**ABSTRACT**

Pancreatic cancer is often identified on the terminal stage and at the moment of diagnosis the tumor resectability does not exceed 10-15%, which is linked with long latent period, as well as to low informativity of generally accepted methods of early stage examinations. The aim of present study was the optimization of CT examination of pancreatic head cancer, by elaborating diagnostic criteria for defining the indications and possible surgical intervention scope. CT conclusions were received from 68 patients prior to the operation (31 – native, 37 – with contrast enhancement), who were diagnosed with pancreatic head neoplasm and were morphologically verified with pancreatic head cancer after surgery. It was established that native CT examination may have only an orientation value, since the pancreatic head tumor cannot be precisely differentiated from pancreatic parenchyma without the application of contrast media. Diagnosis divergence was observed in 14 cases; moreover, the number of divergences is more by separate CT criteria (e.g. metastatic lesions, tumor primary localization, etc.). Among CT criteria maximal frequency is revealed in dilatation of bile ducts (95.6%), then – the dilatation of main pancreatic duct more than 5 mm (in 45.6% cases); atrophic change of pancreatic body and tail, duodenum deformation and presence of fluid inclusions within the limits of pathological process were established in similar frequency – in 36.8%. It was shown that practically one third of patients, who underwent the contrast exams, had an involvement of the superior mesenteric vein: from partial surrounding of the vessel to entire obturation of the vessel lumen by the tumor. Portal, splenic and inferior cava veins, as well as the superior mesenteric artery, celiac trunk and proper hepatic artery were seldom involved in the process.

The size of tumor revealed in 70.6% of patients was more than 2.6 cm in size, and T3 and T4 stages were found out in 85% of them. Pancreatoduodenal resection (Whipple procedure) was carried out in 14 (20.6%) patients, bypass surgery – in 53 (77.9%) patients. The obtained data indicate on the late detectability of patients with pancreatic head cancer.

Therefore, the pre-operative complex radiological evaluation of patients with biliopancreatoduodenal zone neoplasms, taking into account the individual peculiarities of pathological process prevalence in certain cases, will allow to elaborate proper treating tactics, to fully outline the volume of surgical intervention, which in its case will reduce the surgical time and post-operation rehabilitation period.

**Keywords:** computed tomography, visualization, head cancer, pancreas.

**INTRODUCTION**

Pancreatic head cancer is on the 9th place among oncological diseases, but among gastrointestinal tract tumors – in the 3rd place (following the cancer of stomach and colon). According to the data of some authors the annual incidence of pancreatic head cancer is 217000 people worldwide [Hariharan D et al., 2008]. Statistics of recent years has indicated about steady increase of morbidity rate and mortality due to pancreatic head cancer. The morbidity rate has increased 3 times as much and reaches the level of 12.0 per 100000 of population during recent 50 years in industrially developed countries (Canada, Great Britain). In the western countries mortality from pancreatic cancer is ranked 4th among oncological diseases [Ouaissi M et al., 2012].
Dissatisfying treatment results of patients with malignant tumors of biliopancreatoduodenal zone organs, to which pancreatic head cancer refers to, are mainly explained by their late diagnosis [Furu-kawa H, 2002; Buchs N et al., 2010] linked to peculiarities of its clinical manifestation – prolonged hidden course, late manifestation of the disease and similarities with clinical image of inflammatory diseases of these organs, as well as low informativity of generally accepted methods of examination on early stages of the cancerous process [Moniaux N et al., 2008]. Clinical data show that pancreatic cancer is usually revealed on the terminal stage of the disease, moreover at the time of diagnosis, tumor resectability is not exceeding 10-15%, and the rest 85-90% of patients have non-resectable tumor or metastases to other organs with fatal outcome within 12 months after the diagnosis establishment [Cooperman A et al., 2000].

Among the serological biomarkers, carbohydrate antigen 19-9 is the most informative and experienced tumor marker, which is used in complex diagnosis of biliopancreatoduodenal zone cancer, however its specificity is limited because of increase of its concentration, in case of other organ cancers and in cases of non-tumorous etiology (chronic pancreatic, liver and kidney disease) [Itoi T et al., 2005; Ohike N et al., 2010]. A significant lack of carbohydrate antigen 19-9 is also the fact that its level is normal at early stages, which excludes its application for screening examinations of patients while suspecting cancer [Porta M et al., 2005]. Another frequently used tumor marker is cancer embryonic antigen revealed in 49% of cases among patients with pancreatic cancer, which limits its application at differential diagnosis of cancer and non-tumorous diseases [Ahrens W et al., 2007].

The early disclosure of biliopancreatoduodenal zone tumors is one of the most complicated questions of radiology. The precise estimation of manifestations of any pathological process influences treatment tactics, and therefore, the immediate and long-term results [Wang X et al., 2016]. According to the literature data, the treatment of patients with pancreatic cancer depends on the volume of surgical removal of the tumor. Moreover, the surgical resection volume depends on the careful pre- and intra-surgical tumor disclosure [Long E et al., 2005; Zakharova O et al., 2011].

Among available scientific data with big number of works devoted to the general questions of diagnosis of biliopancreatoduodenal zone tumors, less attention is paid on pre-surgical evaluation of local-regional prevalence of the tumor process and the establishment of its resectability. Tumor staging including criteria of tumor, node, metastasis (TNM) is of special principal importance.

The aim of present study is the optimization of computed tomographic examination of patients with pancreatic head cancer, with application of developed diagnostic criteria, to solve the problem of indications and determination of the volume of surgical resection. To reach the goal, presurgical CT results have been analyzed with postsurgical conclusions, morphologically verified (structural bases were identified).

**Material and methods**

The medical history of 68 patients (42 men and 26 women from 46 to 86 years of age, with average age 63.3±9.4 years), who had undergone surgical intervention due to pancreatic head cancer or with similar pathology, were analyzed. The surgical intervention and morphological verification proved pancreatic head cancer in 68 patients.

Pancreatoduodenal resection (Whipple procedure) was carried out in 14 (20.6%) patients, bypass surgery – in 53 (77.9%) patients, diagnostic laparoscopy in one patient (1.5%).

CT was performed in different medical institutions of Yerevan on Somatom Sensation 64 (Siemens, Germany), Somatom Emotion 6 (Siemens, Germany), Somatom Emotion 1 (Siemens, Germany), Somatom Perspective (Siemens, Germany) devices, the data of which were preoperatively analyzed. All patients underwent native examination, CT with per oral contrast administration with water (10 ml water-soluble contrast was diluted in 200 ml water and the patient takes 100 ml during 10 min in portions prior to the exam and remaining 100 ml – immediately before the exam). For data analyses image post-processing programs were utilized – MPR, MIP and VRT.

Intravenous contrast enhancement was performed in 37 patients in two phases: arterial and venous. The main goal of contrast enhancement is determination of vessels status in region of interest, in cases of massive tumors – determination of...
its vascularization character and accurate tumor border outline.

For visual and quantitative analysis of structural densities by CT, the scale of X-ray attenuation is used, which is called the scale of Hounsfield (its visual display on the screen is the black and white spectrum of the image). Calculated X-ray attenuation coefficients are expressed in relative values, which are so called the Hounsfield Units (HU).

Clinical classification suggested by International Union against Cancer was used in present study, which lights out the degree of the tumor process prevalence in details to determine the accurate treatment tactics.

According to the tumor prevalence character on great vessels, patients were divided into the following types (Table 1).

<table>
<thead>
<tr>
<th>Vascular involvement in the pathological process of pancreatic head</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor relation to regional vessels</strong></td>
</tr>
<tr>
<td>Fatty interlayer separates the tumor from the vessels</td>
</tr>
<tr>
<td>Tumor is delimited from vessels by non-altered parenchyma</td>
</tr>
<tr>
<td>Tumor borders on the vessels</td>
</tr>
<tr>
<td>Tumor partially surrounds the vessel</td>
</tr>
<tr>
<td>Tumor tightly adjoins to the vessel and there is a local thickening of vessel walls</td>
</tr>
<tr>
<td>Circular envelopment</td>
</tr>
<tr>
<td>Narrowing of lumen</td>
</tr>
<tr>
<td>Vessel lumen is entirely blocked by pathological mass</td>
</tr>
</tbody>
</table>

“Investigation was approved by Institutional committee on bioethics and corresponds to principles indicated by Helsinki declaration” (Br. Med. J. 1964; p.177) with further additions.

Data of patients were chosen by retrospective methods from 2004 to 2014. For the elaboration of data the statistic programs SPSS 17.0 and Excel 2013 were used. Descriptive analysis was realized to describe portion-percent content for categories as well as average value, average value error, minimal and maximal data for persistent variables. Checking on symmetry of distribution for persistent data was carried out by Kolmogorov-Smirnov method.

**Results**

Based on TNM criteria the patients were distributed according to primary tumor (T) stage: T1 – 2 (2.9%), T2 – 5 (7.4%), T3 – 25 (36.8%) and T4 – 36 (52.9%); according to the involvement in the process of regional lymph nodes (N): N0 – 9 (13.2%), N1 – 8 (11.8%), N2 – 2 (2.9%), N3 – 1 (1.5%) and N4 – 48 (70.6%) patients. Distal metastases (M) were revealed in 28 (41.2%) (M1) and were absent in 40 (58.8%) patients.

CT data prior to surgical resection and the results of surgical intervention with morphological verification were analyzed: the coincidence of diagnoses was observed in 54 (79.4%) patients, the divergence – in 14 (20.6%).

Infiltration of the pathological process beyond the limits of the pancreatic capsule and invasion into the parietal peritoneum, or ingrowth into the surrounding organs and tissues (duodenum, liver etc.) are one of the most important CT criteria, which identifies not exact borders of the gland, nondifferentiability of borders between the affected pancreatic head and mentioned organs. Depletion (disappearance) of fatty interlayers between organs and structures also has great value in such image formation. In present study, the tumor was interstitially arranged in the limits of intact parenchyma in 5 (6%) patients, infiltrated out of the limits of capsule in 32 (37%) and grows into neighboring anatomical structures in 49 (57%) patients (in duodenum, biliary tracts, great trans-pancreatic vessels).

Neoplastic process of pancreatic head leads to distortion of its normal anatomic form, i.e. the pyramidal shape of the uncinate process is being changed, the head contours rounds off, which has a respective reflection on CT-scans, particularly in volume reconstructions. During massive neoplasms the tumor growth occurs irregularly in different parts, and it appears as irregularity of the gland head contours. In most cases clinically relevant pancreatic head neoplasms leads to the increase of its size. Pancreatic head absolute dimensions are represented much bigger respectively on CT images, compared to average statistic values of the normal size and are not proportional related to the body and tail. Particularly, it is more obvious when the tumor is developing simultaneously with trophic changes of the body and tail of pancreas. Moreover, the CT criterion that has prognostic
value is the size of the space-occupying lesion by which the patients were conditionally divided into three groups: 0-1 cm, 1-2.5 cm (20 patients; 29.4%) and more than 2.6 cm (48 patients; 70.6%). There were not revealed patients having lesions with less than 1 cm in size.

Pancreatic head neoplasms may have solid homogeneous structure in the primary stages of tumor development. In any case the vascularization of the neoplasm is not complete compared to the unchanged or less changed tissue of gland, and on native CT image the pathological focus of the head is hypodense (Fig. 1a). Depending on vascularization degree at contrast enhancement, this or other degree of enhancement of the densitometric measures of the tumor mass are observed, but the latter in any case are lower of those of the unchanged tissue (Fig. 1 b, c).

With the growth of the tumor, necrotic zones with discharge of pancreatic juice and blood can be developed and it is shown as tumor heterogeneity on computed toograms. Vascularization of such tumors is particularly not complete and they are obviously hypodense both in native scanning and with contrast enhancement. The growth of pancreatic head tumor undoubtedly leads to compression or pathological involvement of common biliary and main pancreatic ducts, which leads to the dilatation of the latter. It appears on CT by the presence of additional tube-like structures in proximal zone of compression. Almost half of patients (45.6%) had dilatation of the main pancreatic duct (diameter more than 5 mm) in this study. Practically all patients (95.6%) showed dilatation of the bile ducts. Disorders of evacuation of gastric content were revealed in 4.4% of patients. Calcifications in the limits of neoplasm were revealed in 2 (2.9%), fluid involvements in 25 (36.8%) patients. Atrophic changes of pancreatic body and tail and duodenum deformation (compression by the lesion) were established in 25 patients (36.8%).

Determination or precise estimation of structural modification of lymph nodes is also of great value. CT evaluation of regional lymph nodes status is carried out based on the visualization of node, their structural changes and growth. Majority of unchanged lymph nodes are not visualized on CT. Lymphadenopathy was observed in 39 (57.4%) patients with the involvement of different groups of regional lymph nodes into process (Table 2). As table 2 shows, lymphadenopathy is often observed in the superior mesenteric region (30%), then – celiac trunk (29%). Paraaoortic lymph nodes were sufficiently often involved as well (21%). Other groups of regional lymph node involvement

<table>
<thead>
<tr>
<th>Localization of lymph nodes</th>
<th>Number of lymphadenopathy cases N=77</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior mesenteric</td>
<td>23</td>
</tr>
<tr>
<td>Celiac</td>
<td>22</td>
</tr>
<tr>
<td>Gastric</td>
<td>6</td>
</tr>
<tr>
<td>Perihepatic</td>
<td>7</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>16</td>
</tr>
<tr>
<td>Paracaval</td>
<td>3</td>
</tr>
</tbody>
</table>

**TABLE 2.**

**Figure 1.** Dispersion variations of the densitometric measures of pancreatic head lesion in native (a), arterial (b) and venous (c) phases of scanning.
Lymphangitis (edema of fatty tissue) of lesser omentum was observed in 14 (20.6%) patients. Presence of the secondary neoplastic lesions is also an important prognostic and treatment determining factor during pancreatic tumors. Metastatic lesions were discovered in 15 patients (22%): liver – in 9 (56.2%), lungs – 4 (26.7%), adrenals – 1 (6.2%) patients. Carcinomatosis of peritoneum with development of ascites was revealed in one case (6.2%).

Vessel changes have different exhibitions such as neighboring with neoplasm, growing into the wall and total lumen obturation. These processes have a respective reflection on CT with contrast enhancement as changes of external and internal contouring and lumen alterations of vessels. Patients were divided into types based on tumor prevalence onto the great vessels revealed with contrast enhancing examinations, as it was mentioned above. The biggest number of changes was observed in superior mesenteric vein: 13 patients (35%) were considered to type A, 5 (14%) – type B, 7 (19%) – type C1, 5 (14%) – type D1, 2 (5%) – type D2, 3 (8%) – type E1, 2 (5%) – type E2. C2 type was not discovered in any case. It was revealed that prevailing number of patients (26-70%) had type A in portal and spleen veins, i.e. the fatty interlayer separates the tumor from vessels and only in unique cases types C1, C2, D1, D1, E1 and E2 were observed. Inferior cava was involved in the process only in one case of patient who had a vessel lumen contraction (type E1). From the great arteries the maximal involvement was observed in superior mesenteric artery. Rarely celiac trunk and proper hepatic artery were involved in the process. Mainly the type A was determined.

**DISCUSSION**

The research analysis conducted that early symptoms of cancer of biliopancreatoduodenal zone organs do not exist. Cancer of the given localization, as it is aforementioned, may occur over a long period of time with no symptoms, but the appearing of the first clinical features of the disease, as a rule coincides with tumor extension, which excludes the possibility of radical surgical removal [Ruemmele P et al., 2009]. The latter makes it a quite actual topic: deep study of structural bases of pathological changes in the given region, particularly systematization of computed tomographic criteria of pancreatic head cancer. The change of macroscopic structures of organs and tissues in the region of interest, particularly biliopancreatoduodenal zone, changes of the form and topographic relationships, disorder of the integrity of natural contoural formations (capsules, serous cover of organs, vascular walls and bile ducts), redistribution of fluid and tissue components in organs and tissues, accumulation or discharge of biological fluids (bile, blood, etc) are implied under the structural bases. These changes may be determined as morphological substrate for respective CT image formation.

Many researchers note that anatomic mutual connections differ on computed tomograms better, than on ultrasound images [Miura T et al., 2010]. CT application is also informative in those cases, when biliopancreatoduodenal zone lesion is identified on ultrasound images, but the resectability of the tumor is still not verified.

According to research data, pancreatic head tumor is hypodense in contrast enhancement, i.e. it is hypovascular compared to unchanged pancreatic tissue. The tumor is isodense in 10-15% cases, due to diffuse changes of pancreatic parenchyma, which is the cause of its hypovascularization (fibrosis, dystrophic processes); it makes the differentiation of the pathological focus from diffusely changed parenchyma of the pancreas difficult on CT images. Some researchers claim that spiral CT is the most informative method of differential diagnosis of pancreatic diseases [Vargas R et al., 2004]. According to the analysis, the native CT may have only an orientation value for detection of pancreatic head neoplasm, since the tumor cannot be precisely differentiated from parenchyma without the contrast enhancement; the native CT determines the approximate value of the pathologic region, its irregular contours, estimates the state of common bile and main pancreatic ducts, orients to changes of regional lymph nodes. The lesion is differentiated better in the late arterial phase, when pancreatic parenchyma is enhanced most intensively; contrasting gradient is the highest between pancreatic tissue and pathological zone. The pathologic process is not clearly identified on the native images (Fig. 2 a, b). The mentioned peculiarities of
pancreatic tissue contrast enhancement are related to its relative proximity to the great vessel of the celiac-mesenteric pool. In the venous phase the wash-out of contrast media from the neoplasm takes place with delay compared to surrounding unchanged pancreatic tissue, which is also explained by deficient vasculature of the pathological zone (Fig. 1).

Recently many surgeons have considered the tumor size as of great importance in determining prognosis. Most researchers predict favorable prognosis if the tumor size is not exceeding 2 cm (3-year survivability – 23%, 5-year survivability – 18%, at the tumor size exceeding 2 cm there is no 5-year survivability) [Patyutko Yu, Kotelnikova A, 2007; Ohike N et al., 2010]. Results of the studies indicate that the detectability of pancreatic head cancer is sufficiently low, because 70.6% (48) of patients had a tumor with more than 2.6 cm. This fact is proven by the idea that early stages of cancer of the given localization passes without any clinical symptoms. Tumors with less than 0.5 cm in size, even using contrast enhancement, are very difficult to reveal on CT images, in these cases indirect features are used, particularly: “double duct” syndrome, atrophy of pancreatic tail, edema of pancreatic head, as well as loss of lobulation (waving) of external contour of the gland [Karmazanovsky G, 2004].

According to the literature data, the main features of pancreatic cancer on CT are local growth, organ deformation, capsule disorder, change of densitometric measures, dilated ducts and sharp demarcation of distal part of common bile duct with the precise level of occlusion [Karmazanovsky G, 2004; Suda K et al., 2007; Lazebnik L et al., 2012].

Based on the results, the dilatation of bile ducts (95.6%) are found out with maximal frequency among computed tomographic criteria (Fig. 3), then – the dilatation of the main pancreatic duct more than 5 mm (45.6%); atrophic changes of the body and tail of pancreas, deformation of the duodenum (compression by lesion) and presence of fluid inclusions within the limits of the pathological process were established equally – in 36.8% of cases.

Nowadays CT with intravenous contrast enhancement is the method of choice for the determination of indications and planning of pancreate-duodenal resection (Whipple procedure) in bilio-
pancreatoduodenal zone neoplasms [Karmazanovsky G, Akhlinova O, 2009]. The main factor in resectability determination is the identification of invasion into the great vessels of celiac-mesenteric pool, particularly in celiac trunk, superior mesenteric and in common hepatic arteries, as well as the determination of tumorous process extension into retroperitoneal space posteriorly from superior mesenteric artery [Yashina N et al., 2010; Lovecek M et al., 2016]. The studies showed that practically one third of patients, who underwent CT with contrast enhancement, had involvement of superior mesenteric vein from partial surrounding of the vessel by the tumor to total obturation of the vessel lumen by pathological mass (Fig. 4). Portal, spleen and inferior cava veins, as well as superior mesenteric artery, celiac trunk and common hepatic artery were rarely involved in the process. Type A is mainly determined.

From all great vessels of biliopancreatoduodenal zone the superior mesenteric vein is mostly nearly situated to pancreatic head and forms its own bed on the posterior surface of the gland; it is one of the factors determining the partial involvement of the superior mesenteric vein during the pancreatic head cancer. As it is known, the vascular wall of veins differs from arteries by little degree of muscle layer development. The medial layer of venous walls is represented by smooth muscle cells, which do not form solid layer, as it is in arteries, and are situated as separate groups of fibrillar conjunctive tissue. Elastic fibrils are less relevant. It is an additional factor, promoting the tumor invasive growth into the vein.

Analyzing the data Buchs N.S. and co-authors (2010) mentioned that the invasion into superior mesenteric and portal veins is not a contraindication to perform pancreatoduodenal resection. According to some authors, metastases to the liver or to any other organ, canceromatosis of peritoneum, involvement of great arteries in the celiac-mesenteric pool are the absolute criteria for not performing resection in biliopancreatoduodenal zone cancers [Karmazanovsky G, Akhlinova O, 2009; Yashina N et al., 2010]. Though metastatic processes are revealed only in 15 patients from 68, 14 (20.6%) patients underwent pancreatoduodenal resection examination and 53 (77.9%) patients – bypass procedures. The metastatic process particularly in the liver was not pre-surgically diagnosed in 13 patients, due to insufficient informativity of the native CT exams.

The big number of bypass surgeries is explained by the local expansion of the pathological process at the moment of the primary diagnosis (stages T3 and T4) and these cases compose almost 85% of all cases of pancreatic head neoplasms. The final estimation of possible pancreatoduodenal resection procedure is intraoperatively carried out. Traditionally “sparing” approaches of surgeons of CIS countries have a relevant value in the solution of this problem. Surgical resections of biliopancreatoduodenal zone have more radical approaches in Japan and western countries (tumorous invasions of veins are not considered to be an obstacle for pancreatoduodenal resection). Resectability criteria of tumors are not the same in different clinics. In the majority of clinics of CIS countries infiltration into the portal vein or into its branches is considered to be non-resectable state, moreover, in the abroad countries, particularly in Japan, single-moment resection of the portal vein and pancreatoduodenal resection realization are acceptable surgical interventions [Nimura Y, 2010]. The refusal from attempts of radical treatment is common if metastatic lesions of the liver and tumor insemination over the peritoneum are revealed [Shoup M et al., 2004].

It should be mentioned, that the number of biliopancreatoduodenal zone tumor cases has recently increased in which the problems of resectability
are arguable. This problem needs further investigation by radiologists and surgeons to solve the question about how reasonable surgical intervention is. Pre-operative estimation of tumor resectability has an important significance for the determination of validity of vessels involvement, which is possible to conduct by CT imaging with intravenous contrast enhancement. Resolution of this problem is quite topical, because the changes according to CT are evaluated as the signs of invasive growth, but in fact they are not precise.

Results of the studies prove that pre-operative CT estimation of the tumor localization and the process prevalence is quite difficult. From 31 patients who had not undergone contrast enhancement, 13 cases of metastases were not identified. In 6 from 37 patients who underwent contrast enhancement CT, errors concerned the primary tumor localization, as pancreatic head tumor was described as a mass of major duodenal papillae or the distal common bile duct. As it was noticed above, the diagnosis divergence was observed in 14 cases, moreover it should be mentioned as well that based on the separate CT criteria, (metastatic lesions, primary tumor localization, involvement of lymph nodes, etc.) the number of divergences is much bigger. In both groups some cases were observed when the mass was not identified on CT.

Therefore, the pre-operative complex radiological evaluation of patients with biliopancreatoduodenal zone neoplasms, taking into account the individual peculiarities of pathological process prevalence in certain cases, will allow to elaborate proper treating tactics, to fully outline the volume of surgical intervention, which in its case will reduce the surgical time and post-operation rehabilitation period. The possibility of creating virtual models of morphological substrate is subjected to possible surgical correction (as further scientific study viewpoint).

REFERENCES


