Original Research Paper

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Surgery

THE USE OF CA 19-9 IN DETERMINING THE OPERABILITY OF CARCINOMA PANCREAS

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ABSTRACT **Introduction:** Adenocarcinoma of pancreas remains a relatively incurable disease despite advances in surgical care of resected patient, the move toward enrolling patients in clinical trials and advances in systemic treatment for other solid tumors of GIT1. Approximately 25% of patients will be found to have unresectable tumours during surgery even though CT has demonstrated that they are resectable. At our tertiary care centre, we wished to find out if there is an optimum cut off value for CA 19-9 level preoperatively that will indicate that pancreatic cancer is unresectable despite radiologic imaging. Moreover there is a controversy regarding use of CA19-9 to decide resectability of pancreatic adenocarcinoma5. Hence the present study is conducted. **Objectives:** 1. To study the use of CA 19-9 in determining the operability of carcinoma pancreas. **Methodology:** This was a prospective study which included 69 patients and study period was from December 2021 to December 2022. Data collected from all patients with carcinoma of the pancreas who underwent surgical managements. CA 19-9 levels were measured and recorded. During surgery the operative findings on respectability were documented and tabulated against corresponding CA 19-9 levels and CECT findings. **Results:** Of the 69 patients who were operated, 38 patients had resectable tumors and underwent whipples procedure and 31 of them had nonresectable tumors and had to undergo palliative bypass procedures. Among the 31 patients who's tumor was nonresectable, only 4 were diagnosed nonresectable preoperatively with CECT, and the other 27 were found to be nonresectable only during surgery. That shows the relevance of this study. Of the 31 nonresectable cases 14 (45.2%) patients had elevated CA 19-9 values more than 501 and rest 17(54.8%) patients having low CA 19-9 values. Among the 38 resectable cases 12 patients (31.6%) having elevated CA 19-9 more than 501 and 26 patients (68.4%) having low values. On concluding, among nonresectable cases 45.2% had raised CA-19-9 and among operable cases 31.6 % showed raised CA 19-9. Hence CA 19-9 seems to be insignificant predictor of tumor resectability. **Conclusion:** It was found that the need for a preoperative predictor for resectability of carcinoma pancreas is relevant, while considering mortality and morbidity in operating carcinoma pancreas cases. On evaluating CA 19-9 as a preoperative predictor we found that CA 19-9 has no significant role as an indicator of local advancement or metastasis. Hence we can't consider CA 19-9 as a predictor of resectability of carcinoma pancreas preoperatively.

KEYWORDS : Carcinoma Pancreas, CA 19-9

INTRODUCTION

Adenocarcinoma of pancreas remains a relatively incurable disease despite advances in surgical care of resected patient, the move toward enrolling patients in clinical trials and advances in systemic treatment for other solid tumors of GIT[1]. CA19-9 is the most common tumour marker used to diagnose/monitor pancreatic malignancy[2]. It is mainly produced by pancreatic tumour cells and it was first identified in mouse colorectal malignancy[3]. Apart from pancreas CA19-9 is also present in hepatobiliary system. so disease of biliary tract can also cause raised CA19-9 levels[4]. It's sensitivity and specificity are inadequate for accurate diagnosis, but it can be used to predict the extent of disease and outcome after resection. Pancreatic cancer carries a poor prognosis at operation. Approximately 25% of patients will be found to have unresectable tumours during surgery even though CT has demonstrated that they are resectable.

At our tertiary care centre, we wished to find out if there is an optimum cut off value for CA 19-9 level preoperatively that will indicate that pancreatic cancer is unresectable despite radiologic imaging. Moreover there is a controversy regarding use of CA19-9 to decide resectability of pancreatic adenocarcinoma**5**. Hence the present study is conducted.

MATERIALS AND METHEDOLOGY

Study Design

Prospective observational study.

Study Setting

Hospital based study centered at Dept. of General Surgery, Government Medical College Hospital, Kottayam

Study Duration

12 months after getting IRB clearance(November 2021-November 2022).

Sample Size

Based on previous study of **Mehmet Kiliç et al**, of the Department of Fifth Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey, Accepted for publication Nov. 29, 2004 Sample size is calculated using the formula N= 4Sd2/D2

Where

N = Sample size,

Sd = Standard deviation of CA 19-9 among Resectable group, 33.2

D = 20 % of mean CA 19-9 among Resectable group

20% of 68.8 = 13.7

So we are taking Absolute precision as 8

N = 4x(33.2)2 /82

N = 69 subjects

Inclusion Criteria

All carcinoma pancreas patients underwent surgical procedure, who were admitted in general surgery ward of Kottayam Medical College.

Exclusion Criteria

Patients with age less than 18,(uncommon age for carcinoma pancreas).

Method of Study

After getting approval for thesis from institutional review board, written informed consent would be taken from all patients undergoing study. This study includes observation of levels of CA 19-9 among all carcinoma pancreas patient (operable and non operable), who were admitted in the Department of General surgery in Medical college Kottayam. All patients will be assessed according to the following protocol.

Protocol

1. Detailed history
2. Complete clinical examination
3. CT Scan findings
4. CA 19-9 values
5. Intra operative findings

CA 19-9 is now being done routinely for all carcinoma pancreas patients. Collect that data and observe whether the carcinoma is resectable or not. Observe the value of CA 19-9 among the resectable and non resectable groups. Check for any relation between resectability and CA 19-9 value. Collected data will be recorded on a case record form and subjected to statistical analysis. During every phase of the study the personal details of the patients participating in the study shall be kept confidential and the patient has every right to

withdraw at any phase of the study without affecting his/her future treatment.

Data Analysis

Data was entered in Microsoft Excel and was analysed using SPSS software version 18

RESULTS

Age Distribution In Carcinoma Pancreas

Table 1

Age in years	Frequency	Percent
<50	6	8.7
51-60	20	29
61-70	26	37.7
>70	17	24.6
Total	69	100

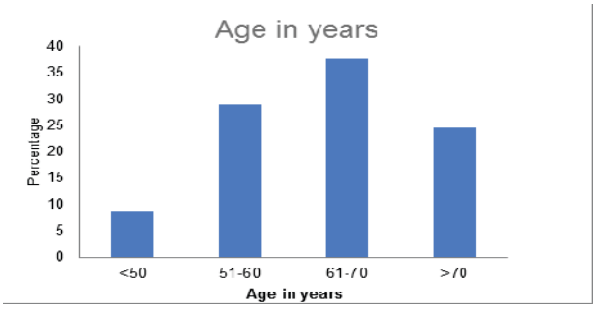

Chart 1

In my study it was observed that carcinoma pancreas is a disease of elderly.Most incidence found in patients above 60 years

Gender Distribution In Carcinoma Pancreas

Table 2

SEX	Frequency	Percent
Male	47	68.1
Female	22	31.9
Total	69	100

Chart 2

In the study it was observed that more incidence is in male gender. Chance of bias will be there ,as preoperatively nonoperable cases were not included in this study.

Unresectability Based On Metastasis

Table 3

Inoperable based on intraoperatively showing metastasis	Frequency	Percent
No	45	65.2
Yes	24	34.8
Total	69	100

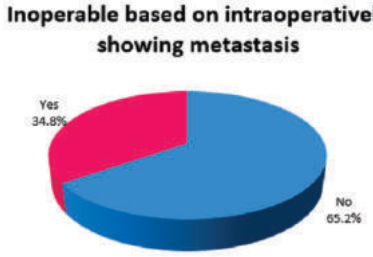

Chart 3

In the study there is around 34.8 % patients are unresectable due to metastasis.As metastasis becomes one of the leading cause of poor prognosis in case of carcinoma pancreas.

Unresectability Based On Unreconstructible Vascular Invasion

Table 4

Inoperable based on intraop shows unreconstructible vascular invasion	Frequency	Percent
No	56	81.2
Yes	13	18.8
Total	69	100

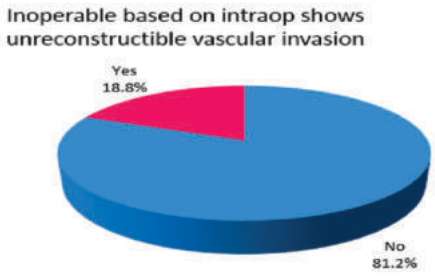

Chart 4

In the study there is around 18.8 % patients are unresectable due to unreconstructible vascular invasion. Also becoming a leading cause of poor prognosis in case of carcinoma pancreas.

Relation Between Ca 19-9 And Unresectability Based On Vascular Invasion

Table 5

CA 19-9	Inoperable based on intraop shows unreconstructible vascular invasion				Total		χ2	df	p
	No		Yes						
	N	%	N	%	N	%			
<100	5	8.9	1	7.7	6	8.7	2.57	3	0.463
101-500	32	57.1	5	38.5	37	53.6			
501-1000	18	32.1	6	46.2	24	34.8			
>1000	1	1.8	1	7.7	2	2.9			
Total	56	100	13	100	69	100			

Table 6

		Inoperable based on intraop shows unreconstructible vascular invasion		Total
		Yes	No	
CA 19-9	>500	7	19	26
	<500	6	37	43
Total		13	56	69

Sensitivity	53.8
Specificity	66.1
PPV	26.9
NPV	86.0
Accuracy	63.8
LR+	1.6
LR-	0.70

By analysing my study it was found that , as the 'p' value is > 0.05, the relation between CA 19-9 and inoperability based on unreconstructible vascular invasion is not significant.Even considering 500 as cut of value for CA 19-9,sensitivity and specificity of the CA 19-9 in predicting unresectability is found low.Making it a bad tool for predicting unresectability in carcinoma pancreas

Relation Between Ca 19-9 And Unresectability Based On Metastasis

Table 7

CA 19-9	Inoperable based on intraop shows mets				Total		χ2	df	P
	No		Yes						
	N	%	N	%	N	%			
<100	5	11.1	1	4.2	6	8.7	1.15	3	0.764
101-500	24	53.3	13	54.2	37	53.6			
501-1000	15	33.3	9	37.5	24	34.8			

>1000	1	2.2	1	4.2	2	2.9			
Total	45	100	24	100	69	100			

Table 8

		Inoperable based on intraop shows mets		Total
		No	Yes	
CA 19-9	>500	16	10	26
	<500	29	14	43
Total		45	24	69

Sensitivity	41.7
Specificity	64.4
PPV	38.5
NPV	67.4
Accuracy	56.5
LR+	1.2
LR-	0.91

By analysing my study it was found that , as the 'p' value is > 0.05, the relation between CA 19-9 and inoperability based on metastasis is not significant. Even considering 500 as cut of value for CA 19-9,sensitivity and specificity of the CA 19-9 in predicting unresectability is found low. making it a bad tool for predicting unresectability in carcinoma pancreas

Relation Between Ca 19-9 And Unresectability Based On Cect Abdomen

Table 9

		CECT ABDOMEN Showing e/o inoperability		Total
		Yes	No	
CA 19-9	>500	2	24	26
	<500	2	41	43
Total		4	65	69

Sensitivity	50.0
Specificity	63.1
PPV	7.7
NPV	95.3
Accuracy	62.3
LR+	1.4
LR-	0.79

By analysing my study found that with a low sensitivity and specificity values, CA 19-9 becomes insignificant role in predicting operability even based on CECT abdomen.

Distribution Of Ca 19-9 In Unresectable Cases

Table 10

CA 19-9	Inoperable based on intra op showing either metastasis or unreconstructible vascular invasion	
	Frequency	Percent
>500	14	45.20
<500	17	54.80
Total	31	100.00

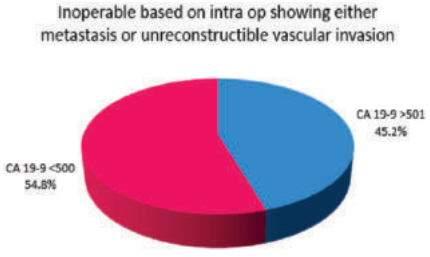

Chart 5

Distribution Of Ca 19-9 In Resectable Cases

Table 11

CA 19-9	RESECTABLE CASES OF CARCINOMA PANCREAS	
	FREQUENCY	PERCENTAGE
>501	12	31.6
<500	26	68.4
TOTAL	38	100

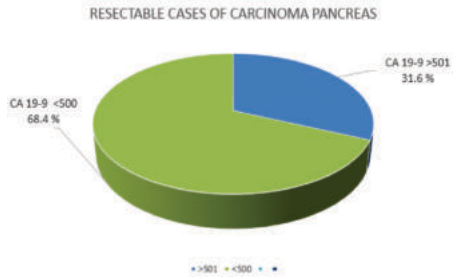

Chart 6

In my study it was observed that around 45.2 % of unresectable cases and around 31.6 % of resectable cases of carcinoma pancreas having CA 19-9 values >501.Making it a less predictable factor for unresectability of carcinoma pancreas.

CA 19-9 as a tumor marker has been proven to be useful in predicting outcomes and in follow up of patients with carcinoma of head of pancreas. With lack of definitive evidence regarding the role of CA 19-9 in predicting operability in a case of carcinoma of pancreas, I have chosen to analyse the same in a prospective study including 69 patients who underwent surgery for carcinoma pancreas, either curative or palliative.

In my study, it was observed that the incidence of pancreatic malignancies were more with patients above 50 years of age. Of the 69 cases, 63 patients were above 50 and only 6 patients found to be younger than 50.Pancreatic cancer found to be a disease of elderly. The incidence of pancreatic malignancies were found more common in males. Of these 69 patients, 47 were males and 22 were females. A male gender preponderance was noted.

As a part of the pre-operative evaluation Contrast enhanced CT (CECT) of abdomen and pelvis and serum CA 19-9 levels were done routinely. In the 69 patients with carcinoma of the pancreas included in the study,4 patients found to be nonresectable preoperatively by CECT abdomen. In that 4 patients 2 Patients found elevated CA 19-9 levels more than 501 and other 2 having values less than 500. Hence CA 19-9 found to be irrelevant in predicting nonresectability in CECT basis.

When the 69 patients were taken up for surgery it was found that 38 of the patients with the malignancy was operable and they underwent classical Whipples pancreaticodudenectomy. In the other 31 patients the tumor was deemed nonresectable and a palliative bypass procedure was done. Among the 31 patients who's tumor was nonresectable, only 4 were diagnosed nonresectable preoperatively with CECT, and the other 27 were found to be nonresectable only during surgery. Of the 31 nonresectable cases 14 (45.2%) patients had elevated CA 19-9 values more than 501 and rest 17(54.8%) patients having low CA 19-9 values.

Among the 31 nonresectable cases 24 patients had metastasis and 13 patients had unreconstructible vascular invasion intraoperatively. In 24 patients with metastasis 10 cases having elevated CA 19-9 more than 501 and 14 having low values.in the 13 patients with unreconstructible vascular invasion 7 cases having elevated CA 19-9 more than 500 and 6 having low values. Among the 38 resectable cases 12 patients (31.6%) having elevated CA 19-9 more than 501 and 26 patients (68.4%) having low values. Among nonresectable cases 45.2 % had raised CA-19-9 and among operable cases 31.6% showed raised CA 19-9. Hence CA 19-9 seems to be insignificant predictor of tumor resectability.

CONCLUSION

It was found that the need for a preoperative predictor for resectability of carcinoma pancreas is relevant, while considering mortality and morbidity in operating carcinoma pancreas cases.

On evaluating CA 19-9 as a preoperative predictor we found that CA 19-9 has no significant role as an indicator of local advancement or metastasis.Hence we can't consider CA 19-9 as a predictor of resectability of carcinoma pancreas preoperatively.

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