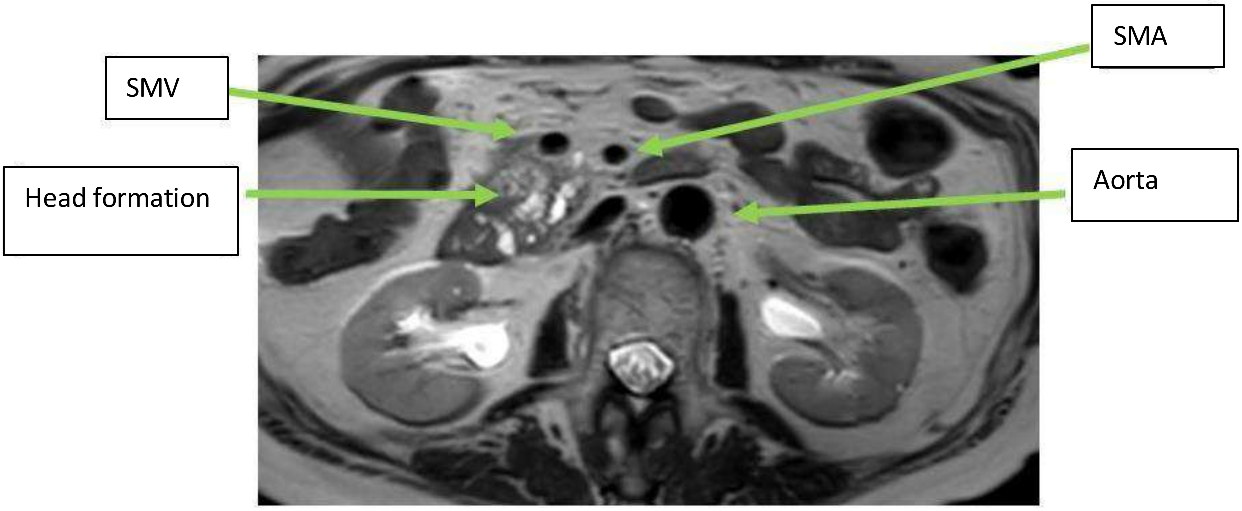


Figure 8 - Patient N., 56 years old, on T2-VI in the head of the pancreas a solid mass with dimensions up to 30*25*32mm, spreading into the surrounding tissue, with intimate adhesion to the superior mesenteric vein was visualized in the head of the pancreas

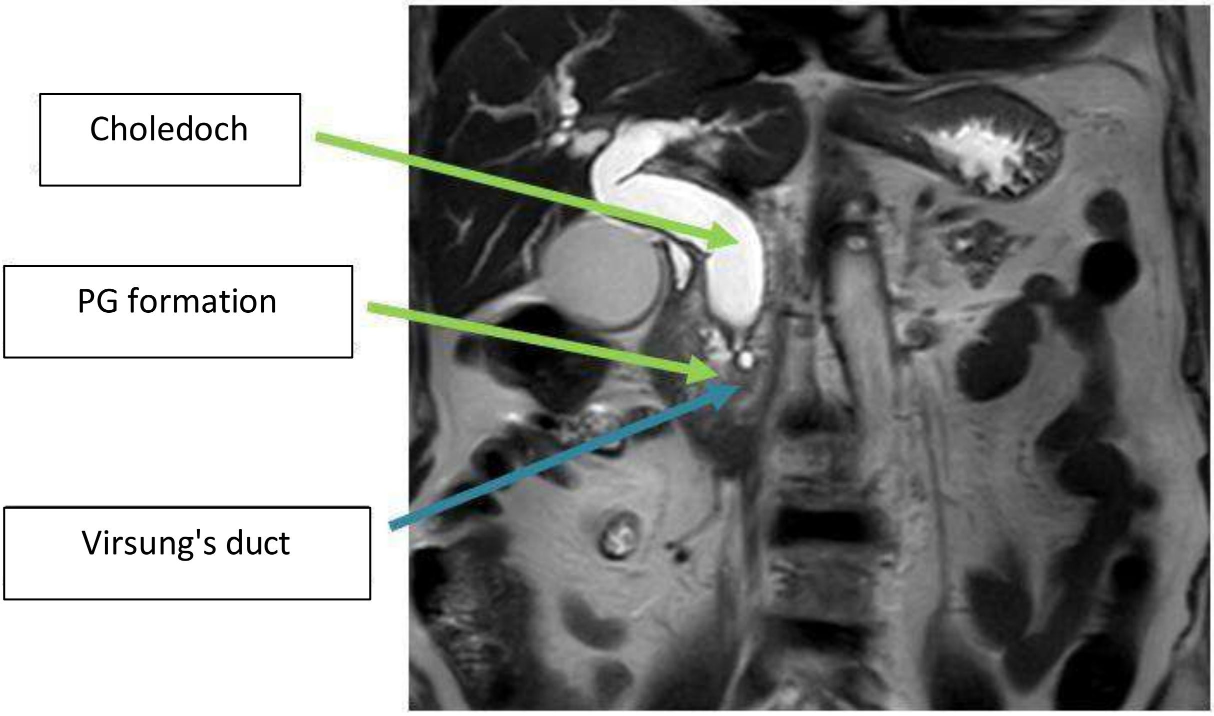


Figure 9 - Patient N., 56 years old, on T2-VI according to the described technique a pancreatic head mass with formation of biliary hypertension is visualized, choledochus is dilated up to 18 mm

MRCPG is a T2-VI-weighted, high-TE time-weighted three-dimensional image of the biliary tree. If biliary hypertension develops, this sequence allows accurate assessment of the level at which bile duct block occurs, as well as evaluation of its type, extent, suprapancreatic and intraduodenal choledochal involvement. The parameters are summarized in Table 4. The obtained images are presented in Figure 10.

Table 4 - MR-scanning parameters in the MRCPG mode

Tomo-graph	Sequence name	Projection	Type	Fat suppression	TR, ms	TE, ms	FOV, mm	Slice thick-ness, mm	Gap between slices, mm	Voxel size, mm	Number of slices
Philips Ingenia	MRCP	oblique coronal	3D	no	1000	500	380x440	2	-1	1x1x1	80
Philips Ingenia	MRCP	axial	3D	no	1000	500	380x440	3	-1	1x1x1,5	90

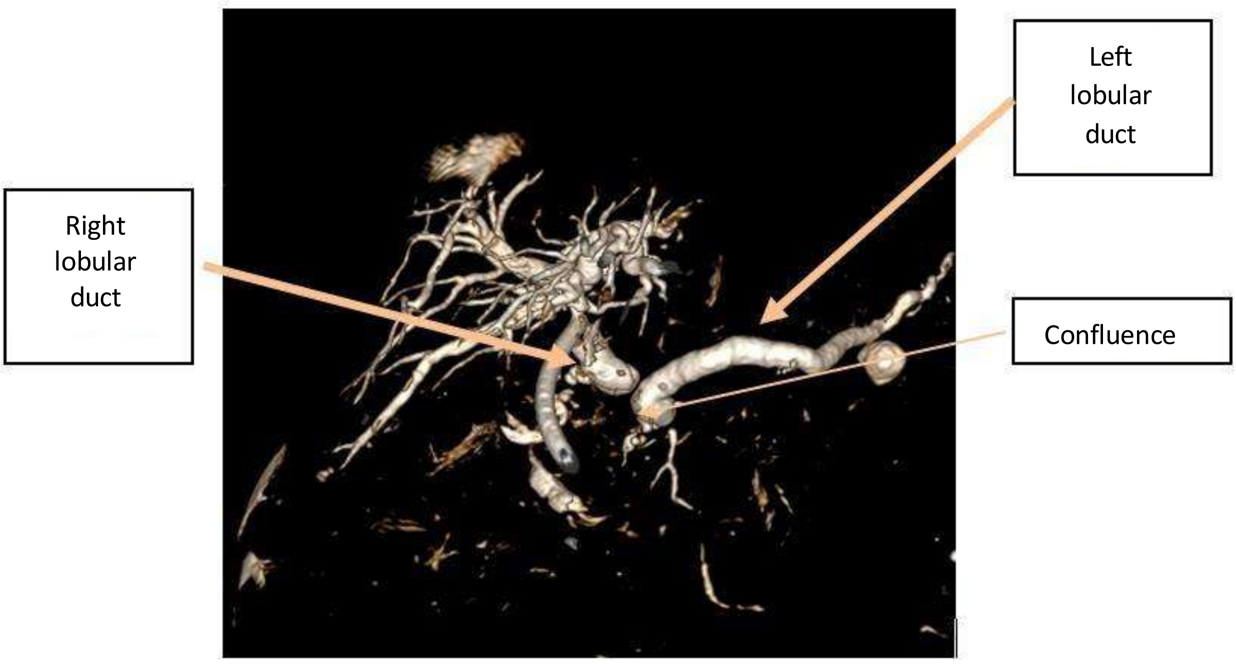


Figure 10 - Patient N., 56 years old, MRCPG revealed irregular dilation of bile ducts and main pancreatic duct due to blockage at the level of the head of the pancreas

After evaluation of the exact localization of the biliary tree lesion, targeted images were performed to assess the local prevalence and, together with this, the resectability of the mass. For this purpose, high-resolution T2-VI images were performed using breath-hold compensation as described above. High-resolution T2-VI was used to correlate the extent of the mass with TNM. Oblique axial planes perpendicular to the course of the duodenum were used. To assess the relationship with the branches of the ventricular trunk, portal vein, in some cases the inferior vena cava, and the duodenal wall. The oblique-coronal plane constructed along the isthmus and head of the pancreas was used to evaluate the structural changes. The same plane was necessary for visualization of unchanged gland tissues and those affected by neoplastic process.

These sequences were of interest for 3D modeling, which, in turn, determined the requirements for zero slice spacing.

Contrast enhancement was performed dynamically to assess neoangiogenesis and the interstitial compartment for more accurate localization of the borders of the mass, as well as the vascular structure of the prural trunk. Data were collected in the arterial, portal, and delayed phases, taking into account arterial blood inflow due to branches of the trunk and branches of the mesenteric artery, as well as outflow to the splenic vein and other portal vein tributaries. Of particular interest were sequences of 4D-THRIVE type, which use partial filling of K-space and allow obtaining images with the highest temporal resolution without losing spatial resolution. The parameters of the sequences used are summarized in Table 5.

In an additional study with a vasopressin analog, 1 minute before the study, the drug was administered intravenously to patients and a standard study protocol was performed twice, during which the ratio of the tumor to the main venous vessel was evaluated. In the case of the occurrence of a fatty layer in the structure of the vessel-tumor against the background of the action of the vasopressin analogue, the invasion was not confirmed.

Table 5 - Parameters of data acquisition during dynamic contrast enhancement

Tomograph	Philips Ingenia
Sequence name	4D-Thrive
Projection	axial
Type	3D
Fat suppression	dixon
TR, ms	3
TE, ms	1,3
FOV, mm	400x350
Slice thickness, mm	3
Gap between cuts, %	-2
Voxel size, mm	2x2x2
Number of slices	115
Time	3 sec

Main characteristics and parameters that are evaluated when describing a magnetic resonance study

Initially, we assessed the localization of the mass and its type, namely, whether it was solid, cystic, and whether it had predominantly periductal spread. In the presence of periproctal spread along the course of the choledochus, the involvement of its suprapancreatic and intraduodenal parts was determined.

Further, we evaluated the size of the mass in three planes, as well as the size of the head, body and tail of the gland in the coronal and axial planes. The next step was to analyze the local prevalence by assessing the involvement of:

- the surrounding plaque;
- the portal vein and its tributaries;
- of the trunk of the jejunum and its branches;
- the superior mesenteric artery;
- superior mesenteric vein.

When analyzing the vascular involvement, its type was evaluated - adjoining or enveloping, for which we used oblique-axial and oblique-coronal and oblique-sagittal sequences, as well as SPACE-type sequences.

At the next stage we analyzed the severity of biliary hypertension, the type of bile ducts structure and also evaluated the secondary changes of liver parenchyma to decide on the possibility of percutaneous hepatic cholangiostomy.

Along with that we evaluated the changes of lymph nodes, taking into account the size and shape of the node, as well as the presence of fat gates. Localization of lymph nodes was performed according to the accepted JSED classification.

The sensitivity and specificity of the method were determined by ROC-analysis.

2.2.2 Endoscopic ultrasonographic study in assessing the degree of invasion and lymphogenic metastasis of pancreaticoduodenal masses

To assess the invasion of pancreatic head tumors into vessels and to determine the presence of regional metastasis, patients underwent endoscopic ultrasonography of the pancreaticoduodenal zone using the push end pull technique. 12 hours before the study the patients stopped food and liquid intake to avoid the formation of ultrasound artifacts in the lumen of the upper gastrointestinal tract. In order to ensure maximum patient comfort and safety, as well as to complete the study, intravenous sedation was used. To perform the mentioned study we used convex echoendoscope UCT 180 of "Olympus" company with radial transducer and diameter of working part 13,4 mm and combined process EUPREMIER PLUS which are integrated into video system EVIS EXERA II-180CV of "Olympus" company. The sector of view in the axial plane was 170 degrees, scanning frequency from 7.5 to 20 MHz. At EVIS it was possible to evaluate the degree of tumor invasion, its localization and extent, as well as the severity of intra-abdominal lymphadenopathy and tumor connection with adjacent main vessels.

The sensitivity and specificity of the method were determined by ROC-analysis.

2.2.3 Evaluation of tumor invasion using three-dimensional modeling

Building three-dimensional models

Three-dimensional models were STL (Stereolithography) files that described a three-dimensional object as a surface with a defined normal (a unit vector perpendicular to the surface). The method consists of two stages. At the first stage, the patient underwent MRI of the abdominal cavity organs in the native and then in the arterial and venous phase with intravenous dynamic contrast enhancement (Omniscan at a dose of 0.2 ml/kg body weight). To build 3D models we used free programs 3D-slicer, Mimics, which allowed semi-automatic model building for further assessment of anatomo-topographic relations. Then we performed computer modeling by integrating data on regional lymph nodes according to EUS data with subsequent color mapping of the affected nodes (Figs. 11 and 12).

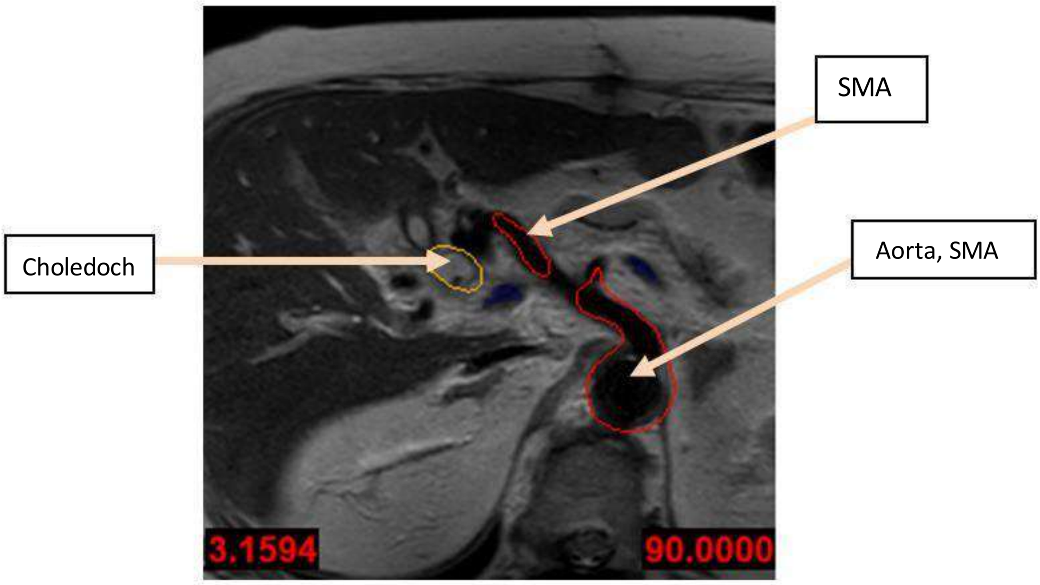
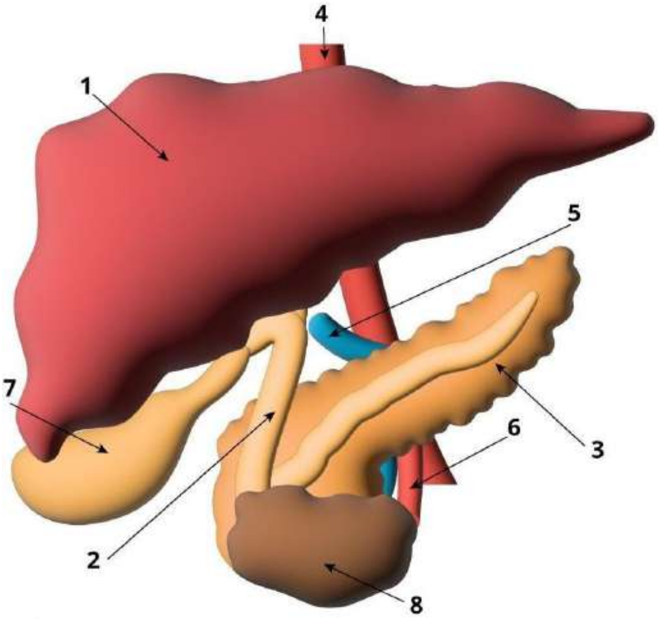


Figure 11 - Formation of semi-automatic segmentation by the rate of fluid flow through the system of the primal trunk, superior mesenteric artery, choledochus



1. Liver
2. Choledoch (bile duct)
3. Pancreas
4. Aorta
5. Superior mesenteric vein
6. Superior mesenteric artery
7. Gallbladder
8. Formation

Figure 12 - Three-dimensional model of the pancreaticoduodenal zone

Three-dimensional models were also built on the basis of X-ray computed tomography (RCT). In RCT, the result of the study was a series of slices made at a constant interval (step), which is set with regard to the purpose of the study and usually ranges from 0.5 mm to 5 mm. The obtained planar slices were studied using medical computer programs, 3D-slicer, Mimics, which are equipped with the ability to build three-dimensional models. The method of three-dimensional model generation from serial images is based on "lofting" (fusion) - the process of obtaining three-dimensional figures from flat objects.

When creating a three-dimensional object from CT images, the obtained slices are sequentially arranged and then merged by a computer program according to the contours of the objects marked on them. That is why, the smaller the interval between slices, the more reliable will be the obtained three-dimensional object. In case a large section of the study is missed, the information on it will be absent and the features of any damage, pathological change or disease will be impossible to assess.

The peculiarity of the created three-dimensional model is that it is not hollow, as models created by three-dimensional scanning, and, therefore, analyzing the three-dimensional model created on the basis of CT images, it is possible to identify separate systems and tissues, as well as to measure and evaluate various processes in three planes of the coordinate system. The three-dimensional model can be exported to various graphic editors for further work with it, which is already used in various fields of medicine.

The sensitivity and specificity of the method were determined by ROC analysis.

CHAPTER 3. COMPARATIVE RESULTS OF PREOPERATIVE STAGING OF PANCREATIC HEAD CANCER AND INTRAOPERATIVE FINDINGS

At present, magnetic resonance imaging is actively used to assess the local spread of pancreatic head cancer and is supplemented by endoscopic ultrasonography (EUS), which allow to reliably assess the local spread of carcinoma and the presence of secondary changes (local and distant).

Patients with distant metastases according to the instrumental examination data were not included in this observation.

3.1 Magnetic resonance imaging findings in the diagnosis of the degree of invasion and regional metastasis of pancreatic head cancer

Magnetic resonance imaging (MRI) of the abdominal region was performed in 93 patients, according to which 21 (22.58%) had unresectable pancreatic tumor. Patients with diagnosed tumor of the pancreas head, having signs of resectability or relative resectability, were subsequently operated in the volume of pancreaticoduodenal resection with lymphadenectomy.

Subsequently, the MR examination data were compared with the intraoperative picture and the results of pathologoanatomic report.

When assessing the extent of the pancreatic head tumor according to MR data, 26 (27.96%) patients were found to have invasion corresponding to T2, 35 (37.63%) patients were found to have invasion corresponding to T3 criteria, and in 32 (34.41%) patients the tumor was defined as T4 stage.

According to the intraoperative picture and pathologic response, 24 (25.81%) patients had T2 invasion, 41 (44.09%) patients had T3 invasion, and the remaining 28 (31.11%) patients had T4 invasion (Table 6).

Table 6 - Distribution of patients in assessing the extent of pancreatic head tumor according to MRI and intraoperative findings

Degree of invasion	MRI assessment of resectability	Intraoperative assessment of resectability
T2	17 (29%)	15 (25%)
T3	22 (37%)	26 (44%)
T4	20 (34%)	18 (31%)

Thus, the sensitivity of the MRI method in assessing the tumor node size was 93.2%, specificity - 98.2% ($p < 0.05$).

When analyzing the degree of pancreas head tumor invasion into the main vessels (according to Anderson's system) to estimate resectability according to magnetic resonance imaging, 27 (29,03%) patients had cancer recognized as resectable, 37 (39,78%) patients showed signs of borderline resectability, and in 29 (31,18%) patients the tumor met the criteria of non-resectability.

According to the intraoperative picture in 12 (12,90%) patients the degree of invasion exceeded the criteria of resectability, which is presented in Table 7.

Table 7 - Distribution of patients in assessment of resectability of pancreatic head tumors according to MRI and intraoperative findings

Category	MRI assessment of resectability	Intraoperative assessment of resectability
Resectable	17 (29,03%)	46 (55,91%)
Borderline resectable	24 (39,78%)	—
Non-resectable	18 (31,18%)	13 (44,09%)

In the subsequent ROC analysis, the sensitivity of the method in assessing tumor invasion into trunk vessels was 90.6% and specificity was 76.9%, as shown in Figure 13

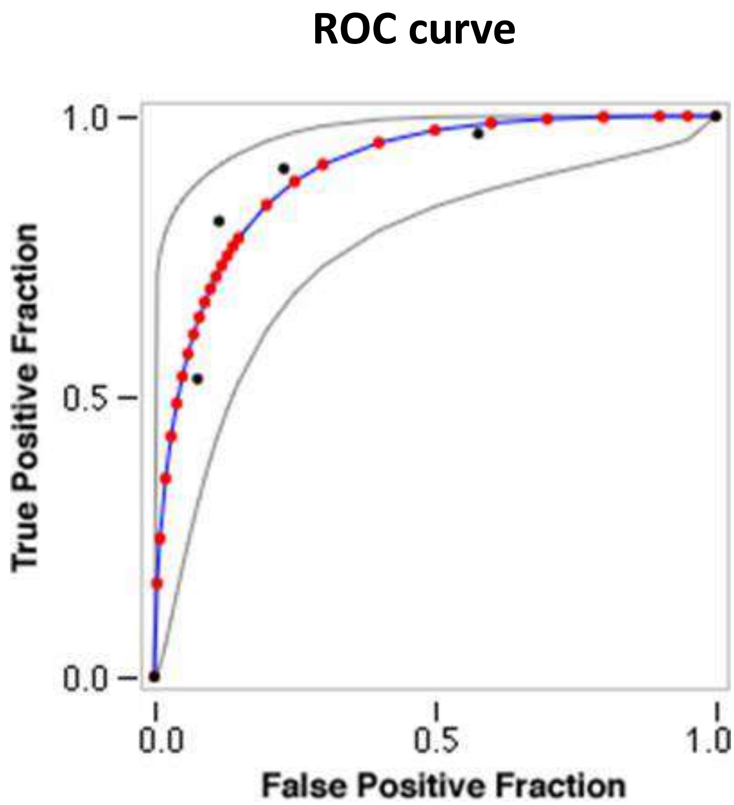


Figure 13 - Results of ROC analysis of tumor invasion into the main vessels

At intraoperative and pathologoanatomical evaluation of lymphatic collectors in 13 (22,0%) out of 59 patients MRI diagnosed secundar lesion of lymph nodes, in 10 (17,2%) patients the data were confirmed histologically.

In 8 (14%) out of 59 patients, who according to MRI data had changes of lymph nodes, which were considered as nonspecific lymphoadenopathy, 3 of them had metastatic lesion at histologic evaluation, in the rest secondary lymphadenopathy was not revealed.

The sensitivity of MRI in detecting metastatic lesion of regional lymph nodes in the area of pancreatic head tumor was 50%, specificity - 84,9%.

Thus, MRI is an informative method of preoperative staging of pancreatic head cancer, but the severity of regional lymphadenopathy cannot always be estimated accurately enough. Therefore, magnetic resonance imaging cannot be considered as an independent method for reliable assessment of lymph node changes and, therefore, for determining the scope of surgical intervention.

3.2 Results of endoscopic ultrasonography in the diagnosis of the degree of invasion and lymphogenic metastasis of pancreatic head cancer

Endoscopic ultrasonography was performed in 59 patients. Of these, 40 patients underwent surgical interventions in the form of pancreaticoduodenal resection, as well as palliative interventions in the form of bypass gastrojejunoanastomosis. Then the results were compared with the intraoperative picture and the results of histologic examination. According to the EUS data the presence of volumetric formation of the pancreas head was visualized in 52 (88,1%) patients. At that, in 6 (10,2%) patients the degree of spreading was estimated as T4, and at histologic examination it corresponded to T3. In 4 (6.7%) patients, the stage of spread was designated as T3, and at histologic evaluation was T2. In 2 (3.4%) patients, the stage of spread was designated as T2 and on histologic examination was T3, as shown in Table 8.

Table 8 - Comparative analysis of EUS and pathohistologic examination data

EUS data		Pathohistologic examination	
Degree of invasion (cT)	Number of patients (n)	Degree of invasion (pT)	Number of patients (n)
T2	15	T2	15
T3	20	T3	26
T4	24	T4	18

As can be seen from Table 8, complete concordance of EUS results with pathologic data was determined in 40 (67.8%) cases. The sensitivity of EUS in assessing T stage was 76.9%, specificity - 50%.

According to EUS data secondary altered lymph nodes were visualized in 18 (30,5%) patients out of 59 examined, which was confirmed by the results of histological examination. At the same time in 2 (3,4%) patients secondary lymphadenopathy was not confirmed. Thus, the sensitivity of EUS in detection of metastatic lymph nodes was 90,0%, and specificity - 100%.

Consequently, EUS of the pancreaticoduodenal zone is an effective method to determine the local prevalence of pancreatic head tumors, as well as the severity of regional lymphadenopathy. It allows planning the volume of surgical intervention, which is most important when choosing the volume of lymphadenectomy. However, the disadvantage of the method was subjective assessment of the size of the mass, which was accompanied by an increase in the number of false-positive results.

3.3 The role of three-dimensional modeling in the diagnosis of local spread of cancer process

The proposed method allows to assess the size and localization of the tumor, the stage of invasion and the relationship of the cancer with adjacent anatomical structures and, most importantly, with the main vessels. These parameters of the tumor process make it possible to plan the sequence of treatment of patients, as well as the volume of surgical intervention with individual selection of lymphodissection variant.

The main objective of this method is to increase the reliability of the preoperative stage of the oncological process in pancreatic head cancer by forming an individual three-dimensional model of the pancreaticoduodenal zone with a visual picture of regional lymph nodes. The 3D model was created on the basis of multiplanar reconstruction of MRI images of abdominal cavity organs and supplemented with integrated EUS data of regional lymph nodes for each specific patient. The presented three-dimensional model allows combining the advantages of both methods and achieving preoperative visualization of the tumor process, the degree of its invasion into vessels and regional lymphogenic metastasis.

The presented method is distinguished by the most accurate model of pathological changes in the pancreaticoduodenal zone, built individually for each patient, which differs from all known ones. By changing the viewing planes of the three-dimensional model, there is a possibility of its comprehensive visual evaluation. In addition, the color image facilitates the perception of the preoperative picture by the attending physician planning surgical intervention. The hybrid nature of the three-dimensional model increases the diagnostic capabilities and value of the method.

As a result, by means of three-dimensional visualization on a multimodal basis of the obtained color images with integration of altered lymphatic collectors, the positive result of the method is provided, in the form of preoperative assessment of the oncological process, planning of the primary treatment method and surgical intervention taking into account the volume of lymphatic dissection.

To illustrate the obtained results we present several clinical examples.

Patient S., 65 years old, was hospitalized on 20.09.2012 in the Mariinsky Hospital of St. Petersburg. On admission, he complained of jaundice of the skin, unmotivated weight loss of up to 13 kg. No clinical data for acute surgical pathology were revealed at the initial examination. In the course of further examination in the hospital the patient was diagnosed with pancreatic head mass TxNxM0. MRI and EUS data revealed a tumor of the pancreas head with signs of relative resectability (the tumor contacts the superior mesenteric vein by more than 180°), without signs of lymphogenic metastasis (Fig. 14,15,16).

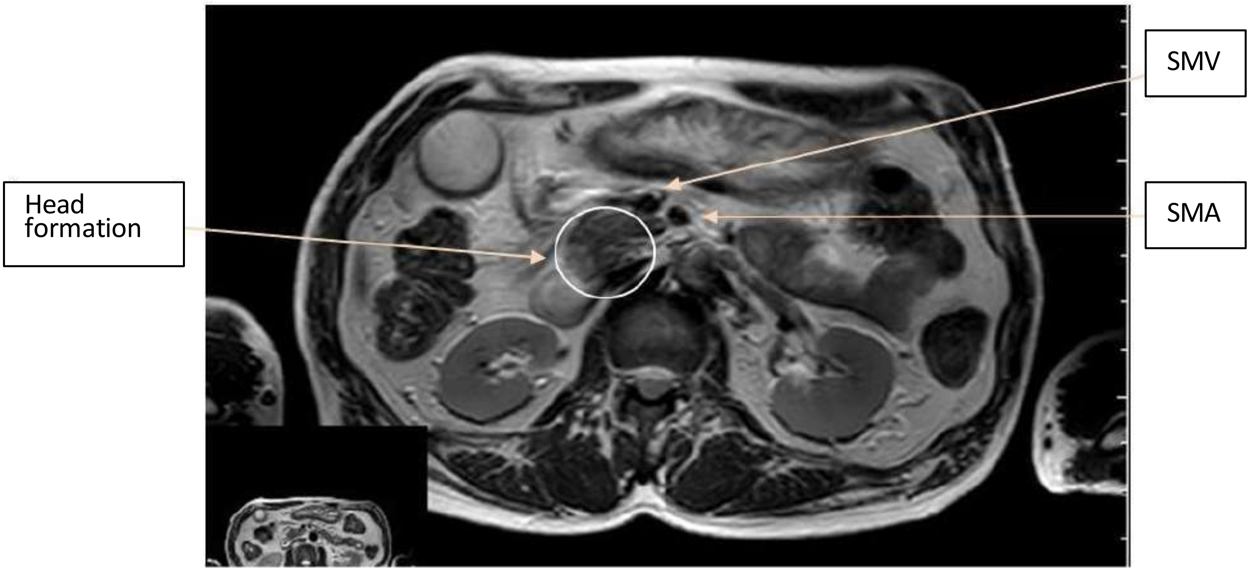


Figure 14 - Magnetic resonance imaging, T2-VI. A volumetric mass of the pancreatic head is visualized, encircling the SMV >180°

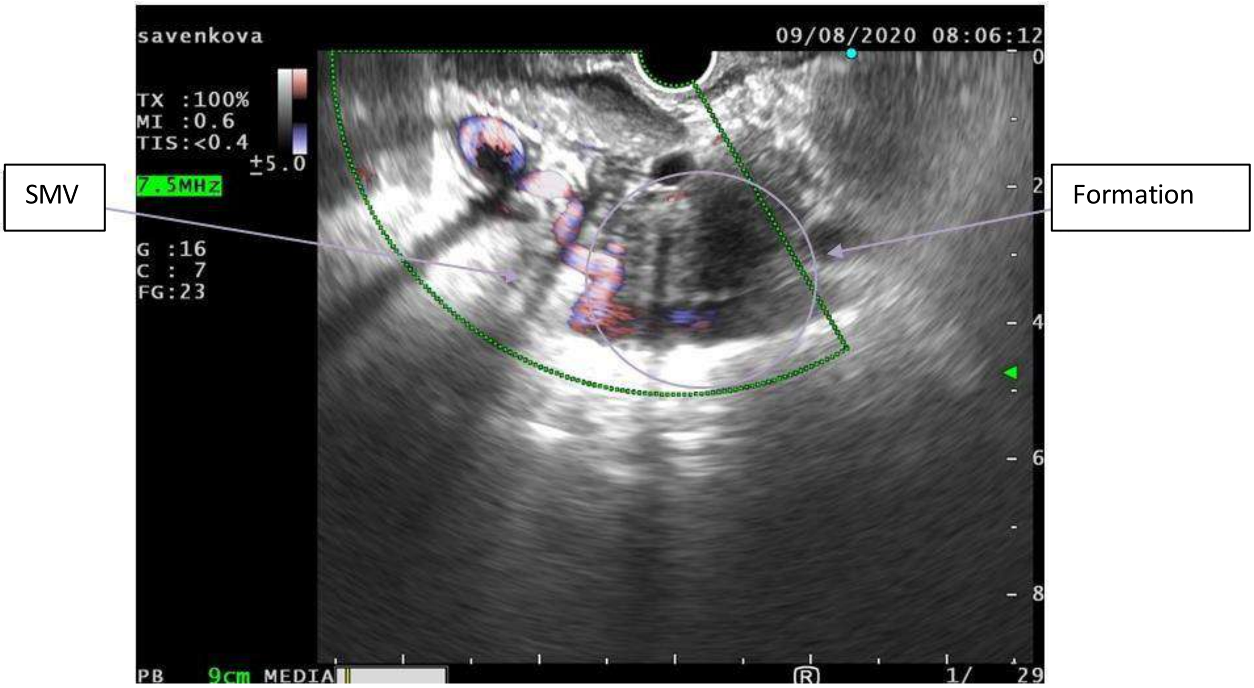


Figure 15 - Endosonogram. An irregularly shaped hypoechogenic mass with signs of invasion into the SMV is detected in the projection of the pancreas head

Three-dimensional modeling of the pancreaticoduodenal region was performed on the basis of graphic data using the above method, and the extent of tumor contact with the superior mesenteric vein (SMV) was determined to not exceed 180° of circumference, up to 5 mm, which is a sign of resectability of the pancreatic head and corresponds to stage T3 N0 (Fig. 16).

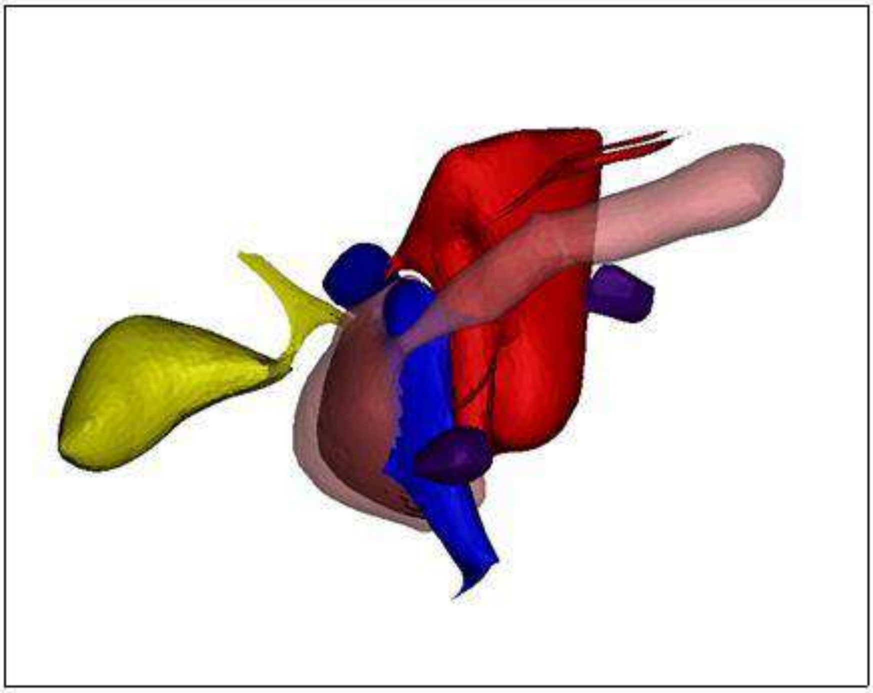


Figure 16 - 3D model of the pancreaticoduodenal area of patient C.

Intraoperatively, a tumor of the pancreas head with the size up to 3.3 cm, extending beyond the organ, with intimate adherence to the SMV, without signs of its invasion was detected (Fig. 8). The patient underwent pancreaticoduodenal resection and lymphodissection in the volume of D2.

The patient was discharged in satisfactory condition on the 13th day after the operation under the supervision of oncologist at the place of residence. At the control examination of the patient in 6 months there was no evidence of continued tumor growth.

Patient M., 77 years old, was admitted to the Mariinsky Hospital of St. Petersburg with complaints of jaundice of the skin and moderate abdominal pain. After hospitalization, a comprehensive examination was performed, which revealed a T3 Nx M0 pancreatic head mass. According to the magnetic resonance imaging data, in the head of the pancreas a mass with the size up to 4.5 cm, intimately adjoining the IVC, involving the SMV, was determined (Fig. 17). Structurally altered lymph nodes were visualized according to EUS.

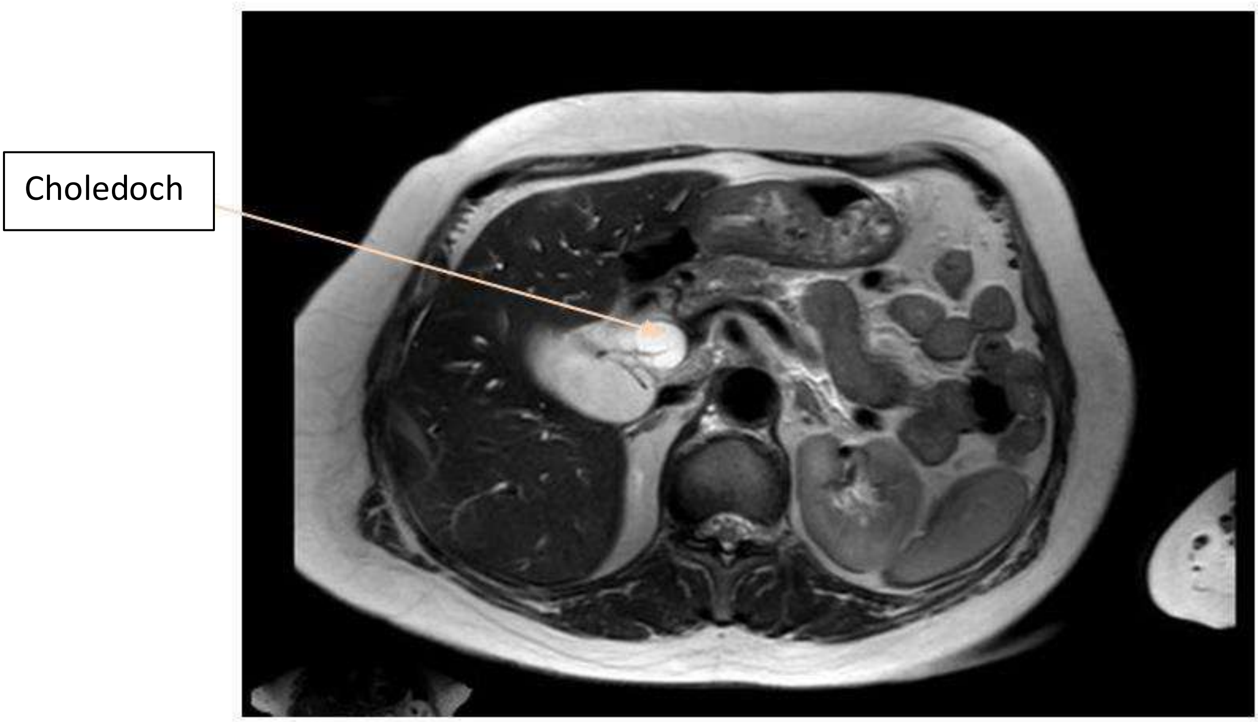


Figure 17 - Magnetic resonance imaging of the abdominal cavity. Volumetric formation of the head of the PG is visualized, with the formation of biliary hypertension.

On the basis of MRI graphic data, we performed 3D-modeling of the pancreaticoduodenal zone. We visualized a tumor of the head of the PG intimately adjacent to the inferior vena cava, without its invasion, but with signs of invasion of the superior mesenteric vein, less than 180° of circumference (Fig. 18). The data correspond to stage T3 N1.

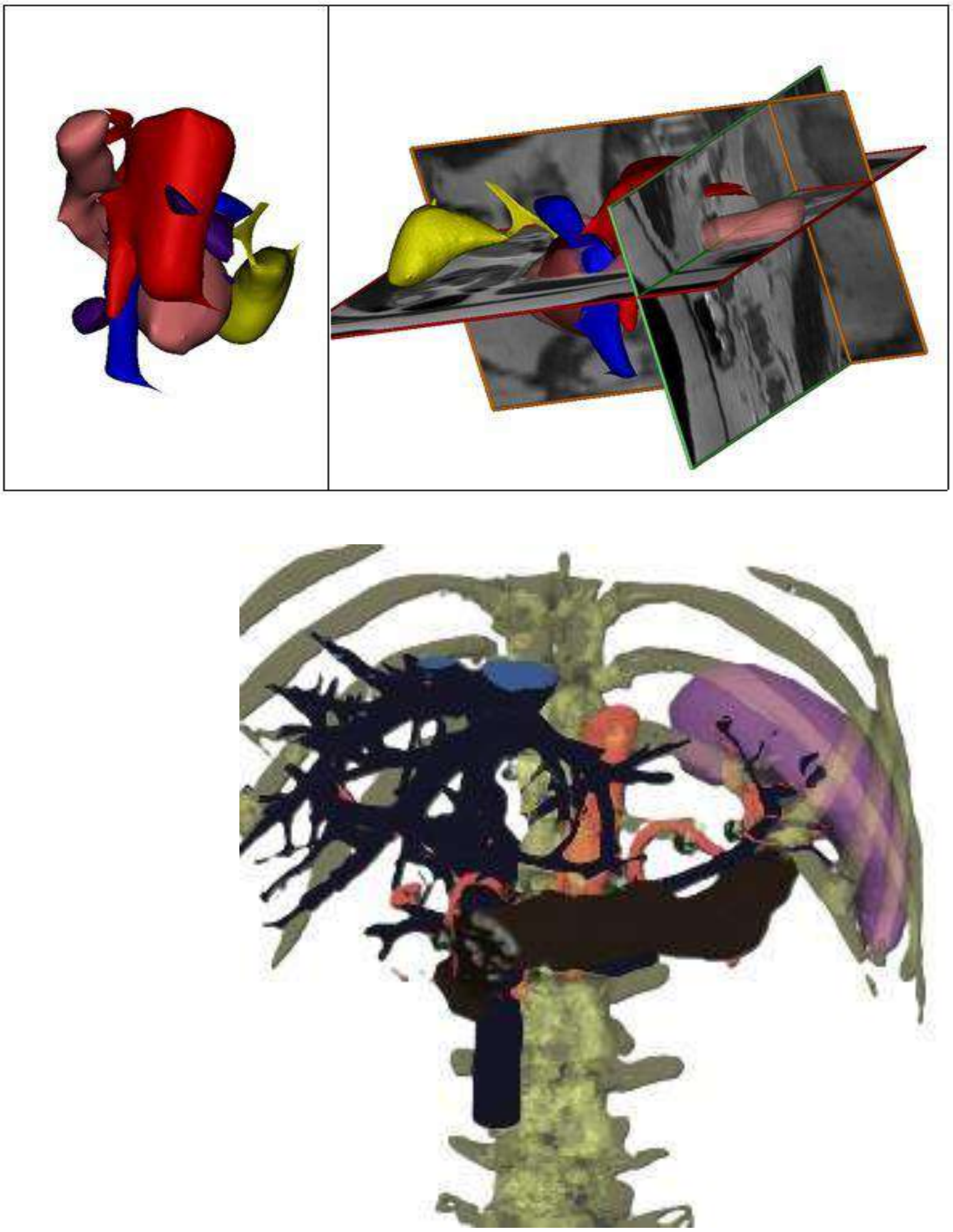


Figure 18 - 3D model of the pancreaticoduodenal zone

Taking into account the signs of tumor resectability, the patient underwent surgery in the volume of pancreaticoduodenal resection with lymphodissection in the volume of D2 (Fig. 19).

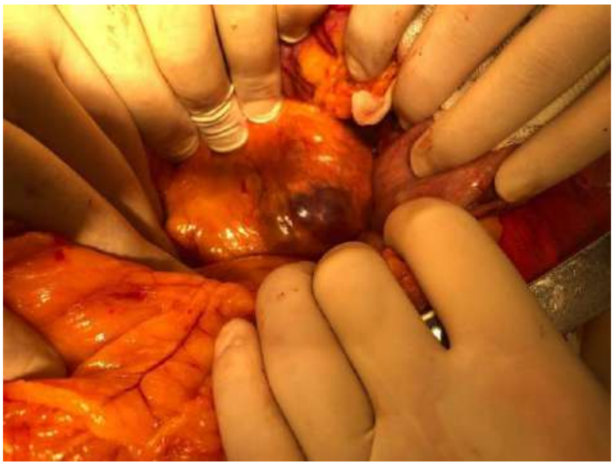


Figure 19 - Intraoperative photograph. A volumetric mass with signs of SMV invasion is visualized in the area of the head of the PG

The postoperative period was complicated by postoperative gastrostasis. The patient was discharged under the supervision of an oncologist at the place of residence on the 22nd day after surgery.

Thus, three-dimensional images gave the operating surgeon a visual idea of the proposed scope of surgical treatment at the preoperative stage, thereby optimizing the tactics of patient management.

3.4 Results of preoperative 3D modeling in patients undergoing surgery

In 58 (100%) patients who underwent surgical treatment, the localization and size of the pancreaticoduodenal tumor, its relationship with adjacent anatomical structures and main vessels, the degree of regional lymphadenopathy were assessed based on the results of preoperative 3D-modeling (MRI). Based on the available data the sequence of treatment and the volume of operations with variants of lymphodissection were planned. Based on the complex examination of the patients no signs of distant metastasis were revealed.

According to the data of examination, intraoperative picture, pathohistological study the most frequent localization of the tumor in the patients for whom 3D-models were built was in the head of the PG in 47 (81%) patients.

According to 3D-modeling data the tumor prevalence up to T2 stage was revealed in 19 patients (32,76%), up to T3 stage in 24 (41,38%), T4 stage was determined in

15 (25,86%) patients. At intraoperative evaluation and pathohistologic examination, T2 stage was confirmed in 19 patients (32,76%), T3 stage in 25 (43,10%), T4 stage was determined in 14 (24,14%) operated patients (Fig. 20).

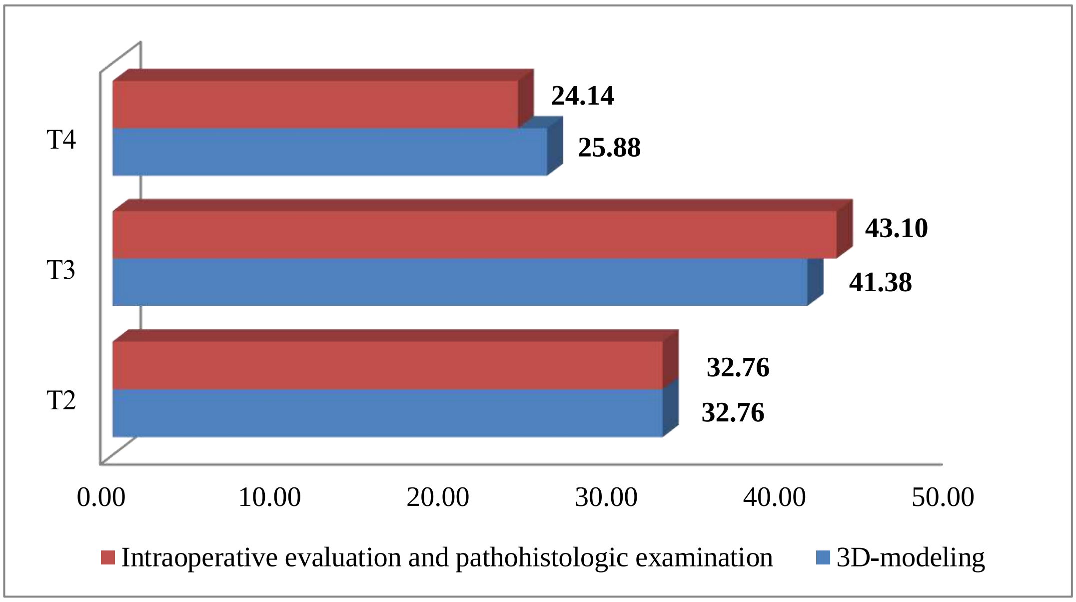


Figure 20 - Tumor prevalence according to three-dimensional modeling, intraoperative evaluation and pathohistological description %

In ROC analysis of tumor extent, sensitivity was 98.3% and specificity was 66.7% ($p < 0.05$) (Figure 21).

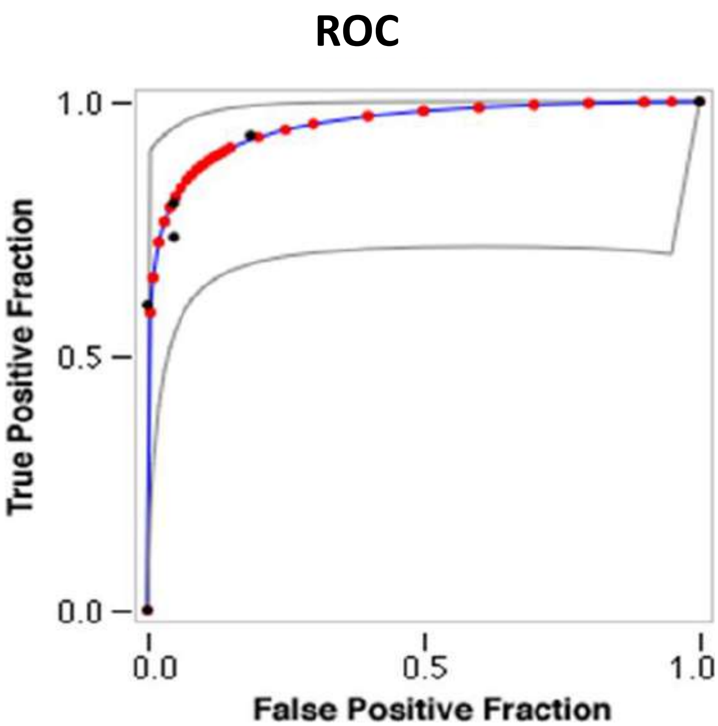


Figure 21 - Results of ROC analysis of tumor extent

According to the presented data, predominantly T3 stage of tumor process prevalence was determined, which was also stated during intraoperative revision and pathomorphological report. Thus, locally spread tumors of the head of the pancreas were observed in the majority of patients.

Magnetic resonance tomography and three-dimensional modeling were used to assess the resectability of the pancreatic tumor. According to MRI data, tumor invasion into the superior mesenteric vein was determined most often in 15 (25.9%) patients, but according to 3D-modeling data only in 10 (17.2%) patients.

Intraoperatively, the invasion into the SMV was confirmed in 12 (20.1%) cases of non-resectable lesion of the superior mesenteric vein. According to MRI data, the invasion of the prural trunk occurred in 3 (5.2%) cases, which was confirmed by the data of three-dimensional modeling and intraoperative picture. Invasion of the superior mesenteric artery could not be excluded at MRI examination in 12 (20.1%) people, but at 3D modeling in only 4 (6.9%) cases, which was confirmed intraoperatively. The exaggeration of data for portal vein and inferior vena cava invasion according to MRI data, which were not confirmed by 3D model construction and intraoperative evaluation, was also noteworthy, which is presented in Table 8.

Table 8 - Lesion of trunk vessels by tumor of the head of the PG according to MRI, 3D-modeling and intraoperative data

Vessels	MRI (n=58)	3D-model (n=58)	Intraoperative picture (n=58)
Ventral trunk	3 (5,2%)	3 (5,2%)	3 (5,2%)
Upper mesenteric artery.	12 (20,1%)	4 (6,9%)	4 (6,9%)
Upper mesenteric vein	15 (22,1%)	10 (17,2%)	12 (20,1%)
Portal vein	2 (3,4%)	0	0
Inferior vena cava	9 (15,5%)	7 (12,1%)	7 (12,1%)
Tumor without signs of vascular invasion	17 (29,3%)	34 (58,6%)	32 (55,2%)

In the ROC analysis of three-dimensional modeling in the assessment of trunk vessel lesions by tumorigenesis, the sensitivity was 98.3% and specificity was 94.1% ($p < 0.05$) (Figure 22).

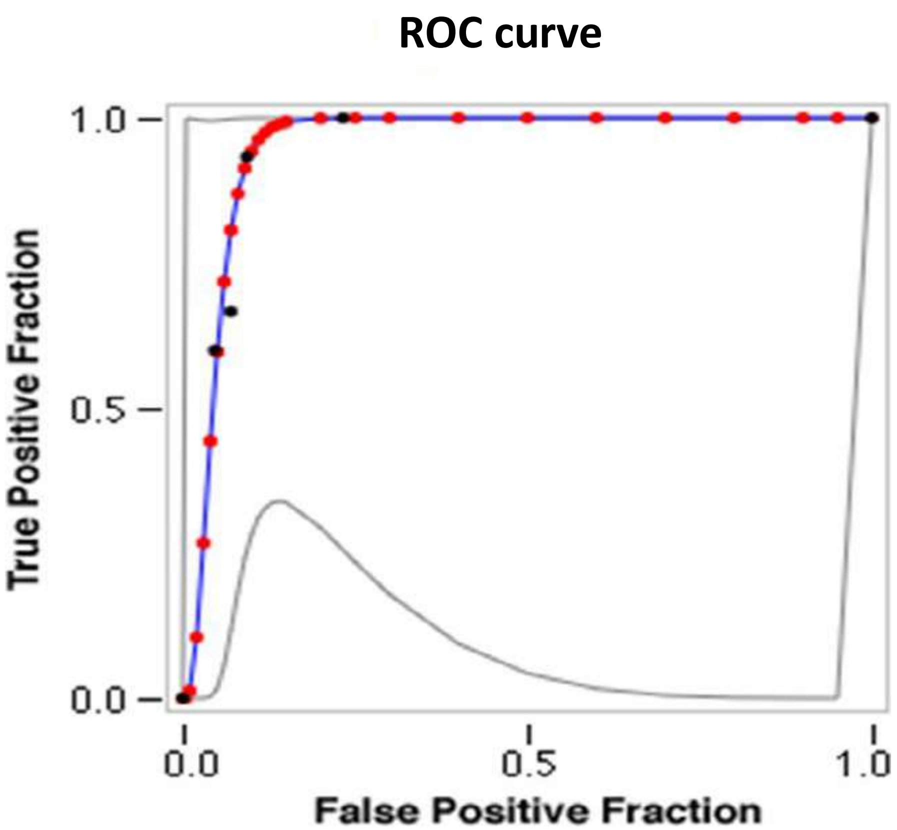


Figure 22 - Results of ROC analysis of three-dimensional modeling in the assessment of trunk vessels lesion by tumor process

Thus, only in 17 (29.3%) patients according to the magnetic resonance study no data on invasion of the pancreatic head cancer into the adjacent main vessels were obtained, while according to the three-dimensional modeling data these numbers reach 34 (58.6%) patients. Intraoperatively the possibility to perform radical resection was achieved in 32 (55,2%) patients.

For planning the volume of lymphodissection in 43 (74,1%) patients the integration of EUS data into 3D-model was performed. The obtained 3D-models allowed planning a more sparing volume of surgical treatment and the volume of lymphodissection in each specific patient. Metastases to regional lymph nodes were detected in 17 (39.5%) according to 3D-model (MRI+EUS)/ data and in 20 (46.5%) according to pathohistologic examination. The spread of the cancer process to the regional lymph nodes of the abdominal cavity was detected in 2 (4.6%) people according to the EUS and 3D-model data, but pathohistologically it was revealed in 3 (6.9%) operated patients.

Thus, the sensitivity in assessment of lymphogenic metastasis of the pancreatic head tumor according to the combined 3D model was 85% and specificity was 60% (p < 0.05), which is presented in Table 10.

Table 10 - Final staging of the cancer process

Stage	3D-model (n=43)	Intraoperative picture and pathomorphologic findings, (n=43).
IIA	2 (4,6%)	2 (4,6%)
IIB	4 (9,3%)	4 (9,3%)
III	20 (46,5%)	21 (48,8%)
IV	17 (39,5%)	16 (37,2%)

In ROC analysis of the 3D model in determining the stage of the tumor process, the sensitivity was 92.0% and specificity was 67.8% (p <0.05) (Figure 23).

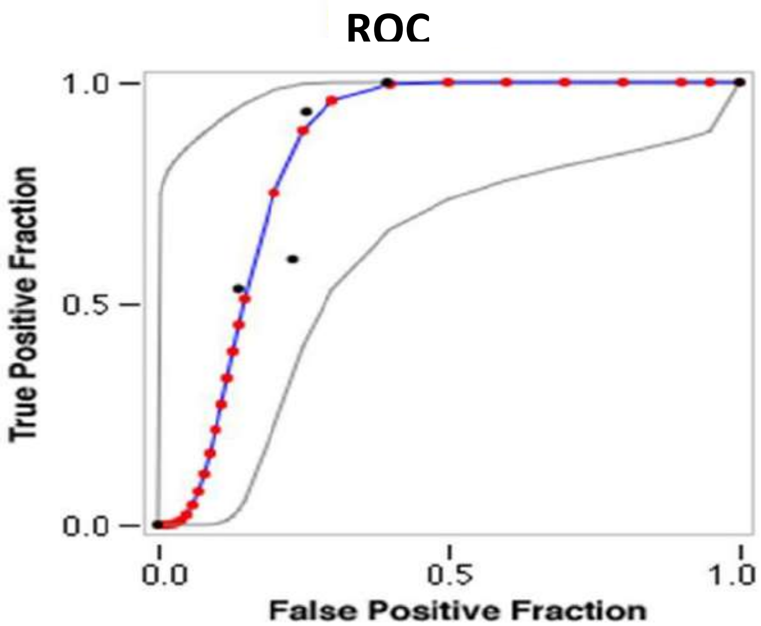


Figure 23 - Results of ROC analysis of 3D model in determining the stage of tumor process

3.5 Comparative analysis of CT and MRI-based 3D modeling

Three-dimensional models were built for 26 patients out of 58 (44.83%), both on the basis of MRI and CT, which allowed for comparative analysis.

According to the CT-based 3D modeling data, tumor prevalence up to T2 stage was detected in 9 (34.62%) patients, up to T3 stage - in 10 (38.46%), T4 stage was determined in 7 (26.92%) patients, which was fully consistent with the MRI-based models. However, the data differed slightly from intraoperative evaluation and pathohistologic examination. T2 stage was confirmed in 9 (34.62%) patients, T3 stage in 11 (42.30%), and T4 stage in 6 (23.08%) operated patients (Figure 24).

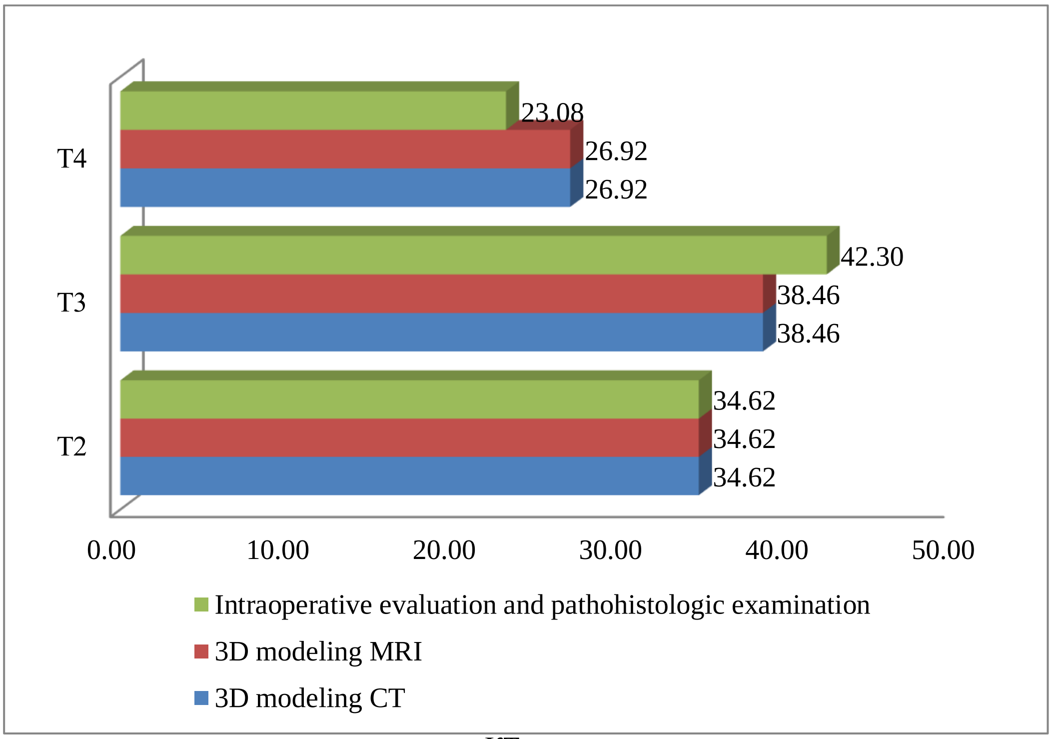


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Figure 24 - Tumor prevalence according to 3D modeling, intraoperative evaluation and pathohistological description (in %)

The sensitivity of three-dimensional CT-based modeling in determining tumor extent was 98.3%, specificity - 66.7% ($p < 0.05$).

Three-dimensional CT and MRI modeling was used to assess the resectability of the pancreatic tumor. According to the CT modeling data the tumor without signs of vascular invasion was determined most often in 14 (53,85%) patients, which was confirmed by the intraoperative picture, but 3D MRI models revealed this type of tumor in 16 (61,54%) cases.

The tumor invasion into the superior mesenteric vein was detected in 6 (23,06%) patients as a result of CT 3D-model construction, whereas on MRI models - in 4 (15,38%), and intraoperatively in 5 (19,23%) patients.

According to both CT and MRI modeling data, the invasion of the ventral trunk occurred in 1 (5.2%) cases, which was confirmed intraoperatively. Inferior vena cava invasion on CT and MRI models was detected in 3 (11,54%) patients, whereas intraoperatively - in 4 (15,38%) patients, superior mesenteric artery - 2 (7.69%) coincided, which was fully confirmed intraoperatively, as presented in Table 11.

Table 11 - Lesion of main vessels by pancreatic head tumor according to 3D-modeling (CT+MRT) and intraoperative images

Vessels	3D-model CT (n=26)	3D-model MRI (n=26)	Intraoperative picture (n=26)
Ventral trunk	1 (3,85%)	1 (3,85%)	1 (3,85%)
Upper mesenteric artery.	2 (7,69%)	2 (7,69%)	2(7,69%)
Upper mesenteric vein	6 (23,06%)	4 (15,38%)	5 (19,23%)
Inferior vena cava	3 (11,54%)	3 (11,54%)	4 (15,38%)
Tumor without signs of vascular invasion	14 (53,85%)	16 (61,54%)	14 (53,85%)

The sensitivity of CT-based 3D modeling in assessing tumor invasion of trunk vessels was 98.7%, specificity - 94.5% ($p < 0.05$).

Thus, CT-based 3D models were more sensitive to small vessel invasion and minimal invasion, but did not differ from MRI models in assessing tumor extent. However, in 2 patients CT did not detect the tumor due to its small size, also in 3 cases CT did not detect liver metastases and in 1 case lymph nodes were not evaluated.

Summing up, it should be noted that three-dimensional modeling, both on the basis of MRI and CT models, is a rather informative method in preoperative staging of the cancer of the head of the PG and the category of its resectability. This method allows to objectively determine the localization and prevalence of tumor process on adjacent anatomical structures, as well as visually demonstrate the metastatic lesion of regional lymph nodes. These parameters present a plastic picture, maximally close to the intraoperative one, which allows planning both the volume and the course of surgical intervention.

DISCUSSION OF THE FINDINGS AND CONCLUSION

Pancreatic head cancer occupies the 6th-7th place among oncologic diseases and the 4th-5th place among the causes of mortality, with only 5% of patients achieving five-year survival [38, 48, 56, 127, 150].

Despite the successes of modern diagnostics and surgical treatment, the problem of early detection, staging of oncologic process and, as a consequence, combined treatment of oncologic process of pancreatic head cancer remains urgent. By the time of tumor detection, a significant number of patients are considered non-resectable due to tumor spread to the main vessels, which is the reason for refusing radical surgical intervention. But due to the introduction of such methods of research as computer and magnetic resonance tomography, endoscopic ultrasonography, it became possible to obtain the necessary diagnostic information and plan the volume of surgical intervention in the preoperative period, avoiding surgery in obviously non-resectable patients. These methods, however, have limitations and need further improvement.

The disadvantages of computed tomography include relatively low evaluation of the tumor according to the T-criterion in case of its location within the head of the pancreas. Certain difficulties arise in the assessment of secondary lesions of abdominal cavity organs in case of small size of metastases. In N-criterion staging the common accepted criteria are lymph node diameter $\geq$ 1 cm, signs of central necrosis or disruption of lymph node capsule integrity, lack of differentiation of cortical and cerebral layers, which is not always an absolute indicator of secondary lesion. Taking into account the incomplete data on the primary tumor stage, as well as the impossibility of radical treatment, the patients received various types of combined and surgical treatment.

Taking into account the abovementioned, it is necessary to have an objective idea about regional invasion and lymphogenic metastasis of carcinoma of this localization in order to optimize the diagnosis of pancreatic head tumor stage and preoperative planning of surgical intervention [20].

The aim of the work was to improve the accuracy of diagnostics and assessment of resectability of pancreatic head cancer on the basis of complex use of radiation methods with 3D-reconstructions of the pancreaticoduodenal zone.

On the basis of the studied literature, the main objectives of the study were set in accordance with the goal, including clarification of the possibilities of multimodal approach using EUS and MRI in preoperative assessment of resectability of pancreatic cancer.

Between 2019 and 2022, 93 patients diagnosed with mechanical jaundice were evaluated in the surgical department of the Mariinsky Hospital.

Patients were sorted by stage according to the seventh revision of the TNM classification from 2010. In 68 (73.12%) patients pathohistologically revealed adenocarcinoma of various degrees of differentiation, in 5 (5.38%) people - cystadenoma.

Also, masses of the duodenum were detected in 7 (7.53%) people, terminal choledochus - in 12 (12.90%) and duodenum - in 1 (1.08%) patient.

Tumor process that corresponded to stage II was found in 10 (14.71%) patients, stage III - in 33 (48.53%) patients and stage IV - in 25 (36.72%) patients.

Out of 93 examined patients 46 (49,46%) patients underwent surgical intervention - pancreaticoduodenal resection with different variants of lymphodissection. Palliative interventions were performed in 37 (39,78%) patients and 10 (10,75%) patients underwent chemotherapeutic treatment.

All 93 patients (100%) underwent MRI of abdominal cavity organs, 59 (63,44%) patients underwent EUS of pancreaticoduodenal zone. Postprocessing 3D-modeling was performed in 58 (62,37%) patients, 43 (46,24%) of them with integration of EUS graphic data into 3D-model. Also, 26 (44.83%) patients out of 58 had 3D models built both on the basis of MRI and CT, which allowed comparative analysis.

Magnetic resonance examination was performed on an MR tomograph "Ingenia" (Philips Medical Systems, the Netherlands) with a magnetic field induction of 3 Tesla. The patients underwent native study of the abdominal cavity and retroperitoneal space, supplemented with the protocol of MRCPG, and dynamic contrast enhancement with data collection in arterial, portal and delayed phases was performed.

Endoscopic ultrasonography was performed by echoendoscope UM 160 of "Olympus" with radial sensor with the working part diameter of 11,2 mm. The obtained data were integrated into the video system EVIS EXERA II-180CV of "Olympus". The field of view in the sagittal plane was 360 degrees, scanning frequency from 7.5 to 20 MHz.

Subsequently, to obtain a three-dimensional image, the MRI and EUS data were integrated into medical systems of three-dimensional modeling (3D-slicer, Mimics, USA), where 3D-models in .stl format were built in semi-automatic mode.

Resectability of the tumor was determined in the operated patients on the basis of MRI data by evaluation of the degree of invasion of the main vessels. As a result, in 27 (29,03%) patients the cancer was recognized resectable, in 37 (39,78%) patients the signs of borderline resectability were revealed due to the involvement of the superior mesenteric vein and artery <180° into the tumor structure. In 29 (31.18%) patients the tumor met the criteria of non-resectability due to the involvement of the superior mesenteric vein and artery >180° in the tumor structure and invasion of the portal vein and the ventricular trunk. Three-dimensional modeling allowed us to reconsider the possibilities of radical surgical intervention.

Tumor invasion into the superior mesenteric vein was most often detected according to MRI in 15 (25.9%) patients, according to 3D modeling - in 10 (17.2%) patients and it was confirmed intraoperatively in 12 (20.1%) operated patients.

According to MRI data, the invasion of the ventral trunk was observed in 3 (5.2%) patients, which was confirmed according to the 3D-modeling data and intraoperatively.

Invasion of the superior mesenteric artery according to MRI could not be excluded in 12 (20.1%) of the examined, at the same time, when constructing the

3D-model only in 4 (6.9%), which was confirmed intraoperatively. The exaggeration of data indicating invasion of the portal vein and inferior vena cava according to MRI data, which were not confirmed when building a 3D model and intraoperatively, also drew attention [19].

According to the data of foreign authors, CT signs of arterial and vein invasion are different. To improve the accuracy of vascular infiltration diagnosis and to correctly assess tumor resectability, it is very important to pay attention to these differences and to be able to correctly interpret CT data [131, 150].

High image quality is one of the main factors in the visualization of abdominal organs and the pancreas in particular. Fast acquisition of scanning data, postprocessing of data with obtaining high-resolution images in multiplanar reformatting, allow good visualization of the pancreas and vascular bed [144].

Computed tomography is considered the gold standard in the diagnosis of pancreatic cancer and in the assessment of tumor resectability in most centers [100, 101]. The sensitivity of CT in assessing the resectability of pancreatic cancer ranges from 81% to 96.3% [18, 19, 46, 52]. Because of the peculiar anatomical relationship of the pancreas and surrounding vessels, the construction of three-dimensional reconstructions is useful in presenting additional information [4, 20, 140].

It is important for the surgeon to see the tumor in a three-dimensional image at the preoperative stage and to visualize its relationship with surrounding organs and vessels. In addition, the surgeon needs to visually assess the tumor volume in relation to the healthy pancreatic parenchyma. By free rotation of the three-dimensional image, the surgeon can visualize the degree of venous invasion more clearly (even before the operation), in contrast to two-dimensional images - axial, coronal and sagittal. Thus, the surgeon already plans the intervention steps before surgery.

Automatic processing of CT images of pancreatic tumors is usually not possible, especially in hypovascular tumors, where segmentation is difficult due to the small density gradient between the organ and the tumor. Based on the definitely narrow range of CT numbers, the software is not able to segment only the region of interest, with tissue delineation often erroneous. However, promising studies to create automatic organ segmentation have been described in the literature [134]. Based on 32 liver models, the authors present three types of gray scale grading. Using these types, a template is created in the program, based on which automatic selection of the organ parenchyma and its boundary is performed.

When planning the volume of lymphadenectomy by 3D-modeling, the degree of regional lymphogenic metastasis of PCa head cancer was estimated. Graphic data of EUS and 3D-modeling were combined in 43 patients. The obtained 3D-models served as a reason for planning a more sparing volume of lymphodissection. Secondary lesion of regional lymph nodes was detected in 17 (39,5%) patients according to 3D-model data and in 20 (46,5%) patients according to pathohistologic examination. Absence of oncologic process in the regional lymph nodes of the abdominal cavity was found in 2 (4.6%) patients according to EUS data, and respectively according to 3D-model, but pathohistologically metastasis was revealed in 3 (6.9%) operated patients.

The results of the study were processed using ROC-analysis with sensitivity and specificity. The sensitivity of the 3D model in determining the stage of tumor process was 92.0%, specificity - 6 7.8% ($p <0.05$).

We built 3D models both on the basis of MRI and CT in 26 (44.83%) patients out of 58. This allowed us to perform a comparative analysis of the 3D models obtained by CT and MRI. According to the CT-based 3D-modeling data, tumor prevalence up to T2 stage was detected in 9 (34.62%) patients, up to T3 stage - in 10 (38.46%), T4 stage was determined in 7 (26.92%) patients, which fully corresponded to the MRI-based models. However, the data differed slightly from intraoperative evaluation and pathohistologic examination. T2 stage was confirmed in 9 (34.62%) patients, T3 stage - in 11 (42.30%), T4 stage was determined in 6 (23.08%) operated patients.

The sensitivity of three–dimensional CT-based modeling in determining tumor extent was 98.3%, specificity was 66.7% ($p <0.05$).

The sensitivity of three-dimensional CT-based modeling in determining tumor extent was 98.3%, specificity - 66.7% ($p < 0.05$).

Three-dimensional CT and MRI modeling was used to assess the resectability of the tumor of the PG head. The most frequent CT-modeling data showed tumor without signs of vascular invasion. It was found in 14 (53,85%) patients and confirmed by intraoperative picture. However, the 3D model constructed by MRI, this type of tumor was detected in 16 (61.54%) patients.

As a result of CT 3D-model construction, tumor invasion into the superior mesenteric vein was detected in 6 (23.06%) patients, whereas on MRI models - in 4 (15.38%), and intraoperatively - in 5 patients (19.23%).

Inferior vena cava invasion was detected on CT and MRI models in 3 (11.54%) patients, whereas it was detected intraoperatively in 4 (15.38%) patients.

The CT and MRI 3D models coincided with the data on the invasion of the ventral trunk in 1 (3.85%) patient, and of the superior mesenteric artery - in 2 (7.69%), which was fully confirmed intraoperatively.

The sensitivity of CT-based 3D-modeling in the assessment of trunk vessels lesion by tumor process was 98.7%, specificity - 94.5% ($p < 0.05$).

CT-based 3D models were more sensitive to small vessel invasion and minimal invasion, but did not differ from MRI models in assessing tumor extent. However, in 2 patients, CT did not detect the tumor of the head of the PG due to its small size. Also, in 3 cases, CT did not detect metastases to the liver and in 1 case to lymph nodes.

Thus, 3D modeling based on MRI and CT studies is an informative method in preoperative staging of the head of the PaCa and its resectability. This method allows to objectively determine the localization and prevalence of tumor process on adjacent anatomical structures, as well as visually demonstrate the metastatic lesion of regional lymph nodes. In terms of diagnostic efficiency, 3D models are maximally close to the intraoperative picture, which allows planning both the volume and the course of surgical intervention.

DEDUCTIONS

1) For objective preoperative assessment of resectability of the tumor of the head of the PG and the exact volume of surgical intervention, it is necessary to use the possibilities of multimodal radiation diagnostics of the pancreaticoduadenal zone to the maximum extent possible. In evaluation of T stage the sensitivity of MRI and EUS methods was 93,2% and 76,9%, and specificity - 98,2% and 50%, respectively

2) A hybrid (MRI-EUS) 3D model of the pancreatoduodenal zone allows to stage the oncological process with high accuracy and determine the volume of lymphadenectomy; in determining the stage of the tumor process, its sensitivity is 92.0% and specificity is 67.8%.

3) The sensitivity and specificity indicators of 3D models based on MRI and CT data in the assessment of invasion of the main vessels are close, amounting to 98.7%, 67.8% versus 94.5%, 66.7%, respectively. Both 3D models are quite informative methods in the preoperative assessment of the resectability of pancreatic head cancer.

4) 3D reconstruction of modern tomographic methods of the pancreatoduodenal zone is comparable to the intraoperative picture.

PRACTICAL RECOMMENDATIONS

1) It is reasonable to perform MRI and EUS of abdominal cavity organs in patients with established diagnosis of mechanical jaundice and presence of volumetric mass of the head of PG according to ultrasound in order to estimate the tumor process prevalence.

2) For preoperative staging of head cancer, a 3D reconstruction of the pancreaticoduodenal zone is performed based on CT or MRI data, which allows to determine the criteria of tumor resectability.

3) In order to select the lymphodissection volume, it is necessary to integrate the graphic data of EUS into a 3D model based on MRI of the pancreaticoduodenal zone.

LIST OF ABBREVIATIONS

2D	–	Two-dimensional images
3D	–	Three-dimensional images
HAC	–	Higher Attestation Commission
SMA	–	Superior mesenteric artery
SMV	–	Superior mesenteric vein
VC	–	Vena cava
DWI	–	Diffusion-weighted image
MDC	–	Measured diffusion coefficient
CT	–	Computed tomography
IARC	–	International Agency for Research on Cancer
MPR	–	Multiplanar reconstruction
MPI	–	Magnetic resonance imaging
MRCPG	–	Magnetic resonance cholangiopancreatography
MSCT	–	Multispiral computed tomography
IVC	–	Inferior vena cava
GHA	–	General hepatic artery
PG	–	Pancreatic gland
X-ray CT	–	X-ray computed tomography
RNA	–	Ribonucleic acid
PaCa	–	Pancreatic cancer
USE	–	Ultrasound examination
CDM	–	Color Doppler mapping
VT	–	Ventral trunk
EUS	–	Endoscopic ultrasonography
AJCC	–	American Joint Committee on Cancer
EUS-FNA	–	Endoscopic ultrasound-guided fine-needle aspiration
FGF	–	Fibroblast growth factor
FOV	–	Field of View or scanning field
HR	–	High resolution
IVIM	–	Model of incoherent motion
miR	–	MicroRNA
NCCN	–	National Comprehensive Cancer Network
PanIn	–	Pancreatic intraductal neoplasia
PDGF	–	Platelet-derived growth factor
TE	–	Echo time
TGF -1	–	Transforming growth factor
TR	–	Repetition time
TSE	–	Turbospin Echo Sequence

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