

An attempt at assessing the efficacy of combined positron emission tomography and computed tomography (PET/CT) imaging in the diagnosis of pancreatic carcinoma – own experiences

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Introduction. Positron emission tomography (PET) with the use of fluoride-18-fluorodeoxyglucose (FDG) is one of the most modern methods of obtaining a functional image of the entire body, the trunk or a selected organ. In case of oncological diagnosis the method bases upon the phenomenon that neoplastic cells show an increased uptake of glucose. Thus, glucose is labeled with a positron radioisotope, which allows for tumour imaging. When FDG-PET is combined with CT scanning the efficacy of the method is enhanced.

Aim. To perform a retrospective analysis of the clinical value of PET/CT for the diagnosis of suspected pancreatic tumours or postoperative pancreatic tumour recurrence.

Material and method. Between march 2003 and December 2004 PET/CT was performed in 22 patients (13 men, 9 women; mean age 55.9 yrs) with diagnosed or suspected pancreatic cancer (in 11 cases the pancreatic tumour was found in the course of other imaging examinations, in 5 cases there was a distinct suspicion of a pancreatic tumour, but the imaging examinations were negative, and in the remaining 6 cases there was a distinct suspicion of postoperative pancreatic tumour recurrence)

Results. In all the 11 patients with pancreatic tumours we discerned foci of increased glucose utilization (increased FDG uptake). PET/CT provided data to diagnose pancreatic tumours with a high probability in 2 cases. In the case of the remaining patients it was impossible to differentiate between pancreatic cancer and chronic pancreatitis. In 4 cases the results of PET/CT suggested that the local advancement of the malignant process was lesser than that recognized intraoperatively. In 5 patients, in whom pancreatic cancer was suspected although no tumour mass had been diagnosed in the course of other imaging analyses, the results of the PET/CT were unequivocal. In 4 out of the 6 postoperative patients we diagnosed recurrence in the form of distant metastases.

Conclusion. PET/CT scanning may have significant clinical value in the early diagnosis of postoperative recurrence of pancreatic cancer and in the diagnosis of distant metastases. Its clinical value for the differentiation between pancreatic cancer and pancreatitis and for the evaluation of the local advancement of pancreatic cancer is probably lesser.

Próba oceny połączenia pozytonowej tomografii emisyjnej z tomografią komputerową (PET/KT) w rozpoznawaniu raka trzustki – doświadczenia własne

Wstęp. Pozytonowa tomografia emisyjna (PET) z użyciem F-18-fluorodeoksyglukozy (FDG) należy do najnowszych metod czynnościowego obrazowania całego ciała, tułowia lub wybranego narządu. W diagnostyce onkologicznej metoda wykorzystuje zwiększony wychwyt glukozy znakowanej radioizotopem pozytonowym przez komórki nowotworowe. Połączenie skanerów FDG-PET i tomografii komputerowej (KT) zwiększa możliwości diagnostyczne badania.

Cel pracy. Retrospektywna ocena wartości klinicznej badania PET/KT u chorych z podejrzeniem raka trzustki lub wznowy raka trzustki po operacji.

Materiał i metoda. Badanie PET/KT wykonano u 22 chorych (9 kobiet, 13 mężczyzn, średni wiek 55,9 lat) od marca 2003 r. do grudnia 2004 r. U 11 chorych wskazaniem do badania był guz trzustki stwierdzony w badaniach obrazowych, u 5 chorych podejrzenie raka trzustki bez stwierdzonego guza w badaniach obrazowych, a u 6 chorych podejrzenie nawrotu raka trzustki po operacji.

Wyniki. Ogniska wzmożonej utylizacji glukozy (wychwytu FDG) stwierdzono u wszystkich 11 chorych z guzem trzustki. Badanie PET/KT u dwóch chorych pozwoliło z dużym prawdopodobieństwem rozpoznać raka trzustki. W pozostałych przypadkach różnicowanie raka i zapalenia trzustki było niepewne. W 4 przypadkach wynik badania PET/KT wskazywał na

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mniejsze zaawansowanie miejscowe raka trzustki niż stwierdzone badaniem śródoperacyjnym. U 5 chorych z podejrzeniem raka trzustki bez masy guza w badaniach obrazowych wynik badania PET/KT był niejednoznaczny. U 4 z 6 chorych po leczeniu operacyjnym rozpoznano wznówę raka trzustki, w tym u wszystkich przerzuty odległe.

Wniośki. Badanie PET/KT może mieć dużą wartość kliniczną we wczesnym rozpoznaniu wznowy raka trzustki po operacji oraz w diagnostyce przerzutów odległych. Badanie PET/KT prawdopodobnie ma mniejszą wartość kliniczną w różnicowaniu raka i zapalenia trzustki oraz w ocenie miejscowego zaawansowania raka trzustki.

Key words: positron emission tomography, computed tomography, image fusion, pancreatic cancer

Słowa kluczowe: pozytonowa tomografia emisyjna, tomografia komputerowa, połączenie obrazów, rak trzustki

Pancreatic cancer (PC) is rarely curable and presents as one of the main causes for cancer mortality throughout the world. Overall 5-year survival ranges between 3% and 5%, while a vast majority of patients (80-85%) are disqualified from surgical treatment on diagnosis [1]. In Poland in the year 2000 1917 men and 1847 women died of PC; while the number of PC deaths has increased four times over the last 35 years [2]. In view of these facts it is obvious that early diagnosis is of crucial importance for patient survival, although it is still very difficult to achieve it despite the application of numerous modern methods of imaging. As for now we are not in the possession of a PC-specific marker, while the applicability of the CA 19-9 carbohydrate antigen is limited. Potential risk factors, which could be used in the course of screening, are also unclear, with the exception of hereditary pancreatitis. Different diagnostic methods, such as abdominal ultrasound (USG), computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), EUS-guided fine needle aspiration biopsy and transcutaneous fine needle aspiration biopsy all have sub-optimal sensitivity, specificity and diagnostic accuracy and therefore unclear or erroneous diagnoses are common.

Positron emission tomography (PET) is one of the most modern imaging methods. It may be performed after intravenous administration of a radioisotope, which emits positron radiation. In the course of oncological diagnostics the method bases upon the fact, that malignant cells show increased glucose utilization as compared to healthy tissue cells. The most common radiopharmaceutical preparation used in PET is a glucose derivative called fluoride-18-fluorodeoxyglucose (FDG) and therefore the term PET relates to PET with FDG, while PET performed with any other radioisotope must be specifically named. The increased uptake of FDG (which behaves exactly like glucose within the cell until it enters the phosphorylation stage) shown by neoplastic cells allows registering positron radiation in the places where the isotope is pathologically accumulated. Early studies have shown the high clinical value of PET for the diagnosis of pancreatic lesions, but the more recent publications are not unequivocal [3-5]. One may expect an increased clinical efficacy of PET if it were combined with CT scanning. The fusion of the images allows performing a functional and anatomical survey of the

entire body in the course of one non-invasive examination. Until now it has not been concluded whether PET/CT may be helpful in the diagnosis of PC, including its efficacy for the differentiation between cancer and chronic pancreatitis.

The aim of this study was to perform an initial, retrospective analysis of PET/CT in patients suspected of primary PC and for the diagnosis of postoperative PC recurrence.

Material and method

We performed a retrospective analysis of 22 patients (13 men, 9 women) who had, between March 2003 and December 2004, undergone PET/CT scanning for primary PC or postoperative PC recurrence at the Department of Nuclear Medicine of the Center of Oncology in Bydgoszcz. Patient age varied between 19 and 78 yrs (mean age 55.9 yrs)

In 11 cases the pancreatic tumour was found in the course of other imaging examinations, in 5 cases there was a distinct suspicion of a pancreatic tumour but the imaging examinations were negative, and in the remaining 6 cases there was a distinct suspicion of postoperative pancreatic tumour recurrence. The PET/CT was performed with a Biograph scan (Siemens) 60-90 minutes after the intravenous administration of approx. 370 MBq of FDG. FDG could only be applied if the blood glucose level was <8.4 mmol/l. After the administration of FDG the patient rested for 1 hour, over which he or she had to drink 1 litre of mineral water. The PET/CT scan was performed between two lines – the upper at the level of the eyeballs and the lower directly below the buttocks. The standard uptake value (SUV) was calculated according to the following equation:

$$\text{SUV} = \frac{\text{tissue concentration (millicuries / g)}}{\text{injection dose (millicuries) / body weight (g)}}$$

The results were interpreted in three categories: high likelihood of PC (+); unequivocal results (+-) and low likelihood of PC (-). We also performed a detailed analysis of the patients' histories noting the results of USG, CT, MRCP, ERCP, histopathological analyses (HP), chest X-ray (RTG), follow-up and therapies. After some 6-18 months (mean 11.5 months) from the time of the PET/CT we were able to perform an analysis of the clinical value of the obtained results.

Results

PET/CT scanning presented foci of increased FDG uptake in all 11 patients in whom a pancreatic tumour had been discerned in the course of other imaging examinations (Figure 1). In two cases the diagnosis of PC was highly probable, while in 1 case the results of the PET/CT were suggestive of a benign process. In the

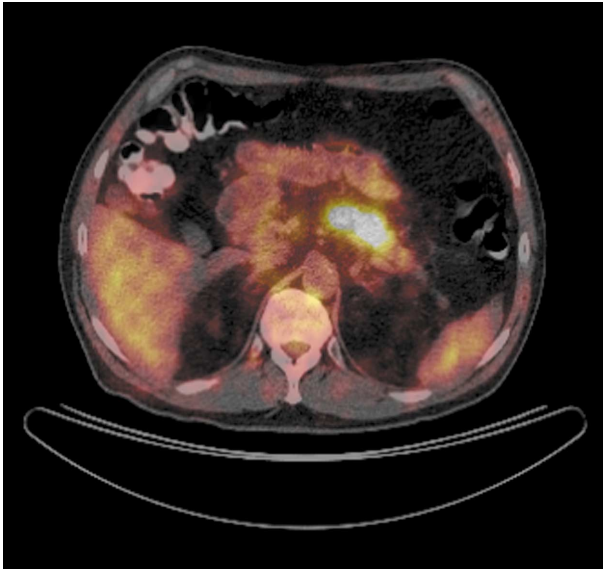


Figure 1. 78-year old man (10) with diagnosed pancreatic carcinoma. Transaxial PET/CT imaging of the abdominal cavity. In the projection of the pancreatic head – an area of increased FDG uptake analogous to pancreatic carcinoma

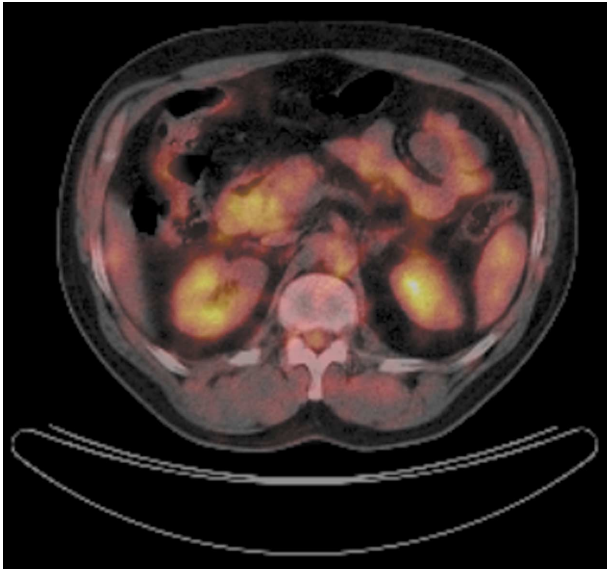


Figure 2. 45-year old man (09) with diagnosed inflammatory pancreatic tumour. Transaxial PET/CT imaging of the abdominal cavity. In the projection of the pancreatic head – presence of focal FDG uptake analogous to an inflammatory pancreatic tumour

remaining case we found the results of the PET/CT to be unequivocal. Basing upon clinical observation, the results of additional analyses (RTG, USG, CT, MRI, MRCP and HP) and intraoperative examination PC was finally confirmed in 7 cases. In two patients with confirmed PC the results of the PET/CT were uniform with the advancement of the disease, as discerned intraoperatively. In the remaining four cases disease advancement was in fact greater than the PET/CT findings had suggested and radical surgical treatment was impossible (allowing only for explorative laparotomy and/or cholangio-duodenic anastomosis). In three cases intraoperative examination allowed to diagnose an

inflammatory tumour, which was resected in 1 case in the course of distal pancreatectomy (Figure 2). In one patient we performed PET/CT 1 hour and 2 hours after the administration of FDG, but we failed to observe a SUV increase in the course of the second hour. In this case follow-up brought the diagnosis of inflammatory pancreatic tumour. The characteristics of the patients undergoing PET/CT with the previous diagnosis of a pancreatic lesion are presented in Table I.

The second analysed group consisted of the 6 patients with a distinct suspicion of PC, but without a discernible pancreatic lesion observed in the course of other examinations. In all of these patients the results of

Table I. PET/CT imaging results in 11 patients with pancreatic tumours diagnosed by means of USG, CT, MRI and MRCP

No	Age	Gender	Size of lesion in imaging diagnostics [mm] (USG, CT, MRI, MRCP)	PET	SUV	Treatment results	Histopathology results
01	47	M	38x49x51	(+ -)	6.1	cholecystectomy	inflammation
02	48	M	38x25x34	(-)	6.1	modo Whipple	adenocarcinoma
03	19	M	22x23x18	(+)	2.4	follow-up	inflammation
04	70	F	44x52x48	(+)	9.2	laparotomy	adenocarcinoma
05	45	M	42x46x44	(-)	2.6	laparotomy	inflammation
06	63	M	45x60x56	(+ -)	5.3	laparotomy	adenocarcinoma
07	53	M	29x28x30	(+ -)	4.0	laparotomy	adenocarcinoma
08	49	F	42x36x48	(+ -)	9.6	laparotomy	adenocarcinoma
09	45	M	15x16x15	(+ -)	3.0	peripheral pancreatectomy	inflammation
10	78	M	38x29x53	(+)	10.5	modo Traverso	adenocarcinoma
11	57	K	23x30x25	(+ -)	2.8	peripheral pancreatectomy	adenocarcinoma

Explanation: high probability (+), equivocal result (+ -), low pancreatic cancer probability (-)

Table II. PET/CT imaging results in 5 patients with suspected pancreatic carcinoma – USG, CT, MRI and ERCP examinations without tumour presence

No	Age	Gender	Imaging diagnostics (USG, CT, MR, ERCP)	PETnik results	SUV	Localisation of lesions	Therapy	Final diagnosis
01	72	M	stenosis and modelling of the choledochus	(+ -)	5.3	head of the pancreas	bile duct prosthesis	acute pancreatitis
02	34	F	hypoechogetic tail and body of pancreas ascites	(+ -)	4.2	whole pancreas	BAC follow-up	inflammation cirrhosis
03	56	F	dilated bile ducts blurred head of pancreas	(+ -)	10.1	head of the pancreas	BAC prosthesis	adenocarcinoma
04	53	F	blurred contours enlarged tail of pancreas	(+ -)	1.1		sphincterectomy	acute pancreatitis
05	53	M	nonhomogenous echogenic pancreas fibrosis	(+ -)	3.5	head tail of pancreas	follow-up	chronic pancreatitis

Explanation: high probability (+), equivocal result (+ -), low pancreatic carcinoma probability (-)

the PET/CT were unequivocal. In one patient we did find a focus of increased FDG uptake within the head of the pancreas (SUV 10.1), yet the result was pronounced as unequivocal due to the presence of a stent within the bile ducts; the results of fine needle aspiration biopsy confirmed a malignant process. In the remaining 4 patients chronic pancreatitis was diagnosed in the course of follow-up. The characteristics of the patients undergoing PET/CT with a previous suspicion of PC but without the presence of a pancreatic lesion in other imaging examinations are presented in Table II.

The third analysed group consisted of 6 patients with a suspicion of postoperative recurrence of PC. In 4 cases PET/CT provided data confirming recurrence in the form of numerous foci of increased FDG uptake within the lungs, the spine, the retroperitoneal space, the pelvis and the abdominal wall (Figure 3 and 4). One person was qualified for surgical treatment – the resection of a single

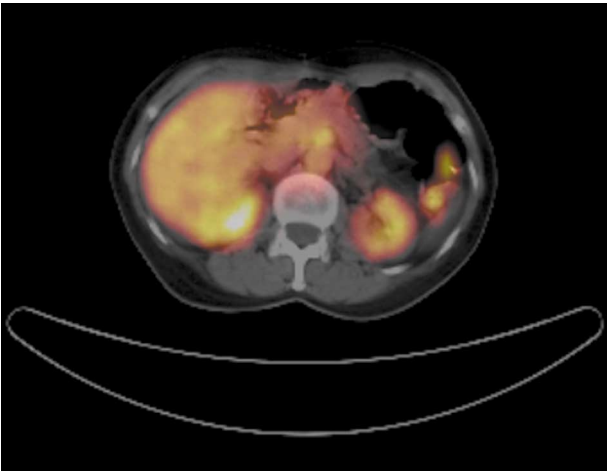


Figure 3. 59-year old woman (06) with diagnosed local pancreatic carcinoma recurrence and pulmonary metastases. Transaxial PET/CT imaging of the abdominal cavity. At the site of the pancreatic cancer – presence of focal FDG uptake analogous to local recurrence

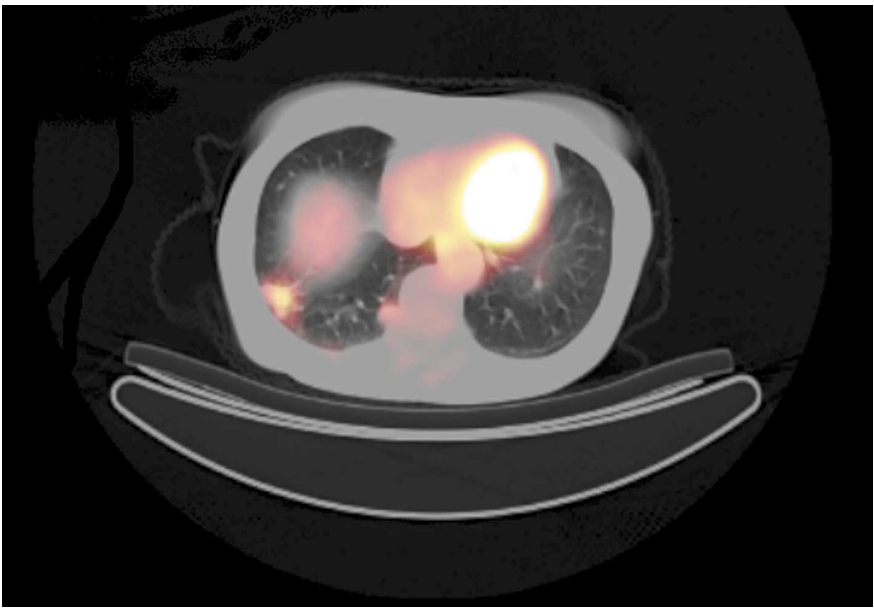


Figure 4. 59-year old woman (06) with diagnosed local pancreatic carcinoma recurrence and pulmonary metastases. Transaxial PET/CT images of the thorax. Presence of focal FDG uptake in the right lung – analogous to a metastasis of pancreatic carcinoma. Local FDG uptake by the liver

Table III. PET/CT imaging results in 6 patients with suspicion of local recurrence or pancreatic carcinoma metastases after surgical treatment

No	Age	Gender	Type of operation	Imaging results (USG, CT, MRI)	PET result	SUV	Localisation of recurrence	Final diagnosis
01	64	M	Traverso	no lesions	(+ -)	6.1	oesophagus	no recurrence
02	72	M	Whipple	irregular lesion 47x30 mm in the rectus abdominis muscle	(+)	5.5	anterior abdominal wall	metastasis
03	52	F	Whipple	hepatic focal lesions	(+)	11.8	pelvis liver	metastasis
04	54	F	Whipple	enlarged paramesenteric nodes	(+ -)	3.0	nodal spine	metastases
05	72	F	Traverso	no lesions	(+ -)	4.8	mediastinum	no recurrence
06	59	F	Whipple	pulmonary lesions	(+) (+ -)	3.2 2.8	lungs tumour site	metastases local recurrence

Explanation: high probability of recurrence (+), equivocal result (+ -), low probability of pancreatic carcinoma recurrence

metastatic tumour from the anterior wall of the abdomen; in the remaining 3 cases dissemination was confirmed. The characteristics of the patients undergoing PET/CT postoperatively are presented in Table III.

Discussion

PET is becoming more and more popular in the diagnosis and treatment of malignancies. In the case of malignant tumours of the alimentary tract PET is especially useful in the diagnosis and evaluation of postoperative recurrences of colorectal cancer and in the early diagnosis of esophageal cancer. The value of PET in the early diagnosis of PC has been, initially, enthusiastically commented. In an analysis of 106 patients with a pathological mass within the pancreas Zimny et al. evaluated the sensitivity and specificity of PET as 85% and 84%, respectively [6], while Delbecq et al. in a study of 65 patients with a strong suspicion of PC have shown a significantly higher sensitivity and specificity of PET (92% and 85% respectively), as compared to CT (65% and 61%) [7]. A similar study has also been conducted by Sperti et al. who have shown higher sensitivity and specificity of PET (94% and 97%, respectively) as compared to CT (65% and 87%) [8]. To summarise – the first studies on the applicability of PET in the differentiation of PC and pancreatitis have shown the diagnostic accuracy of PET to exceed 85%. However, more recent studies question these results – especially for the differentiation of malignant and benign lesions within the pancreas. In a prospective study Sendler et al. have shown a low sensitivity (75%) and specificity (64%) of PET in the diagnosis of PC and a poor diagnostic accuracy in the differentiation of pancreatic tumours (69%) [3]. In a number of patients PET scanning was performed after previous invasive procedures, which could have increased the ratio of false positive results. Higashi et al. have shown, in a study of 53 patients, that in the course of differentiating benign and malignant lesions PET has a relatively low sensitivity (65%) while it possess

higher specificity (93%) and clinical accuracy (81%). In our study it was possible to recognize a tumour, which had been previously diagnosed in the course of other imaging methods, only in two cases. Due to the small number of patients we refrained from analyzing the sensitivity, the specificity and the clinical accuracy of this method.

We would like to stress that not a single one of the present-day imaging methods allows for a positive differentiation between PC and chronic pancreatitis. Final diagnosis can only be made in the course of histopathological analysis of surgically harvested tissue samples. In the case of PET the limitations arise from the fact that the cells within the inflammatory infiltration have an increased glucose uptake, resembling that observed in malignant cells. It is assumed that some 24% of the total FDG accumulation within a malignant tumour has been carried out by the inflammatory cells [9]. Also the accumulation pattern of the radioisotope is not much help in the differentiative diagnostics, because both the inflammatory and the malignant infiltrations may be either localized or disseminated throughout the entire organ. In order to differentiate between PC and chronic pancreatitis one may analyse the quantitative radioactivity of accumulated FDG. Due to the fact that our patient group was rather small we could not arrive at any statistically confirmed conclusions, but we believe that high mean SUV may be characteristic of malignant lesions. Nitzsche et al. have improved their results by performing dynamic PET scanning with an analysis of the uptake curve in relation to time [10]. In the case of PC the FDG uptake curve rises rapidly in the final phase, as compared to the shape of the curve in the case of patients with benign lesions. These observations may be supported further by the case of our one patient with a benign tumour within the head of the pancreas, in whom we had performed PET 1 hr and 2 hrs after the administration of FDG. When analyzing SUV one must, however, keep in mind that they vary significantly depending upon the duration of the scan, the size and structure of the tumour

and upon the blood glucose and insulin concentrations. We believe that high SUV allows for diagnosing PC with a high probability, especially in view of the overall clinical data, increased levels of CA 19-9 and the results of other imaging techniques. In our opinion PET/CT scanning may, despite the listed limitations, be a very useful diagnostic tool in the differentiation of PC and chronic pancreatitis, especially in combination with other diagnostic methods.

An analysis of 5 patients with diffuse abnormalities within the pancreas and a concomitant pathology within the bile ducts has allowed us to conclude that in such cases the differentiative diagnosis of PC also has a number of limitations. PET results may suggest the presence of a malignancy especially in patients with acute or chronic pancreatitis and in the case of choledochitis and/or choledocholithiasis. The false positive result may also be caused by previous invasive techniques (ERCP and BAC) and endoscopic procedures (sphincterectomy, prosthesis of the bile ducts and the pancreatic ducts).

The basic aim of modern-day diagnostics is the early recognition of a malignant lesion and an exact analysis of clinical advancement. The value of PET in PC is best observed in the case of discerning distant metastases. A few studies have shown that the diagnostic accuracy of PET in the recognition of hepatic metastases is higher than that of CT and abdominal USG [11-13]. Frohlich et al. report that the frequency of the recognition of hepatic focal lesions over 10 mm in diameter is 97% with PET, while in the case of lesser lesions it reaches 43% [13]. In the case of hepatic metastases, which are characterized by an avid glucose uptake, the lesions may be considered larger than they in fact are [4]. In the case of lymph node metastases the value of PET is much smaller. Although in the course of the initial studies lymph node metastases were recognized in some 76% of patients [11], more recent reports have shown the clinical accuracy of PET to pose itself between 46% to 56% [4, 6]. Basing upon our material we may also say that in the case of lymph node metastases the specificity of PET/CT is too poor, especially in the case of parapancreatic nodes. Presently, it is assumed that the most exact method of preoperative evaluation of the advancement of PC (i.e. the infiltration of neighbouring organs and large vessels) is EUS [14-16]. Martz et al. [14] have shown, that combined EUS and PET have a higher sensitivity in PC staging than spiral CT. In our patient material in the case of 4 patients the results of PET/CT were characteristic of a lesser local advancement, than that found intra-operatively, i.e. in those cases the results of PET/CT did not allow us to refrain from unnecessary laparotomies. Higashi et al. have found distant metastases and other primary malignancies in 35/132 patients (38%) evaluated with PET for the advancement of PC [4] and they believe that PET scanning performed for the evaluation of the advancement of PC allows to alter the planned treatment course in some 40% of patients. In our patient group this ratio was much smaller while PET/CT influenced the

treatment course only in combination with the results of other examinations and of the overall clinical picture.

Studies on small patients groups have proven the high clinical value of PET for the diagnosis of PC recurrence after surgery. As in the case of colorectal cancer, PET scanning allows for the earliest possible diagnosis of PC in the case of an increase in the activity of markers of malignancy with concomitant negative results of other methods of diagnostic imaging. Our results regarding the 4 patients with PC recurrence confirm these results – this is true both in the case of distant and local failure. Our early experiences show that PET/CT may have significant clinical value in the early recognition of postoperative local failure in PC and in the diagnosis of distant metastases. PET/CT is less effective in the differentiation of PC, and chronic pancreatitis, and for the sake of the evaluation of local advancement of PC. In the latter cases PET/CT may be considered as auxiliary method accompanying other diagnostic procedures. Our results indicate the need for further prospective studies on larger patient groups, including PET/CT scanning with the evaluation of radioactivity over a longer time period. We believe that as PET is replaced with PET/CT and new scanners and radiomarkers are introduced the clinical value of this diagnostic modality in patients with PC will increase.

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