Original Article

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Surgery Section

The Role of CA19-9 in Predicting Tumour Resectability in Carcinoma Head of Pancreas

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ABSTRACT

Introduction: Carbohydrate antigen 19-9 (CA 19-9) is a tumour associated antigen. Blood levels may be elevated in benign as well as malignant conditions. Its sensitivity (70-90%) and specificity (68-91%) are inadequate for accurate diagnosis. It can be used to predict the extent of disease and outcome after resection.

Aim: The aim of the present study was to assess the role of CA 19-9 in predicting the resectability of the tumour in the head of pancreas.

Materials and Methods: This was a prospective study which included 30 patients and study period was from May 2012 to October 2014. Data collected from all patients with carcinoma of the head of pancreas on the basis of contrast enhanced computed tomography/Magnetic resonance cholangiopancreaticography. CA 19-9 levels were measured and recorded. Patients who were medically unfit for surgery or those who didn't warrant palliative surgery were excluded from the study. During surgery the operative findings on operability were documented and tabulated against corresponding CA 19-9 levels.

Results: Of the 30 patients who were operated, 13(43.3%) patients had operable tumours and underwent Whipple's procedure and 17(56.7%) underwent palliative bypass procedure. Of the 30, CA 19-9 levels were elevated in 9(30.0%) and were normal in 21(70.0%). Among 13(43.3%) who had operable tumours, CA 19-9 was elevated in 4(13.3) and was normal in 9(30.0%). Of the 17(56.7%) who had inoperable tumours CA 19-9 was elevated in 5(16.7%) and was normal in 12(40.0%). Among the 17 who had inoperable tumours, 8(47.1%) were diagnosed preoperatively and of them CA 19-9 levels were raised in 2(11.8%) and normal in 6(35.3%). In the group of 9(52.9%) who had inoperable tumours diagnosed intraoperatively, CA 19-9 was raised in 3(17.6%) of them and was normal in the remaining 6(35.3%) of them.

Conclusion: Based on the study findings, it can be stated that there is no significant correlation with resectability of pancreatic adenocarcinoma and CA 19-9 and it doesn't predict vascular involvement and liver metastasis.

Keywords: Liver metastasis, Superior mesenteric artery (SMA), Spleno-Mesenteric-Portal Vein (SMPV)

INTRODUCTION

Adenocarcinoma of the pancreas remains a relatively incurable disease despite advances in surgical care of the resected patient, the move toward enrolling patients in clinical trials, and advances in systemic treatment for other solid tumours of the gastrointestinal tract [1]. The combination of aggressive tumour biology and ineffective therapies usually results in the rapid decline of these patients, resulting in death within a few months after diagnosis. The median age of diagnosis with pancreatic cancer is 72 years with less than 13% of cancers diagnosed prior to the age of 55 and greater than 69% of cancer diagnosed after the age of 65 years.

Tumour markers are biological products and used as indicators of cellular, biochemical, molecular and genetic alterations by which neoplasia can be recognized. Tumour markers are used a diagnostic tool, correlate with the amount of tumour present, allow subtype classification to more accurately stage patients, be prognostic either by the presence or absence of the marker and guide choice of therapy and predict response to therapy [2].

Carbohydrate antigen 19-9 (CA 19-9) is the most common tumour marker used to diagnose or monitor pancreatic malignancy [3]. but it is more useful for monitoring of recurrence following curative surgery rather than for diagnosis [4]. It is mainly produced by pancreatic tumour cells and it was first identified in mouse colorectal malignancy [5]. Apart from pancreas CA 19-9 also present in hepatobiliary system. So disease of biliary tract can cause raised CA 19-9 levels [6].

Immunoassay is used to measure serum CA19-9 levels and the maximum level of CA 19-9 in a normal person is 37U/ml [7]. The sensitivity and specificity of CA 19-9 for diagnosis of pancreatic malignancy varies from 70-90% and 68-91% respectively [8]. Apart from malignant jaundice CA19-9 also elevated in non-malignant jaundice due to biliary tract involvement [9]. There is lot of pit fall for using CA 19-9 as a diagnostic marker in pancreatic malignancy. They are: 1) Negative Lewis blood groups are unable to produce CA 19-9 [10]; 2) Elevated CA19-9 in non malignant hepatobiliary pathology [11]; 3) It can also be elevated in other malignancy like choloangiocarcinoma (95%), colorectal malignancy (15%), adenocarcinoma of lung (13%) and hepatocellular carcinoma (7%) [12]. There is controversy regarding use of CA 19-9 to decide resectability of pancreatic adenocarcinoma [13]. There are studies which showed CA 19-9 predict pancreatic resectability [14] and few studies showed CA 19-9 doesn't predict resectability of pancreatic adenocarcinoma [15].

AIM

Our aim in this study was to identify whether CA 19-9 predict resectability of pancreatic cancer.

MATERIALS AND METHODS

This was prospective study and included 30 patients who were admitted in all the surgical units of Department of General Surgery, Government Stanley Medical College & Hospital, Chennai. The study period was from May 2012 to October 2014. Data was collected from all patients who were diagnosed with carcinoma of

the head of pancreas on the basis of Contrast Enhanced Computed Tomography/Magnetic Resonance Cholangiopancreaticography (CECT/MRCP) were included in the study. During the preoperative evaluation of these patients, CA 19-9 levels were measured and recorded. Patients who were medically unfit for surgery or those who didn't warrant palliative surgery were excluded from the study. After adequate preparation, patients were taken up for surgery with either curative or palliative intent. During surgery the operative findings on operability like tumour size, vascular invasion and local/distant spread were documented and tabulated against corresponding CA 19-9 levels. Diagnosis was confirmed with histopathological report. The operative findings and its relation to the CA 19-9 levels were analysed and the results were interpreted. Significance was analysed by using Chi-square test. The statistical software used was SPSS 22.0 version and Microsoft excel used for generate table and graph.

RESULTS

Present study included 30 patients with high incidence noted in the age group of 51-70 years. There were 33.33% in the age group of 51-60 years and 30.0% in the 61-70 years age group [Table/Fig-1]. All 30 patients were analysed for relationship with CA 19-9 and age of patients. No significant relationship between age of the patient and CA 19-9 (p >0.01). Most of the patient with elevated CA 19-9, 6 (20.0%) belongs to the age above 50 years, so there was poor correlation with age of the patient and CA 19-9 [Table/Fig-2].

In our study, 53.33% were male patients and 46.67% were female patients. This indicates male population had slightly high incidence of pancreatic malignancies compared to female population [Table/Fig-1]. All 30 patients were analysed for relationship with CA 19-9 and sex of patients. No significant relationship between sex of the patient and CA 19-9 (p >0.01). So there was poor correlation with sex of the patient and CA 19-9 [Table/Fig-2].

In our study, CA 19-9 levels were elevated in 30% patients and were within normal limits in 70% patients [Table/Fig-1]. A cut off of 37 IU/ml was used because it was a upper limit of normal adult, based on the study by Ballehaninna UK et al., and M. M. S. Bedi et al., [16,17]. When the 30 patients were taken up for surgery it was found that in 13 (43.3%) patients the malignancy was operable and they underwent Whipple pancreaticoduodenectomy. In the other 17(56.7%) of patients the tumour was deemed inoperable and a palliative bypass procedure was done. Among the 17(56.7%) patients whose tumour was inoperable, 8(47.1%) were diagnosed preoperatively with CECT/MRCP and the other 9(52.9%) were found to be inoperable only during surgery. Of the 13(43.2%) patients who had operable tumours, CA 19-9 was elevated in 4(13.3%) patients and was normal in the other 9(30.0%) patients. Among the other 17(56.7%) patients with inoperable tumours, CA 19-9 was elevated in 5(16.7%) of the patients and was normal limits in the other 12(40.0%) patients. No significant relationship between resectability and CA 19-9 (p >0.01) [Table/Fig-2-4].

Vascular involvement like Superior Mesenteric Artery (SMA) and Spleno-Mesenteric-Portal Vein (SMPV) involvement were analysed. SMV involvement was found in 2 (6.6%) and SMPV involvement in 3 (10.0%) patients. Elevation of CA 19-9 in SMV involvement was found in 1 (3.3%) patient, whereas elevation in 8 (26.7%) with no SMV involvement. There was poor correlation with CA 19-9 and SMV involvement (p >0.01). Elevation of CA 19-9 in SMPV involvement was found in 1 (3.3%) patient, whereas elevation in 8 (26.7%) with no SMPV involvement. There was poor correlation

Characters	Percentage
Age (years)	
31-40	6 (20.0%)
41-50	4 (13.33%)
51-60	10 (33.33%)
61-70	9 (30.0%)
71-80	1 (3.34%)
Sex	
Male	16(53.33%)
Female	14 (46.67%)
Tumour marker (U/L)	
<37	21(70.0%)
>37	9 (30.0%)
Nature of operative procedure	
Whipple's procedure	13 (43.4%)
Palliative bypass	17 (56.6%)
SMV involvement	
Presence of SMV involvement	2 (6.6%)
Absence of SMV involvement	28 (93.4%)
SMPV involvement	
Presence of SMPV involvement	3 (10.0%)
Absence of SMPV involvement	27(90.0%)
Liver mets	
Presence of liver mets	3 (10.0%)
Absence of liver mets	27 (90.0%)

[Table/Fig-1]: Patient characters.

Characters	Level of CA 19-9 <37U/L	Level of CA 19-9 >37U/L	Pearson Chi-Square	p-value
Age (years)				
<50	7(23.3%)	3 (10.0%)	0.000	1.000
>50	14 (46.7%)	6 (20.0%)		
Sex				
Male	10 (33.3%)	6 (20.0%)	0.918	0.338
Female	11 (36.7%)	3 (10.0%)		
Nature of operative procedure				
Whipple's procedure	8 (26.7%)	5 (16.7%)	0.782	0.376
Palliative bypass	13 (43.3%)	4 (13.3%)		
SMV involvement				
Presence of SMV involvement	1 (3.3%)	1 (3.3%)	0.408	0.523
Absence of SMV involvement	20 (66.7%)	8 (26.7%)		
SMPV involvement				
Presence of SMPV involvement	2 (6.7%)	1 (3.3%)	0.018	0.894
Absence of SMPV involvement	19 (66.3%)	8 (26.7%)		
Liver mets				
Presence of liver mets	3 (10.0%)	0 (0.0%)	1.429	0.232
Absence of liver mets	18 (60.0%)	9 (30.0%)		

[Table/Fig-2]: Comparison of epidemiological variables.

Levels of CA 19-9	Preoperatively inoperable	Intraoperatively inoperable	No. of cases
<37 U/L	6 (35.3%)	6 (35.3%)	12 (70.6%)
>37U/L	2 (11.8%)	3 (17.6%)	5 (29.4%)
No. of cases	8 (47.1%)	9 (52.9%)	17 (100%)

[Table/Fig-3]: Relationship with CA19-9 with inoperability.

CA 19-9	Operable	Inoperable	Total
<37U/L	9 (30.0%)	12 (40.0%)	21 (70.0%)
>37U/L	4 (13.3%)	5(16.7%)	9 (30.0%)
Total	13 (43.3%)	17 (56.7%)	30 (100.0%)

[Table/Fig-4]: Relationship with CA 19-9 with operability.

with CA 19-9 and SMV involvement (p >0.01). Liver metastasis was found in 3 (10.0%) patients. Elevation of CA 19-9 in liver metastasis was found in 0 (0.0%) patients, whereas elevation in 9 (30.0%) with no liver metastasis. There was poor correlation with CA 19-9 and liver metastasis [Table/Fig-1,2].

DISCUSSION

CA 19-9 can't be used as a sole diagnostic marker for pancreatic malignancy, but higher levels can aid to diagnose pancreatic cancer [18]. CA 19-9 levels more than 100U/ml has higher sensitivity (60-84%) and specificity (>95%) for diagnose pancreatic malignancy [19]. We can certainly diagnose pancreatic malignancy when CA 19-9 levels more than 1000U/ml [20]. As CA 19-9 can be elevated in benign conditions of bile duct, it can't be used as a marker for malignant stricture of common bile duct.

Haas M et al., reported there is direct correlation between CA 19-9 level and tumour stage [21]. He showed unresectable pancreatic malignancy is associated with higher level of CA19-9 more than 1000U/ml. A better survival rate is seen in patients with normal CA 19-9 levels following curative surgery than with elevated levels [3]. It still remains to be defined whether the CA 19-9 response is a more reliable method for evaluating treatment efficacy compared to conventional imaging [22].

Treatment response of pancreatic malignancy following curative surgery is best assessed by serial monitoring of CA 19-9 levels. Recurrence following curative resection can be detected early by rise in CA19-9 before clinical or imaging evidence [23]. Poor response to chemotherapy in unresectable disease is indicated by failure to fall or rise of CA19-9 levels [24]. However, monitoring of CA19-9 levels is not much useful because lack of other treatment modalities for pancreatic malignancy. When a CA 19-9 level of 256.4 U/ml was used as a cut off point, the specificity and sensitivity was 92.3% and 82.4% respectively for pancreatic cancer respectability [25].

CA 19-9 with resectability: In our study, CA 19-9 levels were elevated in 30% patients and were within normal limits in 70% patients. In our study 13 (43.3%) of patients was operable and remaining 17(56.7%) of patients found to be inoperable. Similar findings of operability was reported by Guopei Luo et al., showed resectability was 35.8% and unresectable 64.2% [26] and Kilic M et al., reported resectable was 36.0% and unresectable was 64.0% [27]. Of the 13(43.2%) patients who had operable tumours, CA 19-9 was elevated in 4(13.3%) patients and was normal in the other 9(30.0%) patients. Among the other 17(56.7%) patients with inoperable tumours, CA 19-9 was elevated in 5(16.7%) of the patients and was normal limits in the other 12(40.0%) patients. It shows there was no significant relationship between resectability and CA 19-9 (p >0.01). Similar findings was reported by Safi et al., showed only pre treatment CA 19-9 more than 300 U/ml associated with unresectable disease in 80% where as 5-10% patient don't demonstrate altered serum CA 19-9 levels [28]. In contrast to our study Schlieman et al., reported low levels of CA19-9 in resectable tumour compared to unresectable tumour [29]. A study conducted by Kilic et al., reported CA19-9 can be used a marker to determine resectability of pancreatic malignancy inspite of resectability on contrast CT scan [27].

CA 19-9 with vascular involvement: As per our study there is no correlation between CA 19-9 and vascular involvement. It doesn't predict superior mesenteric artery (SMA) and spleno-mesenteric-portal vein (SMPV) involvement. This is because CA 19-9 elevated even without vascular involvement. A similar finding was reported by Katz A et al., and Barton JG et al., showed there was no significant relationship between CA 19-9 and vascular involvement [30,31]. In contrast to our study Ferrone et al., reported that perioperative CA 19-9 level can predict stage and survival in patient with resectable pancreatic adenocarcinoma [32]. Apart from vascular involvement CA 19-9 doesn't predict liver metastasis as per our study. Similar findings were reported by Barton JG et al., [31]. In contrast to our study Szwedziak K et al., reported CA 19-9 in portal vein can predict liver metastasis compared to peripheral CA 19-9 levels [33].

LIMITATION

This study has certain limitation. This study conducted in short duration with limited sample. In our study vascular involvement is considered as unresectable. Now-a-days vascular involvement is also not considered as non resectability due to availability of vascular reconstruction.

CONCLUSION

CA 19-9 is one of the tumour markers for pancreatic adenocarcinoma. It can be used as marker to identify pancreatic adenocarcinoma with limited sensitivity and specificity. Even with non resectable tumour there is no significant rise of CA 19-9. There is no significant correlation with resectability of pancreatic adenocarcinoma and CA 19-9 and it doesn't predict vascular involvement and liver metastasis. So, CA 19-9 is used as a marker to identify pancreatic adenocarcinoma, but it doesn't predict the resectability and vascular involvement.

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