Gastroenterology and Hepatology From Bed to Bench


**ORIGINAL ARTICLE**

# Serum $CA_{19-9}$ in patients with solid pancreatic mass

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## ABSTRACT

**Aim**: This study evaluated the results and efficacy of serum CA $_{19-9}$ in determining the nature of a pancreatic solid mass in patients referred for investigation of possible malignancy.

**Background**: A wide variety of tumor markers have been proposed for pancreatic cancer but currently the only one with any practical usefulness for diagnosis, prognosis, and monitoring of treatment is "CA $_{19-9}$".

**Patients and methods**: This present study is a single center 2 year descriptive, prospective and case series studying patients with a pancreatic solid mass.

**Results**: Serum CA $_{19-9}$ was checked in 159 patients .The majority of patients were male (68%) and 81% had mass in the head of pancreas. Pathologic assessment revealed 131 adenocarcinomas (82%), 10 other malignancies (6%), 7 benign lesion (4%) and was non-diagnostic in 11 cases (7%). Mean level of this tumor marker in patients with adenocarcinoma, non-adenocarcinoma malignancy, benign and non-diagnostic pathology was 1094, 1004, 120, 259 U/ML respectively. With regarding 58 U/ML as a cutoff point; sensitivity, specificity, positive predictive value, negative predictive value and accuracy of this tumor marker for diagnosing the adenocarcinoma were 85%, 67%, 88%, 60% and 81% respectively.

**Conclusion**: There was no significant relationship between Serum CA $_{19-9}$ value and histopathology of solid pancreatic mass. This marker has limited sensitivity and specificity and cannot be used as a definite diagnostic test. So the use of CA $_{19-9}$ for the differentiation of pancreatic cancer should be applied on an individual case basis, depending on the clinical situation and imaging findings.

**Keywords**: Pancreatic neoplasm, CA $_{19-9}$.

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## Introduction

The majority of pancreatic cancers are ductal adenocarcinomas. One and five year survival of this malignancy, the fourth leading cause of cancer death, is 26% and 3-6%, respectively (1,2). Early detection, accurate preoperative staging and better treatment options remain a challenge. Appropriate imaging and tissue sampling are needed for a definite diagnosis of pancreatic cancer. Several immunochemical markers have been proposed for pancreatic cancer such as $CA_{19-9}$, $MUC_3$, $MUC_4$, $MUC_1$, and $CA_{125}$ but currently the only one with any practical usefulness is $CA_{19-9}$. Although not suitable for screening, this marker is considered a valuable adjunct in the diagnosis, prognosis, and monitoring of treatment of pancreatic cancer (3-7). Patients with a negative Lewis blood group phenotype (-a-b) do not express the $CA_{19-9}$ antigen, resulting in false-negative results (8, 9). The reported sensitivity and specificity of CA

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$_{19\text{-}9}$ for pancreatic cancer is between 80 to 90 percent (10 -13). Serum level of this marker rises in benign pancreatobilliary disease, so its specificity for adenocarcinoma is limited (8, 14 -16). One study found that $CA_{19\text{-}9}$ serum concentrations above 37unit/milliliter represented the most accurate cutoff value for discriminating pancreatic cancer from benign pancreatic disease (sensitivity and specificity of 77 and 87 percent, respectively) (16). Although, serum levels of this marker increase in benign pancreatobilliary disease, this marker may be useful for differentiating adenocarcinoma from benign disease and/or pancreatic neuroendocrine tumor (17). However accuracy of this marker in small tumors (less than 1 centimeter) is low (10,11,14,15,18). Increased levels of this tumor marker in serum level are also seen in other malignancies such as stomach and colorectal cancer. Serum $CA_{19\text{-}9}$ increases the accuracy of laparoscopic staging (19). Furthermore, in patients who appear to have potentially resectable disease, the magnitude of the $CA_{19\text{-}9}$ level can also help to predict the presence of radiographically occult metastatic disease (3). Serial monitoring of $CA_{19\text{-}9}$ levels (once every one to three months) is useful in the follow up of patients after potentially curative surgery and for those who are receiving chemotherapy for advanced disease (8, 20, 21). Rising $CA_{19\text{-}9}$ levels usually precede the radiographic appearance of recurrent disease, but confirmation of disease progression should be pursued with imaging studies and/or biopsy (21).

This study aims at evaluating the results and efficacy of serum $CA_{19\text{-}9}$ in patients with pancreatic solid mass.

## Patients and Methods

This study is a descriptive, prospective and case series of patients with a pancreatic solid mass referred to either the Tehran Imam Khomeini teaching hospital or Yazd Shahid Sadoghi hospital over a two-year period, from November, 2009. Most of the histopathologic diagnosis have obtained by EUS-FNA and few cases have diagnosed by CT guided biopsy or surgery. To determine the false negative and false positive cases, the patients have been followed up for up to two years. Patients' serum $CA_{19\text{-}9}$ level was measured using a standard immunofluorescence laboratory method. Patients' demographic information, clinical and imaging finding, pathologic result and serum $CA_{19\text{-}9}$ level have been analyzed by SPSS version-16 for correlation with clinical findings. The exact Fisher test, student t- test and Chi-square test were used for statistic evaluation. P-values less than 0.05 were considered statistically significant. Sensitivity and specificity calculated with a 2×2 table. ROC curve was described by plotting the sensitivity on the y-axis against 1-specificity on the x-axis for each of several cutoff values.

## Results

159 patients with pancreatic solid mass were enrolled in the present study. Demographic information, clinical and imaging findings, pathologic results and the serum $CA_{19\text{-}9}$ level are in the table 1. Tissue sampling was diagnostic in 148 patients (93%). The pathologic diagnosis was adenocarcinoma in 129 cases (81%), non-adenocarcinoma malignancy in 12 Patients (table 1) and benign lesion in 7 cases. Pathologic diagnosis of 2 gastrointestinal stromal tumors cases, 4 neuroendocrine tumors and 2 pseudo-papillary tumors was confirmed with IHC. The range of serum $CA_{19\text{-}9}$ level in our patients was 6 to 16000 U/ml. Mean levels of this tumor marker in patients with adenocarcinoma, non-adenocarcinoma malignancy, benign lesions and non-diagnostic cases was 1094, 1004, 120, and 259 unit/milliliter respectively. Our study found that serum concentrations more than 58 unit/milliliter represented the most accurate cutoff value for discriminating pancreatic cancer from benign pancreatic disease (sensitivity, specificity, PPV, NPV and accuracy of 85, 67, 85, 60 and 81 percent respectively). There was no significant relationship between this marker and pathologic diagnosis (p=0.593), patient demographics,

smoking habits, alcohol consumption, tumor size, tumor location in the pancreas, vascular invasion and patient survival.

**Table 1.** Characteristics of patients with pancreatic solid mass*

| | Total (n=159) | Malignant (n=141) | Benign (n=7) | Non-diagnostic (n=11) |
|---|---|---|---|---|
| Age (Year) | | | | |
| Range | 20-80 | 50-80 | 34-65 | 20-75 |
| Mean | 61±12 | 66±7.5 | 51±15 | 52±15 |
| Male/Female | 108/51 | 98/43 | 3/4 | 4/7 |
| Smoking | 81(51%) | 71 (51%) | 2 (29%) | 7(64%) |
| Tumor location | | | | |
| Head | 129(%81) | 111(79%) | 7(100%) | 11(100%) |
| Body | 24(15%) | 24(17%) | 0 | 0 |
| Tail | 6(4%) | 6(4%) | 0 | 0 |
| Tumor size (Mm)† | | | | |
| Range | 105 -20 | 105 -20 | 50-20 | 40- 20 |
| Mean | 15± 41 | 16± 42 | 14 ±33 | 10 ±28 |
| Vascular invasion | 81(51%) | 72(53%) | 0 | 7(64%) |
| Adenocarcinoma | 129(81%) | 129(91%) | 0 | 0 |
| GIST‡ | 2(1.2%) | 2 (1.4%) | 0 | 0 |
| Neuroendocrine tumor | 4 (2.5%) | 4(2.8%) | 0 | 0 |
| Musinous cyst neoplasm© | 1(0.6%) | 1(0.7%) | 0 | 0 |
| Solid-psudeopapillary tumor | 2 (1.2%) | 2(1.4%) | 0 | 0 |
| Giant cell tumor | 1(0.6%) | 1(0.7%) | 0 | 0 |
| Lymphoma | 1(0.6%) | 1(0.7%) | 0 | 0 |
| Metastasis | 1(0.6%) | 1(0.7%) | 0 | 0 |
| Focal fibrosis | 3(1.9%) | 0 | 3(43%) | 0 |
| Focal pancreatitis | 3(1.9%) | 0 | 3(43%) | 0 |
| Autoimmune pancreatitis | 1(0.6%) | 0 | 1(14%) | 0 |
| Non-diagnostic pathology | 11(7%) | 0 | 0 | 11(100%) |
| Serum $CA_{19-9}$ (U/ML)§ Mean | 771 | 946 | 120 | 259 |

* There were no significant differences between groups (NS). †Millimeter, ‡Gastrointestinal Stromal Tumor, © with an associated invasive carcinoma, §Unit/Milliliter

## Discussion

Because tissue sampling from pancreatic masses has risks and complications and also because negative pathologic results of EUS-FNA (the most common tissue sampling method in pancreatic cancer) do not exclude malignancy (22) , additional adjunct tests are needed . Serum $CA_{19-9}$ level is a useful marker for evaluating the likelihood of pancreatic ductal adenocarcinoma. However this marker has limited sensitivity and specificity and cannot be used as a definite diagnostic test. Serum level of this marker increases in some benign and malignant disease such as biliary stone, cholangitis, cirrhosis, HCC, ovary tumor, stomach and colorectal cancer (14-16). Similar to other studies (8,14-16,21), this study did not find any statistical relationship between serum $CA_{19-9}$ and histopathology diagnosis of solid pancreatic masses (p=0.593).

Only 5 adenocarcinoma cases (3%) of our patients were resectable but in some centers 20% of adenocarcinoma cases are resectable at the time of diagnosis (23). This shows that our patients have diagnosed late in advanced stage of disease. This delay can lead to increment in calculated serum $CA_{19-9}$ cut off point in our study (16) (58U/ML Vs 37 U/ML in other similar study). If 37 U/ML value considered as a cut off point for this present study , sensitivity and specificity will be 90% and 37%, respectively. Few studies showed that serum $CA_{19-9}$ level does not rise and so is not reliable in the diagnosis of small pancreatic tumors (less than 1 centimeter) (10,11,14,15,18). There were not any small tumors less than 2.5 centimeter in this study and we did not find statistical relationship between serum $CA_{19-9}$ level and tumor size (p=0.676).

Some studies have recommended periodic serum $CA_{19-9}$ measurement as a useful method for monitoring treatment (3-6). Only 5 cases of our patients with adenocarcinoma treated with surgery, so treatment monitoring with serum $CA_{19-9}$ testing was not possible in our patients.

Our study found that serum $CA_{19-9}$ more than 58 unit/milliliter represented the most accurate cutoff value for discriminating pancreatic adenocarcinoma from benign pancreatic disease or non-adenocarcinoma tumor (sensitivity, specificity, PPV, NPV and accuracy of 85, 67, 85, 60 and 81 percent, respectively). Serum $CA_{19-9}$ level is a useful marker for evaluating the pancreatic ductal adenocarcinoma. However this marker has limited sensitivity and specificity and cannot be used as a definite diagnostic test. The use of $CA_{19-9}$ for differentiation

of pancreatico-biliary cancer should be applied individually, depending on the clinical situation and imaging finding.

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