

THE USE OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY TO ASSESS CLINICAL OUTCOMES OF PATIENTS WITH BORDERLINE RESECTABLE PANCREATIC CANCER

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Borderline resectable pancreatic cancer exemplifies a subset of locally advanced pancreatic cancers. The guidelines clearly emphasize the need of delineating the tumor from superior mesenteric vein (SMV), portal vein, gastroduodenal artery, hepatic artery and superior mesenteric artery (SMA). The guidelines also highlight the characterizing of involvements of these vessels in terms of impingement, abutment, narrowing, occlusion and encasement [14,15]. The term “borderline resectable pancreatic cancer” is used when the tumor fulfills these criteria and shows no evidence of distant metastasis [10].

Unfortunately, only 10-15% of pancreatic cancers are found to be resectable at the time of diagnosis due to late onset of the symptoms [8]. Therefore, well-timed diagnosis and staging is essential to specify the most appropriate treatment and avoid unnecessary surgical risk in the evaluation of patients with PC.

The use of 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (PET/CT) provided better staging and resulted in clinical management variations when applied to a number of tumors in literature [2,5-7,11].

The combination may provide a more comprehensive picture of the area being evaluated. PET scans are done regularly at some but not all cancer centers for diagnosis and staging of the pancreatic cancer. However, it has not yet been considered as a standard test to diagnose pancreatic cancer. A PET scan should not be used alone instead of a high-quality CT scan [12]. Furthermore, the clinical opinion on the role of PET/CT in the routine management of primary pancreatic cancer varies. While numerous studies exist for use of PET in assessment of treatment response for other tumors, there are only four small sized studies concerning with the treatment of pancreatic cancer [11]. There are no studies in literature about the effect of using PET on the change of preoperative strategy in locally advanced pancreatic tumors.

The aim of this study is to prospectively evaluate the effect of PET/CT on patients with borderline resectable pancreatic cancer, including an assessment of the clinical management planning.

Material and methods. Between December 2011 and February 2015, 28 consecutive patients who admitted to

our tertiary hospital and diagnosed as borderline resectable pancreatic cancer were included in this study. In addition to conventional preoperative studies, PET/CT was also performed to patients, and all data was prospectively recorded into a database. All PET/CT scans were performed prior to preoperative chemo-radiotherapy.

Exclusion criteria were recurrent disease, patient refusal of participation in this study and either PET/CT or other conventional preoperative imaging studies performed outside of our institution.

The conventional modalities included an examination with helical+h CT and MRI.

All preoperative CT studies were performed using a CT scanner with 64 parallel detector rows (Toshiba Aquilion 64, Toshiba Medical Systems Corp., Tokyo, Japan). Nonionic intravenous contrast material (Omnipaque 300, Amersham Health, Princeton NJ, USA) was administered to the patients as 2 mL/kg up to a maximum of 180 mL.

PET/CT scans were performed with a Siemens Biograph 16 PET/CT System (Siemens medical solutions, Knoxville, TN) at least one hour after intravenous injection of 18 F-fluorodeoxyglucose (FDG). All patients fasted for six hours prior to the study, but were encouraged to drink water. Patients also received bowel preparation prior to procedure. All PET/CT images were interpreted by a single nuclear medicine specialist prior to surgery. The mean interval between the CI studies and PET/CT was 6 days (range 1-12 days).

A single radiologist with 5 years of experience in CT evaluated the images. The PET/CT findings were directly correlated with previous CI images and rates of over-staging or down-staging and change in the management were evaluated.

SPSS 16.0 software (Chicago, Illinois, USA) was used for statistical analysis. The level of statistical significance with 0.95 and confidence limits was set as P=0.05.

Results and their discussion. Twenty-eight consecutive patients underwent PET/CT scanning. The mean age was 65 years (range 58–76 years), and 45% were male. Twenty-two patients had pancreatic head cancer, while 6 patients had

Table 1. Patients characteristics

Cancer n=28	PET-Ct	ct	MRI
Pancreatic head	19	22	22
Pancreatic body and tail	6	5	6
Metastasis	4	4/2	4/3

Table 2. Corelation between PET Ct and convantional modality

	correlation	PET CT
Ct MRI	Kappa value	p
metastasis	0.502	P<0.01

pancreatic body and tail cancer. Results of conventional studies with regard to tumor or metastasis features of the patients are summarized in Table 1. All primary lesions were detectable with CT scan.

The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of PET/CT assessment based on the results of CI studies were calculated separately for the T and N stages. The sensitivity and accuracy of PET/CT for T staging was also higher when compared to N staging.

The κ agreement coefficient analysis showed that the correlation between PET/CT and CT studies were higher with the T staging. The kappa value for the T staging was found to be 0.502. (Table 2).

PET/CT identified the primary tumor accurately in all patients. Comparing PET/CT with CT studies, there were incidental findings in 4 (14.28%) patients. According to the PET/CT results, the preoperative stage of 1 patients (10%) changed.

PET/CT examination revealed suspicious findings for peritoneal metastasis in 1 and mediastinal metastasis in 3 patients. When compared conventional modality, Pet Ct had detected peritoneal metastasis were better (Table 3). Moreover, All mediastinal metastases were true positive. Furthermore, this process ensured prevention of the surgical procedure for these patients.

Pancreatic cancers have the worst prognosis among the abdominal cancers and they become symptomatic in late period. Therefore, most of the patients admit to clinics with advanced stages. Currently, the main potential treatment for pancreatic cancer is surgery [3,16]. Surgery became very popular in locally advanced pancreatic tumors in recent years. 1 year survival after surgery is 41% longer in cases which were able to be performed R0 compared to those which were not [3]. The most considerable problem in preoperative period is patient selection. Peritoneal or distant metastasis and a long segmental involvement in celiac or superior mesenteric arteries are not amenable. Short segmental involvement in portal vein, superior mesenteric vein or superior mesenteric artery is not a contraindication for resection [14,15]. Borderline re-

sectable pancreatic cancers increased the rate of probability of by 20-30% for pancreatic cancers in recent years [15]. Mostly, a high-quality CT scan is adequate to evaluate intra-abdominal organs in preoperative period and additional imaging methods are not being performed in routine to evaluate distant organs (lungs etc.). There is no data in literature about additional benefit of PET/CT on locally advanced pancreatic tumors. Recently, dual-phase 18F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) was shown to be useful in the discrimination of malignant and benign pancreatic lesions [13]. FDG-PET is a functional imaging method that is specific to metabolically active cancer cells. Sperti et al. reviewed a sum of sixty pancreatic cancer patients who had PET scans and demonstrated that the initial PET scan predicted the clinical outcome when patients were dichotomized at a SUV of 4 [11].

The efficacy of PET/CT at identifying the lesions which were diagnosed before with the imaging methods is 95% [20]. However, the use of PET/CT might be considered to detect peritoneal or distant organ metastasis not yet been detected with other imaging studies that constitutes 5-10% of patients and to identify locally advanced tumors [1,4,17].

In literature [17], performed a small study of 16 locally advanced patients who received pre- and post-treatment 18F-fluorodeoxyglucose (FDG) PET scans. They observed that patients exhibiting a $\geq 50\%$ decrease in SUV following neoadjuvant chemoradiation underwent successful resections while resection was uncommon in non-responders; however, only three patients in the entire cohort proceeded to resection. While these preliminary studies show promising results, further research is warranted before FDG-PET parameter cutoffs are applied in the surgical candidate selection process for BL-PDAC [9].

The most important problem about PET/CT is that it changed the surgery strategy in 3 cases (10%) only. 2 of these were lung metastasis and 1 of them was peritoneal nodule which was suspicious in CT but verified with PET. Our study is not large enough to show the efficacy of PET/CT, however, we propose that performing PET/CT on specific groups with advanced stage pancreatic tumors might prevent surgeries with high morbidities.

Table 3. Sensitivity

Advance pancreatic cancer	Pet ct	MRI/BT
Ppv(disease)	0.96	100
PPV (metastasis)	100	0.75/0.5

In conclusion, ¹⁸F-FDG PET has additional value over conventional radiologic techniques for monitoring the treatment response in locally advanced pancreatic cancer patients. It is feasible to predict early metastasis and patient outcome early (after one course of IC) during therapy.

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SUMMARY

THE USE OF ¹⁸F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY TO ASSESS CLINICAL OUTCOMES OF PATIENTS WITH BORDERLINE RESECTABLE PANCREATIC CANCER

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The aim of this study is to evaluate the effect of ¹⁸F-FDG PET on preoperative staging and clinical management of pancreatic cancer. Between December 2011 and February 2015, 28 consecutive patients with borderline resectable pancreatic cancer were evaluated with both ¹⁸F-FDG PET scans and conventional preoperative imaging studies.

Medical records of all patients were noted prospectively. ¹⁸F-FDG PET findings were compared with conventional imaging studies and over-staging or down-staging rates with changes in clinical management were evaluated. The correlation of ¹⁸F-FDG PET with conventional imaging studies was evaluated with a kappa agreement coefficient. A number of 22 (78.5%) patients had pancreatic head

cancer and 6 (21.4%) patients had pancreatic body and tail cancers. Based on ¹⁸F-FDG PET, additional lesions were found in 4 (14.28%) of the patients which were lung and peritoneal lesions as metastasis. No hepatic metastasis or supraclavicular lymph node involvement was confirmed in patients. Routine use of ¹⁸F-FDG PET for preoperative staging has not an effect on cancer management in 96.8% of our patients. In conclusion, ¹⁸F-FDG PET has additional value over conventional radiologic techniques for monitoring the treatment response in locally advanced pancreatic cancer patients. It is feasible to predict early metastasis and patient outcome early (after one course of IC) during therapy

Keywords: borderline resectable pancreatic cancer, ¹⁸F-FDG PET, preoperative assessment.

РЕЗЮМЕ

ИСПОЛЬЗОВАНИЕ ПОЗИТРОННО-ЭМИССИОННОЙ КОМПЬЮТЕРНОЙ ТОМОГРАФИИ С ПРИМЕНЕНИЕМ РАДИОФАРМАКЕВТИКА 18F-ФТОРДЕЗОКСИГЛЮКОЗА ДЛЯ ОЦЕНКИ КЛИНИЧЕСКИХ ИСХОДОВ У ПАЦИЕНТОВ С ПОГРАНИЧНО РЕЗЕКТАБЕЛЬНЫМ РАКОМ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ

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Целью данного исследования явилась оценка эффективности позитронно-эмиссионной компьютерной томографии при операционном планировании и лечении погранично резектабельного рака поджелудочной железы.

В период с декабря 2011 г. по февраль 2015 г. с помощью ПЭТ/КТ с 18-ФДГ и обычных методов визуализации обследовано 28 пациентов. Истории болезней всех пациентов записывались для дальнейшего анализа. Данные ПЭТ/КТ с 18-ФДГ сравнивались с данными, полученными при обследовании посредством обычных методов визуализации, а также изучались коэффициенты занижения или завышения стадии болезни с клиническим ведением пациента. Оценка соответствия результатов, полученных при помощи ПЭТ/КТ с 18-ФДГ, с данными, полученными при обследовании обычными методами визуализации, осуществлялась с помощью коэффициента каппа. У 22 (78,5%) пациентов выявлен рак головки поджелудочной железы, у 6 (21,4%) – рак тела или хвоста поджелудочной железы. Посредством ПЭТ/КТ с 18-

ФДГ дополнительные повреждения были найдены у 4 (14,28%) пациентов, это были метастазы в легких и перитонеальные поражения. Наличие метастазирования в печень или вовлечения надключичных лимфатических узлов не подтверждено. Исследование выявило, что рутинное использование ПЭТ/КТ с 18-ФДГ при операционном планировании погранично резектабельного рака поджелудочной железы у 96,8% обследованных пациентов не эффективно.

В заключение, ПЭТ/КТ с 18-ФДГ обладает дополнительной ценностью в сравнении с обычными рентгенологическими методами для мониторинга реакции на лечение погранично резектабельного рака поджелудочной железы.

რეზიუმე

კუჭქვეშა ჯირკვლის რეზექტაბელური კიბოს კლინიკური გამოსავლის შეფასება პოზიტრონულ-ემისიური კომპიუტერული ტომოგრაფიის და რადიოფარმეკეპარატ 18F-ფთორდეზოქსიგლუკოზის ერთობლივად გამოყენების პირობებში

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კვლევის მიზანს წარმოადგენდა პოზიტრონულ-ემისიური კომპიუტერული ტომოგრაფიის (პე/კტ 18-ფდგ) მეთოდის ეფექტურობის შეფასება კუჭქვეშა ჯირკვლის მოსაზღვრე რეზექტაბელური კიბოს ოპერაციის დაგეგმარებასა და მკურნალობაში. 2011 წ. დეკემბრიდან 2015 წ. თებერვლამდე პე/კტ 18-ფდგ-თან და ვიზუალიზაციის რუტინული მეთოდების გამოყენებით გამოკვლეული იყო 28 ავადმყოფი. პე/კტ მონაცემები შედარდა ვიზუალიზაციის სხვა მეთოდებით მიღებულ მონაცემებს. პაციენტის კლინიკური მდგომარეობასთან ერთად შესწავლილი იყო, აგრეთვე, ავადმყოფობის სტადიის მომატების და დაკლების კოეფიციენტები. პე/კტ მეთოდით მიღებული შედეგების შესაბამისობის შეფასება ვიზუალიზაციის რუტინული მეთოდებით მიღებულ მონაცემებთან ხდებოდა კაპას კოეფიციენტის მეშვეობით. 22 (78,5%) პაციენტს აღმოაჩნდა კუჭქვეშა ჯირკვლის თავის კიბო, 6 (21,4%) ავადმყოფს - კუჭქვეშა ჯირკვლის სხეულის და მისი კუდის კიბო. პე/კტ გამოყენებით დამატებითი დაზიანება აღმოჩენილი იქნა 4 (14,28%) შემთხვევაში - მეტასტაზები ფილტვებში და პერიტონეული დაზიანება.