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Research Article

**DIAGNOSTIC ACCURACY OF CT-PERFUSION IN
DETECTING HIGH GRADE PANCREATIC
ADENOCARCINOMA USING PEI****Dr. Hafsa Faiz, Dr. Rameesha Tanvir, Dr. Ruqaiya
Punjab Medical College (FMU)****Abstract:**

Objective: To estimate the Diagnostic accuracy of CT perfusion using PEI in detecting high grade pancreatic ductal adenocarcinoma keeping histopathology as gold standard.

Material and Methods: The study conducted in Radiology department of Allied Hospital Faisalabad and the duration of the study was 6 months.

Study Design: Cross sectional (validation) study.

Results: This study is thus being carried out that how accurately CT perfusion can detect high grade pancreatic ductal adenocarcinoma by noninvasive method and by accurate characterization of histologic grade this study will help doctors to opt for targeted treatment and early deaths due to unnecessary surgery can be avoided.

Conclusion

Perfusion CT can predict tumor grade of pancreatic adenocarcinoma. In particular, PEI and BV perfusion parameters proved their efficiency in identifying high grade pancreatic adenocarcinoma

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INTRODUCTION:

Pancreatic cancer is fifth leading cause of cancer deaths worldwide¹. The American society estimates that 45,220 Americans will be diagnosed with pancreatic cancer in 2013 and that 38460 will die from disease². Pancreatic ductal carcinoma is the most common primary malignancy of pancreas patients with pancreatic adenocarcinoma have an overall 1yr and 5yr survival rate after diagnosis below 20% and 5% respectively.³ In last year's expressive development in field of radiology and imaging diagnosis have been observed with advent of multi detector computed tomography(MDCT) and magnetic resonance imaging(MRI).In the context of such evolution and in attempt to obtain not only structural assessment but also metabolic and functional analysis of different organs and types of lesions, new imaging technique have developed⁴. MDCT is first line imaging procedure for preoperative diagnosis of solid pancreatic lesions¹.CT perfusion (CTP) has recently aroused the interest of many researchers given its reproducibility, robustness and efficacy⁴.

Miles et al for first time applied this technique in pancreas⁵. Despite the fact that a combined surgical systemic approach may offer a longer life expectancy the long term outcome remains dismal. The early recurrence of pancreatic adenocarcinoma after resection characterizes the patient population reported in literature as Early Death (ED). The preoperative correct identification of this group is important to minimize unnecessary resections but remain difficult owing to postoperative assessment of some factors such as tumor resection margins and grading.³ CTP provides a noninvasive method to evaluate the variables that provide insight into angiogenesis⁶. The excellent linear relationship between tissue attenuation and iodinated contrast agent concentration allows an objective quantification of perfusion parameters correlated with hemodynamic changes caused by new vessels³Qualitative parameters refers to the descriptors of the enhancement time curves. These include curve shape, time to peak enhancement, peak enhancement intensity (PEI) or area under the enhancement time curve. Quantitative parameters are regional blood flow, blood volume(BV), and permeability surface area product.⁷ The statistically significant difference between high and low grade neoplasm were demonstrated for PEI and BV. Prevalence of high grade ductal adenocarcinoma is 62.5% considering PEI perfusion CT identified high grade lesions with 65% sensitivity &92% specificity³. Sensitivity and specificity for endoscopic ultrasound guided fine needle cytology is 88.6% and 99.3% respectively [8].

This study is thus being carried out that how accurately CT perfusion can detect high grade pancreatic ductal adenocarcinoma by noninvasive method and by accurate characterization of histologic grade this study will help doctors to opt for targeted treatment and early deaths due to unnecessary surgery can be avoided.

OBJECTIVE

To estimate the Diagnostic accuracy of CT perfusion using PEI in detecting high grade pancreatic ductal adenocarcinoma keeping histopathology as gold standard

OPERATIONAL DEFINITIONS**Pancreatic adenocarcinoma**

Pancreatic adenocarcinoma is a tumor that histologically form glands and secrete mucin forming tubular structures or cell cluster. Poorly differentiated lesion with several cytological atypia is a feature of high grade.

Perfusion-CT features of pancreatic adenocarcinoma

On perfusion CT, PEI value of 17.8 HU is used as cut-off for diagnosis of high grade pancreatic adenocarcinoma.

Sensitivity

Ability of perfusion CT to detect those who have high grade pancreatic adenocarcinoma.

Specificity

Ability of perfusion CT to exclude those who don't have high grade pancreatic adenocarcinoma.

True-positive

The cases that will be positive for high grade pancreatic adenocarcinoma on perfusion CT and histopathology.

True-negative

The cases that will be negative for high grade pancreatic adenocarcinoma on perfusion CT and histopathology.

Positive predictive value

Probability of having high grade pancreatic adenocarcinoma if found positive on perfusion CT.

Negative predictive value

Probability of not having high grade pancreatic adenocarcinoma if found negative on perfusion CT.

MATERIAL AND METHODS:

The study conducted in Radiology department of Allied Hospital Faisalabad and the duration of the

study was 6 months.

STUDY DESIGN

Cross sectional (validation) study.

SAMPLE SIZE

By using sensitivity specificity calculator

Sensitivity =65%³

Specificity =92%³

Prevalence rate=62.5%³

Confidence level = 95%

Precision for sensitivity=10%, for specificity=8%

Sample size=100

SAMPLE COLLECTION

INCLUSION CRITERIA

- 1- Patients of any sex
- 2- Age 30 to 65 years
- 3- Patients who have been diagnosed of having irregularly marginated hypoechoic mass lesion in pancreas on ultrasound

EXCLUSION CRITERIA:

- 1- Patients currently undergoing chemotherapy
- 2- Presence of resectable tumor at imaging examination
- 3- Patients who have evidence of metastatic disease
- 4- Patients with deranged renal function test and allergic to contrast agent

DATA COLLECTION PROCEDURE

Permission for research will be sought from hospital ethical committee. Patients will be collected from OPD & indoor of Radiology and surgical department of Allied Hospital Faisalabad. Objective of study will be explained to every subject who fulfills the criteria & informed consent will be taken. Confounding variables will be controlled by restriction (by excluding the subjects with history of metastatic

disease or chemotherapy). Data will be collected by me and verified by senior radiologists CT-Perfusion examination will be performed with the patient in supine position on a 128 slice Optima Multi detector CT scanner by GE. An initial unenhanced wide coverage scan will be acquired with a section thickness of 5mm to correctly localize the tumor and select the volume on which perfusion has to be performed. P-CT consist of acquisition of repeated CT scan of volume being analyzed over time during and after the administration of bolus of iodinated contrast agent. CT scanning parameters included 120kVp, tube current of 150 mAs, gantry rotation time of 0.5 s, increment 5 mm, 5mm slice thickness and 100 mm in length. To obtain P-CT parameter a single region of interest will be drawn within the tumor on the axial slice. Additionally, six smaller ROIs will be drawn within the tumor, of which two in the central portion and four in the periphery. Qualitative information achieved by perfusion CT consists of analysis of color maps automatically generated by software, able to provide an immediate and panoramic representation of perfusion distribution within the tumor. Quantitative information consists of analysis of CT perfusion parameters. The final numeric values will be expressed for each ROI, are the mean values automatically calculated by the system from all measurements performed in each voxel included in ROI. This procedure will be performed in Radiology Department of Allied Hospital. I will interpret it under supervision of my supervisor. Data will be collected by me on predesigned Performa Image guided (CT guided) biopsy will be done on all patients and specimen will be sent to the hospital pathology lab and histopathology will be done by senior pathologist, who will be kept blinded to perfusion-CT analysis

DATA ANALYSIS

All the data will be analyzed by using SPSS V-17. Mean and standard deviation will be calculated for all the quantitative variables like age. Frequency and percentage will be calculated for all the qualitative variables like gender and true positive. Sensitivity, specificity, PPV, NPV and diagnostic accuracy will be calculated by constructing 2x2 table taking histopathology as gold standard

Histopathology

+ve	-ve	
a (TP)	b (FP)	+ve
c (FN)	d (TN)	-ve

P-CT

Specificity = $TN/FP+TN \times 100$

Sensitivity = $TP/TP+FN \times 100$

Positive predictive value = $TP/TP+FP \times 100$

Negative predictive value = $TN/FN+TN \times 100$

Diagnostic accuracy = $TP+TN/TP+FP+FN+TN \times 100$

DISCUSSION:

Perfusion CT (P-CT) is an imaging technique able to quantify the tissue enhancement after contrast material administration. Main P-CT fields of application are Neuroimaging (in diagnosing stroke and choosing its proper treatment) and Oncologic Imaging in terms of tumor assessment, characterization and staging, angiogenesis assessment, response to therapy prediction and response to therapy monitoring [20]. Many other applications are however emerging also in non-oncologic fields such the assessment of changes in organ (liver, pancreas and spleen) perfusion in cirrhotic patients [21]. Regarding the CT perfusion technique applied in this study, although patient should not move at all during image acquisition, the movement provides less impact on image quality by using CT scanners based on slope method than other processing methods as reported in literature [17]. A shallow breathing during images acquisition is considered acceptable and patients must be instructed not to breathe deeply when feeling the hot flush due to the contrast agent.

Pancreatic ductal adenocarcinoma is the most common pancreatic primary malignancy accounting for 80% of pancreatic malignancies. The main aims of imaging consist of tumor detection and characterization, playing an important role in disease management. CT study represents the modality of

choice in diagnosis confirmation, providing accurate staging. In more than 95% of the patient's pancreatic ductal adenocarcinoma is diagnosed at an advanced stage, in presence of locally advanced disease (vascular or perineural invasion) or distant metastases. Prognosis and therapeutic approaches depend on lesion resectability at the moment of clinical presentation. As reported by Barugola *et al.*, up to 30% of resected patients die of disease within 1 year after surgery [4]. In this subgroup recurrence is very early, and survival is similar to that observed in patients with advanced disease undergoing antitumoral therapies alone. These so-called "early deaths" (ED) after resection for curative intent may be attributed either to inadequate pre- or intra-operative staging or to a particularly aggressive behavior of the disease. Thus, the ability to identify patients at high risk of ED before surgery is an important clinical goal to circumvent a demanding surgical intervention.

According to some authors symptoms lasting >40 days, CA 19-9 >200 U/ml and G2 pathological grading are easy-to-obtain preoperative parameters in order to identify patients with a disease not suitable for front-up surgery, even if deemed resectable by high quality imaging [4, 11]. According to Barugola *et al.* [4] those patients with level of CA 19-9 >200 U/ml and symptoms lasting >40 days should undergo fine needle biopsy: if pathology report shows a poorly differentiated or anaplastic tumor, a non-

surgical therapeutically approach should be carried out. After neoadjuvant therapy (or, if necessary, palliative treatment), in case of disease stability or down-staging, patients could undergo surgical intervention. The present study aims to demonstrate P-CT ability in direct and preoperative characterization of high grade pancreatic ductal adenocarcinomas in order to implement the identification of patients at high risk of ED, to provide each patient with the best treatment strategy.

Thirty-two patients with locally advanced pancreatic ductal adenocarcinoma underwent P-CT imaging study and percutaneous US-guided fine needle biopsy. A statistically significant difference between high grade and low grade neoplasms was found in terms of median PEI and BV values resulting both from measurements performed on the large ROI ($p = 0.012$ for PEI and $p = 0.004$ for BV) and from the mean value of the measurements performed on the 6 small ROIs ($p = 0.005$ for PEI and $p = 0.001$ for BV). Using ROC curves the cut-off values for PEI and BV respectively with the best performance in terms of sensitivity and specificity in the characterization of high grade tumors have been chosen. PEI perfusional parameter with a cut-off of 17.8 HU can identify pancreatic high grade adenocarcinomas with a 75% accuracy. BV perfusional parameter with a cut-off of 14.8 ml/100 g can identify pancreatic high grade adenocarcinomas with a 78.1% accuracy. Considering both PEI and BV perfusional parameter with the related cut-off values, it is possible to characterize pancreatic ductal high grade adenocarcinomas with a 60% sensitivity, a 100% specificity, a positive predictive value of 100%, a negative predictive value of 60% and a 75% accuracy.

According to our results, P-CT offers a significant contribution both to clinical and laboratory data in identifying high grade pancreatic ductal adenocarcinoma, and consequently patients at high risk of ED, more accurately than the suspicion given by duration of symptoms and CA 19-9 levels. In everyday clinical practice patients with pancreatic ductal adenocarcinoma classified as high grade at P-CT should undergo biopsy to achieve a grading confirmation even if resectable at imaging. Actually, standard of care for pancreatic lesions typical for ductal adenocarcinoma deemed resectable at imaging is surgical intervention, without pathological confirmation. Considering its accuracy values, P-CT could adequately select all patients with a high grade lesion and justify fine needle biopsy to confirm the grade itself, even in presence of a resectable disease at imaging. The limitations of this study are the

relative small number of patients included and the analysis of a fine needle biopsy sample instead of the whole surgical specimen. Other prospective studies about resectable pancreatic lesions based on a larger population are needed.

CONCLUSION:

Perfusion CT can predict tumor grade of pancreatic adenocarcinoma. In particular, PEI and BV perfusion parameters proved their efficiency in identifying high grade pancreatic adenocarcinoma.

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