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Original Research Article

Can preoperative CT based assessment of remnant pancreatic volume predict pancreatic fistula in pancreatoduodenectomy

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Abstract

Background: Pancreatic fistula is one of the most dreadful complication of pancreatoduodenectomy causing prolonged hospital stay, financial implications and mortality. The aim of the present study was to assess remnant pancreatic volume based on preoperative CECT and to validate it for predicting pancreatic fistula.
Methods: 52 patients undergoing pancreatodudenectomy in which pancreatic protocol CECT was done in the hospital were included, Remnant pancreatic volume was calculated from the CT as the sum of pancreatic tissue area to the left of the presumed pancreatic transection site and its correlation to postoperative pancreatic fistula was done.
Results: n= 9(17.2%) patients had clinically relevant fistula, mean remnant pancreatic volume in patients without fistula was 36.86±10.73 cm3 and those with clinically relevant fistula was 58.03±12.33 cm3 (p value= <.001), on ROC curve analysis remnant pancreatic volume of >48.6 cm3 was found to be 88.8% sensitive and 76% sensitive in predicting clinically significant pancreatic fistula.
Conclusion: Preoperative assessment of remnant pancreatic volume is a useful marker for predicting postoperative pancreatic fistula and may help in better application of preventive measures in high risk group in future.

Keywords: Pancreatic fistula, remnant pancreatic volume, pancreatic protocol CECT, pancreatoduodenectomy

Introduction

Known as the most morbid procedure with high mortality, advances in perioperative and postoperative management have significantly improved results following Pancreatoduodenectomy (PD) with as low mortality of 0-5% [1]. Pancreatic fistula continues to be the nemesis of pancreatic resection. Various risk factors ranging from patient characteristics, Intra-ooperative factors, pancreatic texture etc. has been studied [2]. Recent studies have shown increased remnant pancreatic volume is associated with increased risk of pancreatic fistula [2, 3, 4]. The aim of our study was to assess the remnant pancreatic volume and other anthropometric parameters based on preoperative pancreatic protocol CECT and to

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assess its role in prediction of pancreatic fistula.

Methods

We conducted a prospective cross sectional analytical study in department of Surgical Gastroenterology in Nizam Institute of Medical Sciences Hyderabad from May 2013 to Dec 2014. All patients posted for pancreaticoduodenectomy were taken in study. The preoperative pancreas protocol CT was used to assess the Remnant pancreatic volume, skeletal muscle mass, Visceral adipose tissue, Subcutaneous adipose tissue.

Remnant pancreatic volume

Remnant pancreatic volume (cm3) was calculated as the sum of pancreatic tissue area in each slice multiplied by slice thickness (2 mm), Level of the third lumbar vertebra (L3) will be selected for measurement of the area of adipose tissue and SM mass value is related linearly to whole-body muscle mass and normalized for stature as is conventional for body mass index and body composition components (Picture 1-3).

Visceral adipose tissue

For the Visceral adipose tissuearea (cm2), the inner boundary of abdominal wall muscle using a graph pen. The Visceral adipose tissuearea (cm2) will computed by the number of pixels multiplied by the pixel surface area (picture 4)

Subcutaneous adipose tissue

For the Subcutaneous adipose tissuearea (cm2), the outer boundary of the abdominal wall muscles and paraspinal muscles will selected manually as the area of interest (picture 5)

Skeletal muscle mass

For the Skeletal muscle mass area (cm2), the area between inner and outer boundary of abdominal wall muscles and paraspinal muscles will be selected manually.Skeletal muscle massarea will include paraspinal muscles (psoas, erector spinae, and quadratuslumborum) and abdominal wall muscles (transversusabdominus, external and internal obliques, and rectus abdominus) (picture 6).

Data collection

Preoperative assessment of factors of study with CECT was done in hospital was done. Preoperative data comprising of age, gender, BMI, presence of preoperative stenting, preoperative cholangitis, and presence of comorbidities was recorded. Intraoperative data based on pancreatic texture, type of anastomosis, intraoperative octreotide use, operating time and blood loss was recorded. Post op complications were defined as per ISGPF definitions (5)

Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

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Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. ROC curve analysis has been performed to find the diagnostic value of RPV/VAT in relation to Pancreatic Fistula Grade, Kendal co-efficient of correlation (Concordance co-efficient) was obtained.
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs and tables.

Results

Demographic data

Eighty five PD were done in the study period. N= 52 cases were included in the study. Mean age of the patients was 52.60±9.61 years (51- 60 years), 32 patients were males, 67.3% of patients had comorbidities in form of DM, Hypertension and CAD, coronary artery disease was most common. Mean BMI was 26.05±3.55. 53.8% of patients were stented preoperatively in view of cholangitis (n=18, 34.6%) or high bilirubin values.

Intraoperative data

Forty five patients had malignancy with periampullary and ampullary (Table 1). 67.3% cases pylorus preserving pancreatoduodenctomy was done and classical whipples in rest with 2 patients (GIST) multivisceral resection with right hemicolectomy was done duedirect infiltration of hepatic flexure. 53.8% (n=28) had firm pancreas with duct size >3mm in 73% (n=38) patients. Mean duration of surgery was 6.71±1.27 hrs with mean blood loss of 280.77±114.26 ml. Intraoperative octreotide was given 20 patient with a dose of 150 ug subcutaneously and continued till POD5 in 8 hourly dose in these cases.

Analysis of postoperative outcome

There was no clinical or biochemical evidence (normal drain fluid amylase) of pancreatic fistula in n=31 cases, Grade A pancreatic fistula in n=12, Grade B in n=4, Grade C in n=5 (table2). Delayed gastric emptying was seen in nearly in 50% of cases but was grade A in majority and subsided by itself/ by use of prokinetics. Mean hospital stay in postoperative period was 13.94±7.01 days and the most common cause of prolonged hospital stay was wound infection. Wound infection rate was 57.7% mainly in preoperative stented patients, 100% bactibilia was present in stented patients with E. coli in 68% of cases and kliebsellapneumoniae in rest as main growing organism in bile, sentive to tigecycline and colistin and resistant to rest, however only few patient showed any signs of sepsis in post of (n=5) in which these antibiotics were required. Rest were given on cefoperazone + sulbactum and metronidazole till 2nd postoperative day. Two patients had post pancreatectomy haemorrhage – one had bleed on POD1 for which rexploration was done and found to have ooze from pancreatic bed, 2nd patient had bleed on POD 25 and found to have GDA aneurysm for which angioembolization was done. Both patient fared well in follow up.
There were 4 postoperative mortalities
Case 1- 60 y/m patient case of ampullary carcinoma with BMI of 27.4 kg/m2 and remnant pancreatic volume of 56.8cm3 was operated, intraoperatively pancreas was soft and duct was

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< 3mm; pylorus preserving pancreatodudenectomy was done, post operatively patient had pancreatic fistula which was managed with drainage. Patient died on POD 8
Case 2- 68 y/m patient suffering from duodenal carcinoma with bleed in form of hematemesis and malena with history of double vessel heart disease with BMI of 27.3kg/m2 and remnant pancreatic volume 84.8cm3 was operated, intraoperatively soft pancreas with duct <3mm; classical whipples was done, postoperatively patient had pancreatic fistula, managed conservatively initially, later developed signs of sepsis for which wide drainage was done on POD12, later went into DIC and died on POD 30
Case 3 50 y/m patient of periampullary malignancy with BMI of 25.5kg/m2 and remnant pancreatic volume of 56.8cm3 with soft pancreas, >3mm duct; pylorus preserving pancreatoduodenectomy was done, patient had mild controlled Pancreatic fistula, recovered and discharged on POD 10, however later developed leak from main abdominal wound with excoriation of surrounding tissue with sepsis, readmitted on POD 17, wide drainage was done, later patient developed pulmonary complications with pneumonia and expired on POD 42
Case 4 was a 55 y/f pancreatic head malignancy with history of cholangitis with BMI of 26.4kg/m2 and Remnant pancreatic volume of 53.5 cm3 with hard pancreas and> 3mm duct. Patient was on ventilator support in postoperative period on ionotropic support, drain fluid amylase was 3500 U, died on POD 4

Assessment of risk factors

Remnant pancreatic volume (p=0.0001) and BMI (p value= 0.0002) were the most significant factors in predicting pancreatic fistula (table 3). Mean remnant pancreatic volume of patients with no or grade A pancreatic fistula was 41.08±12.48 cm3 and that of Grade B+C fistula was 58.02±12.32cm3 (table 4). On ROC curve analysis it was found remnant pancreatic volume of >48.6 cm3 was found to be 88.8% sensitive and 76% sensitive in predicting clinically significant pancreatic fistula (Figure 1).
Remnant pancreatic volume was also found to be significantly associated with delayed gastric emptying.
No significant association was found with other anthropomorphic Factors like SAT, VAT, SM.

Discussion

With the development better perioperative and postoperative care mortality rates have drastically reduced to less than 5% in majority of high volume centres, but morbidity still remains high and pancreatic fistula remains important cause of postoperative morbidity ranging from 12 to 32% in various series [6].
Yeo *et al*. [7] reported that pancreatic fistulas were correlated with anastomotic technique, operative time, a surgeon's skills and experience in performing a PD, tumor location, and co-morbid illnesses. Patients with the hard pancreatic parenchyma have been reported to be at lower risk for pancreatic leakage [8]. The texture of the pancreatic parenchyma has been reported to be correlated with the pancreatic duct diameter, in considering the ease in performing a pancreatic duct-to-jejunum mucosa anastomosis, such a simple comparison requires more consideration. The accurate preoperative prediction of postoperative pancreatic fistula is difficult, however, because most of the known predictive factors such as a small MPD, soft pancreas, fatty pancreas, absence of pancreatic fibrosis, pathologic subtype, and amylase activity in the drainage fluid are only available intraoperatively or postoperatively [6]. All this in turn has relation to remnant pancreatic volume as shown in various studies which formed the basis of the study [3].

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Eighty five patients underwent PD in the study period out of which 52 patients were included

into the study. Majority of patients were in age group of 51-60(46.2%) with mean age of 52.60±9.61 years. Our centre being a high volume tertiary care centre received majority of patients with comorbidities (n= 35, 67.3%) who were high risk for surgery. Most of the patients had high bilirubin of > 10mg or had preoperative cholangitis or were evaluated outside and then referred and were stented preoperatively (n= 28, 53.8%) which is associated with high incidence of bactibilia and in turn with wound infection as shown in various studies [7, 8] was also seen in our study with 100% incidence of bactibilia with *E.coli* and Kliebsella 3984 neumonia as the predominant organism and wound infection in n=30 patients which included all the preoperatively stented patients (n=28). All these patients had prolonged hospital stay. One patient had postoperative septic shock and expired on 5th postoperative day
31 patients (59.6%) had no clinical or biochemical evidence of pancreatic fistula, Grade A pancreatic fistula in n=12(23.1%), Grade B in n=4(7.7%), Grade C in n=5(9.6%) as per following the International society of pancreatic fistula definition. 9(17.3%) patients had clinically significant fistula which is comparable to majority of high volume studies [9, 10].
Patients without clinically significant pancreatic fistula had mean remnant pancreatic volume of 36.86±10.73 cm3 while patients with clinically significant pancreatic fistula was 58.03±12.33 cm3 (p value of <.001). Similar study done by Yujiro Kirihara *et al*. [2]. showed the incidence of remnant pancreatic volume of 34cm3 or more was greater in the group with clinically relevant pancreatic fistula (91 vs 31; P<0.0001), Kanda *et al*. showed remnant pancreatic volume ≥25.5 cm3 was the best cut off value for predicting pancreatic fistula, with a high negative predictive value (0.934) and low likelihood ratio of a negative result (0.235). Multivariate analysis including the preoperative CT parameters and well-known risk factors for pancreatic fistula showed that remnant pancreatic volume ≥25.5 cm3 [9]. Farshad Frozanpor *et al*. conducted a study of 51 patients showed large volume of the pancreatic remnant (greater, or equal to, 34 cm^3) increased the subsequent risk of pancreatic fistula (57.1% *vs*. 20.8%; p=0.035) [3]. In our study on ROC curve analysis it was found remnant pancreatic volume of >48.6 cm3 was found to be 88.8% sensitive and 76% sensitive in predicting clinically significant pancreatic fistula. And it can be safely said that patients with pancreatic volume of >48.6 cm3 have high risk of development of pancreatic fistula based on our study. The difference may be accountable for patient body habitus or variations in method of estimating pancreatic volume as there is no developed software similar to estimation of liver volume for pancreas.
Mean remnant volume was higher in soft pancreas (48.6 cm3; p value=0.02). Mean remnant volume was on higher side in <3mm duct group (49.7 cm3) but it was not found to be statistically significant; indicating softer pancreas has higher volume. Kirihara *et al*. showed similar results remnant volume was positively correlated with main pancreatic duct size of less than 3 mm (P = 0.033) and a soft pancreatic gland texture (P=0.001) [2]. Frozanpor *et al*. showed correlation between median PRV was 35.2 cm and the median PDW was 3.9 mm to be associated with higher risk of pancreatic fistula [9].
Greater remnant pancreatic volume may be indicator of larger exocrine secretion which may be a predisposing factor for development of pancreatic fistula. Small remnant volume suggests not only a lack of intrapancreatic fat but may also suggest the presence of obstructive pancreatopathy, especially if the pancreatic duct is dilated (>3 mm) (15). In such a setting, the pancreatic remnant is more firm and at less risk of pancreatic fistula, therefore, it may alert the surgeon to either a greater or a lesser risk of pancreatic fistula. Greater volume may also indicate more steatosis/fatty infiltration of pancreas [13].
While taking into consideration the other anthropometric factors like subcutaneous adipose tissue (p value=0.578), visceral adipose tissue (p value=0.663) and skeletal muscle mass (p value=0.578), no significant association with pancreatic fistula could be found. This was in contrast to previous studies where significant association was found among these factors and development of pancreatic fistula. Kirihara *et al*. showed significant association of these

anthropomorphic factors with pancreatic fistula. Tranchart *et al*. showed Visceral fat area > 85 cm2 was significant association with the development of pancreatic fistula (p value=0.002) however no significant association was shown with subcutaneous adipose tissue.

Remnant pancreatic volume was also found to have significant association with development of postoperative delayed gastric emptying. 50% of patients had delayed gastric emptying with 25% grade A and 25% grade B. Patients with higher pancreatic volume had higher incidence of delayed gastric emptying (52.24±16.03,p value= 0.044). Kirihara *et al*. showed significant association remnant volume(38±20 vs 29± 16; P = 0.008) with development of Delayed gastric emptying .This may be due to higher incidence of pancreatic fistula in patients with high pancreatic volume and pancreatic fistula (whether clinical or biochemical) is one of the major causes of development of delayed gastric emptying [3].

BMI is well known predictive factor for development of postoperative pancreatic fistula as shown multiple studies comparing obesity and high BMI with pancreatic fistula [11, 12]. In our study also patients with BMI of 27.8 and above had higher incidence of both clinically significant and biochemical pancreatic fistula.

Factors like total operating time, interaoperative blood loss or use, pancreatic duct stenting were not found to be significant. Intraoperative octreotide was used in patients with soft pancreas based on surgeon's discretion at the time of division of pancreas and continued till 5th postoperative day subcutaneously in 8 hourly dosage 150 ug, significant role in prevention pancreatic fistula was found (p= 0.016) however use of octreotide for preventing pancreatic fistula is still controversial with mixed results and no confirmed protocol [13, 14, 15].

Another distressing morbidity beside pancreatic fistula was wound infection which occurred exclusively in patients which were stented preoperatively and required opening up of entire wound and secondary suturing later.

Conclusion

Preoperative assessment of remnant pancreatic volume with help of pancreatic protocol CECT is an important parameter in risk stratification of patients into high risk and low risk for postoperative pancreatic fistula with cut of value of 48.6 cm3 can be used to stratify the patients. Anthropomorphic factors like visceral adipose tissue, subcutaneous adipose tissue and skeletal muscle mass has not been shown any significant association with postoperative pancreatic fistula in comparison to other studies and further studies are required to validate these association. Calculation of remnant pancreatic volume is an important parameter in preoperative assessment and helps in predicting high risk patients which may useful for stratifying patients for better application of preventive measures in future.

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