PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

World J Gastroenterol 2004;10(11):1675-1677
World Journal of Gastroenterology
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• BRIEF REPORTS •

Serum level of TSGF, CA242 and CA19-9 in pancreatic cancer

Jing-Ting Jiang, Chang-Ping Wu, Hai-Feng Deng, Ming-Yang Lu, Jun Wu, Hong-Yu Zhang, Wen-Hui Sun, Mei Ji

Jing-Ting Jiang, Chang-Ping Wu, Hai-Feng Deng, Ming-Yang Lu, Jun Wu, Hong-Yu Zhang, Wen-Hui Sun, Mei Ji, Department of Tumor Biological Treatment, the Third Affiliated Hospital of Suzhou University, Changzhou 213003, Jiangsu Province, China
Correspondence to: Dr. Jing-Ting Jiang, Department of Tumor Biological Treatment, the Third Affiliated Hospital of Suzhou University, Changzhou 213003, Jiangsu Province, China. jitnew@163.com
Telephone: +86-519-6180978 **Fax:** +86-519-6621235
Received: 2003-12-19 **Accepted:** 2004-02-01

Abstract

AIM: To establish a method to detect the expression of the tumor specific growth factor TSGF, CA242 and CA19-9 in serum and evaluate their value in diagnosis of pancreatic cancer.

METHODS: ELISA and Biochemical colorimetric assay were used to detect the serum content of TSGF, CA242 and CA19-9 in 200 normal cases, 52 pancreatitis patients and 96 pancreatic cancer patients.

RESULTS: The positive likelihood ratios of TSGF, CA242 and CA19-9 were 5.4, 12.6 and 6.3, respectively, and their negative likelihood ratios were 0.10, 0.19 and 0.17, respectively. With single tumor marker diagnosed pancreatic cancer, the highest sensitivity and specificity of TSGF were 91.6% and 93.5%. In combined test with 3 markers, when all of them were positive, the sensitivity changed to 77.0% and the specificity and the positive predictive value were 100%. The levels of TSGF and CA242 were significantly higher in the patients with pancreatic cancer of head than those in the patients with pancreatic cancer of body, tail and whole pancreas, but the expression of CA19-9 had no correlation with the positions of the pancreatic cancer. The sensitivity of TSGF, CA242 and CA19-9 was increased with the progress in stages of pancreatic cancer. In stage I, the sensitivity of TSGF was markedly higher than CA242 and CA19-9.

CONCLUSION: The combined use of TSGF, CA242 and CA19-9 expressions can elevate the specificity for pancreatic cancer diagnosis. And it shows that it plays an important role to differentiate positions and tissue typing. It is a forepart diagnosis for the pancreatic cancer by combination checking. There is very important correlation between the three markers and the pancreatic cancer.

Jiang JT, Wu CP, Deng HF, Lu MY, Wu J, Zhang HY, Sun WH, Ji M. Serum level of TSGF, CA242 and CA19-9 in pancreatic cancer. *World J Gastroenterol* 2004; 10(11): 1675-1677
http://www.wjgnet.com/1007-9327/10/1675.asp

INTRODUCTION

Early period of pancreatic cancer lacked the typical clinic performances[1,2], was high malignant and had a low survival time in five years[3-6]. And it was difficult to be diagnosed and made the patients lose the chances of radical cures. So it was very important to diagnose pancreatic cancer early[7-9]. But the sensitivity and specificity were not ideal in examining pancreatic cancer with a single method. We assayed the content of TSGF, CA242 and CA19-9 in serum of pancreatic cancer suffers and analyzed their expression in different positions and tissue typing in order to improve the level of early period of the pancreatic cancer diagnosis.

MATERIALS AND METHODS

Materials

To collect 200 normal people who had medical check-up in the hospital as normal group, including 112 males and 88 females with a mean age of 55.0±11.2 (range,22-68 years). To collect 52 pancreatitis suffers as pancreatitis group, including 29 males and 23 females with an average age of 66.0±8.0 (range, 60-74 years). To collect 96 pancreatic cancer suffers as pancreatic cancer group, including 61 males and 35 females with an average age of 67.6±6.7 (range, 60-88 years). There were 64 heads of pancreatic cancer, 18 body of pancreatic cancer and 10 tail of pancreatic cancer, which were all proved by pathology.

Methods

TSGF was assayed by colorimetric of biochemistry from Fujian New Continent Biochemical Technology Limited Company. CA242 and CA19-9 were assayed by ELISA from Sweden CanAg Company. All operations were followed by manuals. All data were showed as mean±SD and calculated by *t* test, and positive ratios were calculated by χ^2 test.

RESULTS

TSGF, CA242 and CA19-9 assay of three groups

Statistical significance of the contents of the three markers was found when pancreatic cancer group was compared with normal group and pancreatitis group ($P<0.01$). No statistical significance was found between normal group and pancreatitis group ($P>0.05$, Table 1).

Table 1 Laboratory parameters of the 3 tumor markers in pancreatic cancer group, pancreatitis group and normal group (mean±SD, $\times 10^3$U/L)

Group	No. of cases	TSGF	CA242	CA19-9
Critical value		>71	>20	>37
Pancreatic cancer	96	80.7±7.6[b]	90.2±10.9[b]	643.5±203.6[b]
Pancreatitis	52	61.4±6.7	21.1±10.5	30.9±5.9
Normal				
22-59 yr	113	54.3±5.1	17.5±8.3	14.5±5.0
60-68 yr	87	56.6±5.8	19.2±9.6	17.2±5.9

[b]$P<0.01$ *vs* normal group.

Evaluate the value of diagnosis in pancreatic cancer by a single tumor marker

When diagnosing pancreatic cancer by a single tumor marker, TSGF had the highest sensitivity of 91.6%, CA242 had the highest specificity of 93.5%; TSGF and CA19-9 had the exactly validity. The positive likelihood ratio of TSGF, CA242 and CA19-9 were 5.4, 12.6 and 6.3, and the negative likelihood ratio were 0.10, 0.19 and 0.17 (Table 2).

Table 2 Evaluation of the value of diagnosis in pancreatic cancer by a single tumor marker of 96 cases

Value of diagnosis	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio
TSGF	91.6 (88)[a]	83.0	5.4	0.10
CA242	82.3 (79)	93.5[b]	12.6	0.19
CA19-9	85.4 (82)	86.5	6.3	0.17

( ), No. of cases; [a]P<0.05, [b]P<0.01 *vs* the other two indexes. sensitivity=truepositive / patients×100%=TP / (TP+FN)×100%, specificity=true negative / normal×100%=TN / (TN+FP)×100% positive likelihood ratio=true positive / false positive=sensitivity / (1-specificity) negative likelihood ratio=(1-true positive) / (1-false positive)=(1-sensitivity) / specificity.

The different combinations of the 3 markers to the diagnosis in pancreatic cancer

When diagnosing pancreatic cancer by any of the 3 markers was over the critical value, the sensitivity, specificity and positive predictive value were 93.8%, 79.0% and 68.2%. When two of the 3 markers were over the critical value, the sensitivity, specificity and positive predictive value were 89.5%, 95.5% and 90.5%. When the 3 markers were all over the critical value, the sensitivity was 77.0% and the specificity and positive predictive value were both 100%. Therefore, the combination diagnosis in pancreatic cancer could increase the specificity of the diagnosis (Table 3).

Table 3 Analyses of The different combinations of the 3 markers to the diagnosis in pancreatic cancer (No. of cases)

Group	No. of cases	1 Item (+)	2 Item (+)	3 Item (+)
Pancreatic cancer	96	90 (93.8)	86 (89.5)	74 (77.0)
Normal	200	42 (21.0)	9 (4.5)	0 (100)
Positive likelihood rate (%)		68.2	90.5	100

( ), sensitivity (%).

The correlation between the different positions of pancreatic cancer and the levels of the 3 markers

International Union Against Cancer (UICC) divided pancreatic cancer into head, body, tail and whole of pancreatic cancer. Statistical significance was found that the levels of TSGF and CA242 in head of pancreatic cancer were extra better than those in the other three kinds of pancreatic cancer (P<0.01). But no statistical significance was found in the levels of the 3 markers in the other three kinds of pancreatic cancer (P>0.05). The levels of CA19-9 had no correlation with the positions of the pancreatic cancer (P>0.05). (Table 4).

Table 4 The content of the 3 markers in the different positions of pancreatic cancer (mean±SD, $\times 10^3$U / L)

Position of pancreatic cancer	No. of cases	TSGF	CA242	CA19-9
Head	64	88.5±9.0[b]	106.4±12.6[b]	653.7±217.8
Body	18	78.2±6.7	82.5±10.4	633.9±192.4
Tail	10	77.1±5.7	81.6±8.2	659.4±211.0
Whole	4	74.5±3.1	83.0±9.5	615.3±187.1

[b]P<0.001 *vs* body, tail and whole of pancreatic cancer.

To compare the sensitivity of the 3 tumor markers in different stages of pancreatic cancer

We analyzed the sensitivity of the 3 tumor markers in serum in different stages of pancreatic cancer (Table 5). The results showed that the sensitivity gradually strengthened by the progress of clinical stages. Statistical significance was found between stage II, III, IV, and stage I (P<0.01). The sensitivity of CA19-9 was higher than that of CA242, but there was no statistical significance (P>0.05). The sensitivity of TSGF in stage I was significant better than that of CA242 and CA19-9 (P<0.01). So TSGF could be regarded as a tumor marker to filtrate pancreatic cancer in early stage.

Table 5 Analyses of the sensitivity of the 3 tumor markers in different stages of pancreatic cancer (No. of cases)

Clinical stages	No. of cases	TSGF	CA242	CA19-9
I	10	6 (60.0)[bd]	3 (30.0)[d]	4 (40.0)[d]
II	12	9 (75.0)	6 (50.0)	7 (58.3)
III	25	22 (88.0)	20 (80.0)	21 (84.0)
IV	49	46 (93.8)	40 (81.6)	42 (85.7)

Note: ( ), sensitivity (%); [d]P<0.01 *vs* the sensitivity of stage II, III, IV; [b]P<0.01 *vs* the sensitivity of CA242, CA19-9.

DISCUSSION

The incidence of pancreatic cancer is rising[10,11]. We want to diagnose pancreatic cancer in early stage by tumor markers[12]. First, we should find one tumor marker of good specificity[13,14]. TSGF was a gene that could promote the growth of tumor blood vessels. It could greatly hyperplasy in the tumor tissues and capillary vessels around. No correlation was found in the hyperplasia of non-tumor blood vessels. TSGF had good sensitivity to malignant tumors. CA19-9 belonged to the ramification of lactotetraose and was a kind of the ganglioside lipoprotein protein[15-17]. It was mucoprotein when in serum and its epipositions was pentaglucose determinant. Despite advances in preoperative radiologic imaging, a significant fraction of potentially resectable pancreatic cancers are found to be unresectable at laparotomy[18]. CA242 was a kind of sialic acid mucoprotein tumor associated antigen linked Mucin pyrenoid by –O-. It existed in the same molecule with CA19-9. But it belonged to the different antigen determinant with CA19-9. Therefore, there was no correlation between CA19-9 and CA242[19]. But they were complemental. They had good sensitivity in pancreatic cancer diagnosis. This result was exactly similar with the report of Ichihara *et al*[20]. This research also showed that 3 tumor markers in pancreatic cancer group were remarkably higher than that of normal group. And the levels of the 3 tumor markers in pancreatitis group were not high.

The research showed that the positive likelihood ratio of TSGF, CA242 and CA19-9 were 5.4, 12.6 and 6.3, and the negative likelihood ratio were 0.1, 0.19 and 0.17. So the three indexes were very important in clinical pancreatic cancer diagnosis. TSGF had good sensitivity in pancreatic cancer diagnosis as 91.6%. CA19-9 was very important to evaluate the curative effect of chemotherapy and to judge the survival time[21-26]. CA242 had good specificity as 93.5%. When diagnosing with the combination assay of the 3 indexes, the sensitivity was 77.0% and the specificity and positive predictive value were both 100%. Therefore, combination diagnosis should be used in pancreatic cancer diagnosis in order to improve the specificity[27-29].

The research of Metsuyama *et al.* proved that there was significant correlation in malignant tumors between the creation of blood vessels and blood transfer[30]. TSGF and CA242 had high levels. It was related to the rich blood supply of the head of pancreas. Pancreas had the priority and step artery pancreaticoduodenalis superior and the forward and back branches down pancereaticoduodenales inferiors. The arteries were connected by anastomosis at the head of pancreas to be arcuate arterial. The arcuate arterial gave out branches to supply the forward and back parts of the head of pancreas and duodenum. It accelerated the head of pancreas circulation. So

it made the carbohydrate antigen excreted by tumors to be a high level in serum. But there was no correlation between the expression of CA19-9 and the position of tumor. This needs further researches. TSGF was a new tumor marker related to the blood vessel hyperplasia of malignant tumors. It was also a result of the hyperplasia of the malignant tumors and the capillary vessels around. It was released to blood with the acceleration of blood circulation. In the different stage of pancreatic cancer, the sensitivity of the tumor markers TSGF, CA242 and CA19-9 increased with the progress in different stages. Statistical significance was found in the sensitivity of stage II, III, IV and stage I. This result disagreed that Frebourg *et al* reported that there was no correlation between the level of CA19-9 in serum and the stage of pancreatic cancer[31]. The sensitivity of CA19-9 was a little higher than that of CA242, but there was no statistical significance. In the stage I of pancreatic cancer, the sensitivity of TSGF was remarkably higher than that of CA242 and CA19-9. Therefore, TSGF can be regarded as a tumor marker to filtrate pancreatic cancer in early stage.

The research shows that there is very important correlation between the levels of TSGF, CA242 and CA19-9 and pancreatic cancer. The combined assay of the 3 indexes does help to diagnose pancreatic cancer in early stage. At the same time they are very important in analyzing the position of pancreatic cancer and the pathology typings. Therefore, the 3 indexes can be regarded as the tumor markers of pancreatic cancer diagnosis in early stage.

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Edited by Kumar M and Xu FM