

Preoperative assessment of pancreatic adenocarcinoma. Value of CT imaging

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ABSTRACT

Background and aim

Pancreatic adenocarcinoma is one of the most malignant cancer forms. It is fourth most common cause of cancer death worldwide, with a poor overall 5-year survival rate of only 4 %. The treatment depends upon tumour resectability at presentation. Therefore, radiological imaging is crucial in the management of the disease. In this study we evaluated the role of computed tomography in diagnosing pancreatic adenocarcinoma and CT diagnostic values in determining resectability of pancreatic.

Material and methods. This was a prospective randomized clinical study, in which 79 patients with resectable pancreatic cancer were studied. All the patients underwent MDCT scan. In all CT images we analyzed location of pancreatic tumor, invasion into adjacent structures, vascular involvement and distant metastases. The results of preoperative CT staging were compared to the postoperative histological data. In order to determine diagnostic values of CT, we calculated the sensitivity, specificity, positive and negative prognostic values (PPV, NPV) as well, as accuracy. All calculations were performed using SPSS for Windows 25.0 software and Microsoft Excel 16.

Results. There was no difference in evaluating T stage pre and postoperatively $\chi^2 = 74,452$, $df = 15$, $p < 0,001$ and no statistically difference in evaluating tumor N stage pre- and postoperatively $\chi^2 = 8,978$, $df = 1$, $p = 0,003$.

Overall CT sensitivity for tumor T stage was 73 %, specificity 85 %, PPV and NPV 67.1 % and 88.2 % respectively, accuracy 81.4 %. CT diagnostic values for N stage: sensitivity 75 %, specificity 59.3 %, PPV 78%, NPV 55.2% and accuracy 69.6%.

Conclusions

- CT is specific and accurate imaging modality in T stage of pancreatic adenocarcinoma.
- CT is quite sensitive, but non specific in N stage of pancreatic adenocarcinoma.

Keywords: pancreatic adenocarcinoma, resectability, CT values

INTRODUCTION

Pancreatic adenocarcinoma is one of the most malignant cancer forms. It is fourth most common cause of cancer death worldwide. Globally, about 338000 people had pancreatic cancer in 2012, making it the 11th most common cancer. The highest incidence and mortality rates of pancreatic cancer is found in developed countries. Prognosis of this cancer remains bad – 5 year survival rate is less than 5 percent. The incidence and mortality of pancreatic cancer worldwide correlated with increasing age and was slightly more common in men than in women [1,3]. Pancreatic cancer is diagnosed late in the natural history of the disease, given the few early indicators of illness, and the lack of screening tests for this disease [2]. In fact, 40% of the pan-

creatic cancer cases are diagnosed in late stages, when the disease has already spread far from the primary cancerous process, where as another 40% of the patients are diagnosed with locally advanced pancreatic cancer.

Early and precise diagnostics and grading are very important for further treatment and prognosis of patients. When the lesion of the pancreas is suspected, the first line diagnostic modality is computed tomography (CT). If any uncertainties occur, the following test after CT is usually magnetic resonance imaging (MRI) [2-4]. Lately, MDCT (multidetector computed tomography) became golden standard for preoperative evaluation and grading, as well as, treatment choice and observation of the pancreatic adenocarcinoma. However, when using CT as a diagnostic test, approximately 11% of the ductal adenocarcino-

ma's are missed, because density of parenchyma of the pancreas and cancerous tissue are the same, as well as differential diagnosis between paraduodenal space pancreatitis and pancreatic cancer is complicated [4]. Moreover, it is complicated to diagnose pancreatic adenocarcinoma in the presence of chronic focal pancreatitis. In the cases mentioned above, computed tomography with perfusion and MRI are diagnostic tests of the first choice.

In this study we evaluated the role of computed tomography in diagnosing pancreatic adenocarcinoma and CT diagnostic values in determining pancreatic adenocarcinoma's resectability.

AIM

To evaluate CT diagnostic values in determining pancreatic adenocarcinoma's resectability.

OBJECTIVES

1. To identify CT diagnostic values in determining the local extension of pancreatic adenocarcinoma (T stage).
2. To calculate CT diagnostic values in determining the spreading of pancreatic adenocarcinoma into regional lymph nodes (N stage).

MATERIALS AND METHODS

This was a prospective randomized clinical study, in which 79 patients with resectable pancreatic cancer were studied.

Inclusion criteria:

1. Older than 18 year old patients with radiologically confirmed pancreatic adenocarcinoma

Exclusion criteria:

1. Patients with renal dysfunction;
2. Sensitivity to iodine.
3. Refusal to participate in the study.
4. Distant metastases.

Patients were treated in clinics of surgery and gastroenterology between June year 2015 – september Year 2018. (TLK-10, C25.9). All the patients gave their written informed consent, and The Kaunas Regional Biomedical Research Ethics Committee approved the study (protocol Nr. BE-10-5, 2015 05 13).

All the patients underwent MDCT scan, using „GE light Speed Pro“ 64 CT scanner.

Native and contrast-enhanced scans were performed with non-ionic intravenous contrast, injecting 100ml of contrast media at high speed (3,5 ml/s). Arterial and venous phases were performed in 30s and 70s after the start of contrast injection, following the standard protocol, used for pancreatic imaging. If any focal liver lesions were found – late phase (after 10 minutes) was performed in order to identify the nature of those focal lesions. Axial CT images and MPR reconstructions were analysed.

According to NCCN (National Comprehensive Cancer Network) guidelines, it is recommended to use CT or MRI for grading. Decision, whether to use CT or MRI should depend on possibilities, accessibility, local practice and local experience. Preoperative assessment is essential in identifying resectable disease, borderline resectable disease, locally advanced disease (unresectable without distant metastases) and metastatic disease (unresectable).

In our study we used NCCN guidelines version 3.2017 (pancreatic adenocarcinoma), for evaluation of resectability of the pancreatic tumor (Table 1).

During analysis of the CT images, we evaluated homogeneity of the tumor, density of cancerous tissue in comparison with normal pancreatic parenchyma, relation with the surrounding vessels. For extrapancreatic evaluation we looked for distant liver metastases, peritoneal and omental nodules, ascites, suspicious lymph nodes and other extrapancreatic disease (invasion of adjacent structures).

After preoperative radiological evaluation, all the patients underwent radical surgical treatment with further histopathological examination of obtained specimens. The results of CT scans were compared with results of surgery and histopathological examination. Pathologic TNM staging system of pancreatic cancer in the 8th edition of UICC cancer staging system is presented in Table 2.

STATISTICAL ANALYSIS

Quantitative values were presented as mean values and standard deviation. Chi-square test

was performed to evaluate correlation between Qualitative values. Statistically significant value was considered when $p < 0,05$. To determine pancreatic adenocarcinoma's local spreading and resectability, we calculated CT prognostic values. We calculated accuracy, the sensitivity, and specificity of this investigation, as well as positive and negative prognostic values. Calculations were performed using formulas [5]:

Accuracy of diagnostic method (percentage) = $a + d / a + b + c + d \times 100$

Sensitivity of diagnostic method (percentage) = $a / (a + c) \times 100$

Specificity of diagnostic method (percentage) = $d / (b + d) \times 100$

Positive predictive value = $a / (a + b) \times 100$

Negative predictive value (percentage) = $d / (c + d) \times 100$

Where: a – fairly positive cases, b – false positive cases, c – false negative values, d – fairly negative values.

Statistical analysis was performed using IBM SPSS Statistics 25.0 software and Microsoft Excel 16.

RESULTS

79 patients were enrolled in this study: 33 (41.8%) males and 46 (58.2%) females. Patient's age distribution was normal. There was no significant difference between male and female age.

After CT imaging in 82.3 % of all cases, pancreatic adenocarcinoma was diagnosed at stage T3 and T4 disease and only 17.7 % in stage T1 and T2.

After surgery there were 74,7 % T3 and T4 disease and 20,2 % of T1 and T2 disease. There was no difference in evaluating T stage pre and postoperatively $\chi^2 = 74,452$, $df = 15$, $p < 0,001$. More detailed characteristics of radiological and postoperative staging are presented in Table 3.

Based on CT scan results, stage N1 was the most common (63.3% of all the cases, $n=50$) and stage N0 was found in 36.7% of the cases ($n=29$). After surgery stage N1 was found in 52 of all cases (65,8 %) and stage N0 in 27 of all cases (34,2 %). There was no statistically difference in evaluating tumor N stage pre and postoperatively $\chi^2=8,978$,

$df=1$, $p=0,003$

Postoperative histological evaluation revealed adenocarcinomas in 76 cases (96,2%), 1 case was confirmed as metastases and two cases were proven to be pancreatic inflammatory changes ($n=3$, 3,8 %)

Table 4 shows accuracy, sensitivity, specificity, positive prognostic value (PPV), negative prognostic value (NPV) and accuracy of T and N staging, using MDCT.

DISCUSSION

Detection and accurate staging of pancreatic carcinoma is essential for providing optimal therapy for the patients; MDCT is the most commonly used imaging modality for diagnosing and staging pancreatic adenocarcinoma. It allows pancreatic imaging with a very high spatial and temporal resolution within a short breath-hold and is still considered the gold standard for evaluation of pancreatic solid tumors [6]. A complete and accurate assessment of the primary tumor, it's relationship with adjacent vascular structures and distant metastatic disease is required for accurate characterization of disease as resectable, borderline resectable or unresectable. The resection criteria include: no invasion into major arteries; short segment of SMV (superior mesenteric vein) and portal vein involvement (in order to allow venous reconstruction) and absence of distant metastases.

The overall sensitivity of CT in the detection of pancreatic adenocarcinoma according to the literature has improved over the recent years, ranging between 75 and 100 %, with specificity of 70-100 % [7-9,11]. CT is considered to be the most reliable technique for evaluating unresectable tumor, with reported sensitivity and specificity of 79-94 % and 82-89 % respectively [10,11].

According to our study results, CT sensitivity of determining T1/T2 stage tumors was quite low - 62.5 %; specificity 94.4 %, positive predictive value 42.9 % (TPV) and negative predictive value 93 % (NPV). But the sample of T1/T2 groups is very small, so the results should be interpreted with caution.

T3 tumors were detected in 68.4% of all cases. CT sensitivity and specificity for T3 were 83.3%

and 48% respectively and TPV and NPV were 77.6% and 57.1% respectively. Figure 1 demonstrates CT image of T2 disease.

T4 stage was detected in 6.3% of cases. CT sensitivity and specificity in T4 disease were 60% and 94.6% respectively and TPV and NPV - 42.9% and 97.2% respectively. These results should be interpreted with caution as well due to a small sample size. Figure 2 demonstrates an example of T4 disease.

We also evaluated overall CT values for N staging of pancreatic adenocarcinoma: 69.6% sensitivity and specificity was 75% and 59.3% respectively, TPV and NPV 78% and 55.2% respectively.

According to different authors, CT accuracy of N staging varies from 44 to 75 % and is not very accurate [11, 12]. In our study sensitivity of N staging based on CT scans is not very high, as well as accuracy and specificity. Although, we had cases when no pathological lymph nodes were visible on CT scans (CT N0 disease), however histological study revealed stage N1 disease. But in general, preoperative detection of peritumoral lymph nodes was estimated as not essential for assessing the resectability of pancreatic adenocarcinoma, because these lymph nodes are resected together with the primary tumor;

In conclusion, contrast enhanced CT is the primary imaging modality for the detection and staging of pancreatic adenocarcinoma; and our study results of preoperative assessment of pancreatic cancer T and N staging are very similar to those reported in the literature.

In the assessment of vessel invasion, the „tear-drop vein sign“ is a diagnostic sign of unresectable cancer [13, 14]. So, in our study we considered this sign as sign of unresectable disease (Figure 3).

CONCLUSIONS

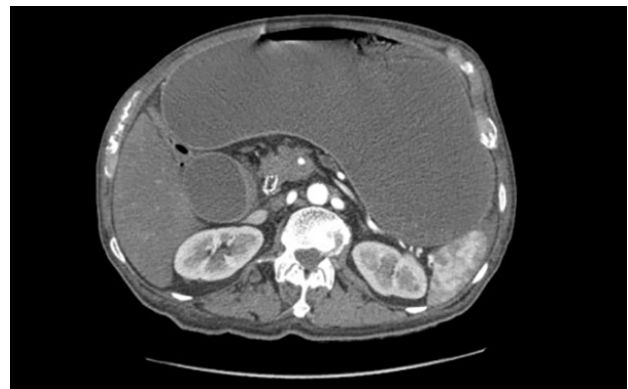
- CT is specific and accurate imaging modality in T stage of pancreatic adenocarcinoma.
- CT is quite sensitive, but non specific in N stage of pancreatic adenocarcinoma.

Figure 1. CT images of T2 disease Our case of T3 stage disease; contrast enhanced CT image, axial plane, venous phase; hypodense mass in the head of the pancreas abutting the superior mesenteric vein (arrow); no narrowing of the vessel is seen.



Figure 2. CT images of unresectable T4 stage disease. The patient with pancreatic head adenocarcinoma with duodenal obstruction and dilatation of the stomach a) axial contrast enhanced CT image, arterial phase; an illdefined hypodense mass in the head of the pancreas (arrow) with circumferential surrounding of SMA b) portal venous phase of the same patient shows involvement of SMV (arrow).

a)



b)



Figure 3. CT image of T4 stage disease with „tear drop deformity“ of SMV. Axial contrast enhanced CT image; venous phase; a hypodense mass in the head of the pancreas involving SMV with teardrop deformity (arrow).



Table 1. NCCN Guidelines Version 3.2017 pancreatic adenocarcinoma [15].

Arterial Evaluation			
SMA Contact		Present	Absent
Degree of solid soft-tissue contact		≤180	>180
Degree of increased hazy attenuation/stranding contact		≤180	>180
Focal vessel narrowing or contour irregularity		Present	Absent
Extension to first SMA branch		Present	Absent
Celiac Axis Contact		Present	Absent
Degree of solid soft-tissue contact		≤180	>180
Degree of increased hazy attenuation/stranding contact		≤180	>180
Focal vessel narrowing or contour irregularity		Present	Absent
CHA Contact		Present	Absent
Degree of solid soft-tissue contact		≤180	>180
Degree of increased hazy attenuation/stranding contact		≤180	>180
Focal vessel narrowing or contour irregularity		Present	Absent
Extension to celiac axis		Present	Absent
Extension to bifurcation of right/left hepatic artery		Present	Absent
Venous Evaluation			
MPV Contact	Present	Absent	Complete occlusion
Degree of solid soft-tissue contact	≤180	>180	
Degree of increased hazy attenuation/stranding contact	≤180	>180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	Present	Absent	
SMV Contact	Present	Absent	Complete occlusion
Degree of solid soft-tissue contact	≤180	>180	
Degree of increased hazy attenuation/stranding contact	≤180	>180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	Present	Absent	
Extension	Present	Absent	

Other			
Thrombus within vein (tumor, bland)	Present: MPV SMV SplenicVein	Absent	
Venous collaterals	Present: Around pancreatic head Porta hepatis Root of the mesentery Left upper quadrant	Absent	

* SMA – superior mesenteric artery, CHA – common hepatic artery, MPV – main portal vein, SMV – superior mesenteric vein

Table 2 . TNM staging of pancreatic cancer(7th edition of the AJCC (The American Joint Committee on Cancer) stage system) [16].

CLINICAL	STAGE CATEGORY DEFINITIONS	PATHOLOGIC
Extent of disease before any treatment		Extent of disease through completion of definitive surgery
y clinical – staging completed after neoadjuvant therapy but before subsequent surgery		y pathologic – staging completed after neoadjuvant therapy AND subsequent surgery
Tx T0 Tis T1 T2 T3 T4	PRIMARY TUMOR (T) Primary tumor cannot be assessed No evidence of primary tumor Carcinoma in situ* Tumor limited to the pancreas, 2cm or less in greatest dimension Tumor limited to the pancreas, more than 2cm in greatest dimension Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor) <i>*Note: This also includes the “PanInIII” classification</i>	Tx T0 Tis T1 T2 T3 T4
Nx N0 N1	REGIONAL LYMPH NODES (N) Regional lymph nodes cannot be assessed No regional lymph node metastasis Regional lymph node metastasis	Nx N0 N1

ANATOMIC STAGE & PROGNOSTIC GROUPS			
GROUP	T	CLINICAL	M
0	Tis	N	M
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1	N1	M0
	T2	N1	M0
III	T3	N1	M0
IV	T4	Any N	M0
Stage unknown	Any T	Any N	M1

Table 3. Radiological and postoperative characteristics of TNM staging of the study.

	T radiologically					T postoperatively						
	T1	T2	T3	T4	Total	T1	T2	T3	T4	Ca in situ	Non tumor	Total
Frequency	3	11	58	7	79	5	11	54	5	1	3	79
Percent	3.8	13.9	73.4	8.9	100	6.3	13.9	68.4	6.3	1.3	3.8	100

Table 4. Sensitivity, specificity, PPV, NPV and accuracy of T and N staging, using MDCT, of our study.

T stage	HISTOLOGICAL STAGING				
	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
CT T1+T2	62.5	94.4	42.9	93	88.6
CT T3	83.3	48	77.6	57.1	72.2
CT T4	60	94.6	42.9	97.2	92.4
T overall	73	85	67.1	88.2	81.4
N stage	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
CT N0	59.3	75	55.2	78	69.6
CT N1	69.2	48.1	72	44.8	62
N overall	75	59.3	78	55.2	69.6

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