RESEARCH ARTICLE

Applicative Value of Serum CA19-9, CEA, CA125 and CA242 in Diagnosis and Prognosis for Patients with Pancreatic Cancer Treated by Concurrent Chemoradiotherapy

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Abstract

Objective: To evaluate the application value of serum CA19-9, CEA, CA125 and CA242 in diagnosis and prognosis of pancreatic cancer cases treated with concurrent chemotherapy. Materials and Methods: 52 patients with pancreatic cancer, 40 with benign pancreatic diseases and 40 healthy people were selected. The electrochemiluminescence immunoassay method was used for detecting levels of CA19-9, CEA and CA125, and a CanAg CA242 enzyme linked immunoassay kit for assessing the level of CA242. The Kaplan-Meier method was used for analyzing the prognostic factors of patients with pancreatic cancer. The Cox proportional hazard model was applied for analyzing the hazard ratio (HR) and 95% confidential interval (CI) for survival time of patients with pancreatic cancer. Results: The levels of serum CA19-9, CEA, CA125 and CA242 in patients with pancreatic cancer were significantly higher than those in patients with benign pancreatic diseases and healthy people (P<0.001). The sensitivity of CA19-9 was the highest among these, followed by CA242, CA125 and CEA. The specificity of CA242 is the highest, followed by CA125, CEA and CA19-9. The sensitivity and specificity of joint detection of serum CA19-9, CEA, CA125and CA242 were 90.4% and 93.8%, obviously higher than single detection of those markers in diagnosis of pancreatic cancer. The median survival time of 52 patients with pancreatic cancer was 10 months (95% CI7.389~12.611).. Patients with the increasing level of serum CA19-9, CEA, CA125, CA242 had shorter survival times (P=0.047. 0.043, 0.0041, 0.029). COX regression analysis showed that CA19-9 was an independent prognostic factor for patients with pancreatic cancer (P=0.001, 95%CI 2.591~38.243). Conclusions: The detection of serum tumor markers (CA19.9, CEA, CA125 and CA242) is conducive to the early diagnosis of pancreatic cancer and joint detection of tumor markers helps improve the diagnostic efficiency. Moreover, CA19-9 is an independent prognostic factor for patients with pancreatic cancer.

Keywords: Pancreatic cancer - tumor markers - CA19-9 - CEA - CA125 - CA242 - prognosis

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Introduction

Pancreatic cancer is one of the common malignant tumors in digestive system, with poor prognosis (Lin et al., 2015). 90% of pancreatic cancer is ductal adenocarcinoma deriving from ductal epithelial cells and only a few deriving from acinous cells. Pancreatic cancer is insidious malignancy of high mortality in clinic, with the overall 5-year survival rate being only 0.4%~4.0% (Jemal et al., 2008). Because patients have no obvious symptoms at an early stage, they are already in middle or advanced stage when diagnosed, losing the chance to optimal treatment. Nevertheless, if patients are diagnosed as pancreatic cancer at an early stage, 20% patients would get cured by early surgical resection. Therefore the early detection plays an important role in diagnosis of pancreatic cancer (Bertsch et al., 2013). At present, although means and methods for the diagnosis of pancreatic carcinoma include imaging, endoscopic and pathological examination, serum tumor markers, there is not effective tumor markers for the early diagnosis and prognosis assessment of pancreatic cancer (Frucht et al., 2004; He et al., 2015). The single detection of tumor markers lacks enough sensitivity and specificity to the diagnosis of pancreatic cancer. In recent years, researches were found that tumor markers such as CA19-9, CEA, CA125 and CA242 are of great significance to the early detection, treatment monitoring and prognosis assessment of pancreatic cancer (Liu et al., 2014). Therefore, this study explored the applicative value of joint detection of CA19-9, CEA, CA125 and CA242 in diagnosis and prognosis assessment for patients with pancreatic cancer treated by concurrent chemoradiotherapy by analyzing the the expression levels of tumor markers in patients with pancreatic cancer.

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Table 1. Levels of Serum CA19-9, CEA, CA125 and CA242 in Different Groups (x-±s)

Groups	Cases	CA19-9(U/mL)	CEA(ng/mL)	CA125(U/mL)	CA242(U/mL)
Pancreatic cancer	52	1494.5±1032.2**	12.3±4.3*	187.7±11.8**	62.5±36.7**
Benign pancreatic diseases	40	45.6±13.8##	7.2±2.3##	23.5±10.0##	13.4±5.4##
Normal control	40	9.4±5.2	3.8±2.6	12.4±8.3	8.4±3.6

**P<0.001, *P<0.05 compared with patients with benign pancreatic disease, ##P<0.01 compared with normal control group (healthy examined people)

Table 2. Value of Single or Joint Detection of Serum CA19-9, CEA, CA125, CA242 in Diagnosis of Pancreatic Cancer (%)

Tumor markers	Sensitivity	Specificity	Diagnostic accuracy
CA19-9	82.7 (43/52)	58.6(47/80)	68.2(90/132)
CEA	53.8 (28/52)	56.3(45/80)	55.3(73/132)
CA125	69.2 (36/52)	67.5(54/80)	68.2(90/132)
CA242	76.9 (40/52)	90.0(72/80)	84.8(112/132)
CA19-9+CEA+CA125+CA242	90.4(47/52)	93.8(75/80)	92.4(122/132)

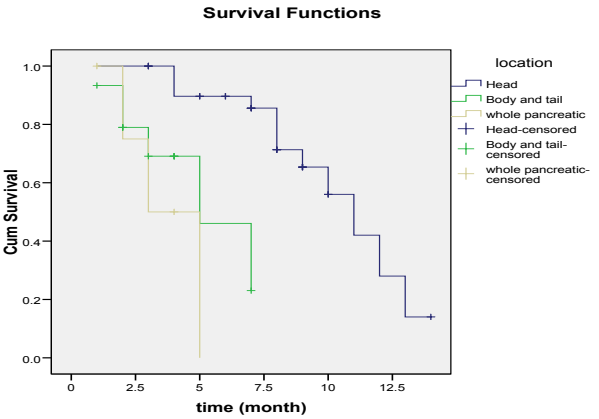

Figure 1. The Influence of Location of Tumor on Survival Time of Pancreatic Cancer. The survival time of pancreatic head cancer was longer than that of pancreatic body and tail carcinoma and the whole pancreatic cancer, P=0.000, HR=1.603 (95% CI 0.487~1.563)

Materials and Methods

General data

A total of 52 patients with pancreatic cancer treated with concurrent chemotherapy admitted in the First Affiliated Hospital of Zhengzhou University from Jan., 2013 to Oct., 2013 were selected, in which there were 29 males and 23 females, aged 32~69 years with the mean age of (56.5±7.3) years. The Karnofsky Performance Status (KPS) of 52 patients scores more than 70 points. All patients had no chemoradiotherapy contraindication. Additionally, 40 patients with benign pancreatic diseases (33 patients with chronic pancreatitis and 7 with pancreatic cyst) at the corresponding period were selected, in which there were 18 males and 22 females, aged 28~71 years with the mean age of (57.5±8.5) years. And 40 healthy examined people were selected as normal control group, 21 males and 19 females, aged 29~70 years with the mean age of (55.5±8.7) years.

Detection of tumor markers

The fasting venous blood (2 mL) at early morning

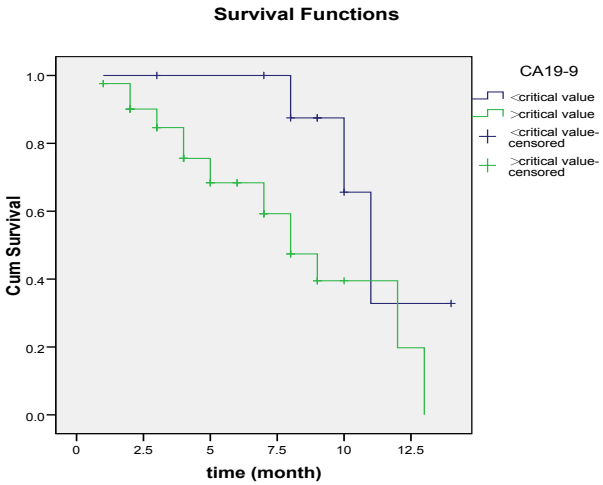

Figure 2. The Influence of Level of CA19-9 on Survival Time of Pancreatic Cancer. Patients with the increasing level of serum CA19-9 had shorter survival time than patients with normal level of serum CA 19-9, P=0.047, HR=3.540 (95% CI 1.035~9.402)

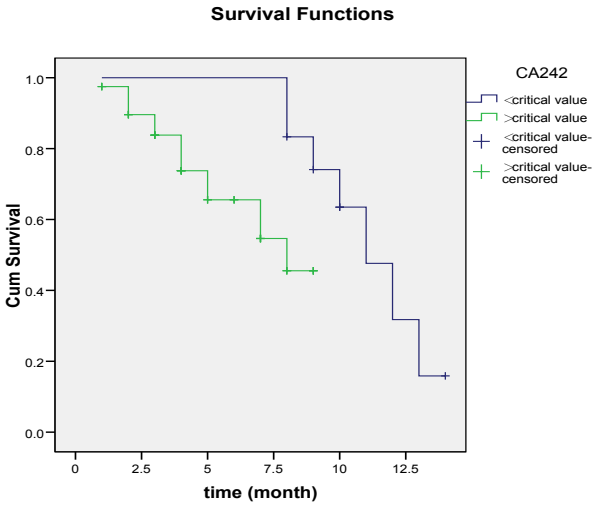

Figure 5. The Influence of Level of CA242 on Survival Time of Pancreatic Cancer. Patients with the increasing level of serum CA242 had shorter survival time than patients with normal level of serum CA242, P=0.029, HR=4.603 (95% CI 2.105~5.124)

of the study objects was drawn and the serum was centrifuged and stored at -20 °Cuntil assayed. The electrochemiluminescence immunoassay method was used for detecting the levels of CA19-9, CEA, CA125, and CanAg CA242 enzyme linked immunoassay kit for the level of CA242. The procedures were conducted strictly according to the instructions of kits. The critical values of CA19-9, CEA, CA125 and CA242 were 37 U/mL, 5 ng/mL, 35 U/mL and 20 U/mL, respectively. The levels exceeding the critical values of 4 tumor markers were deemed as positive.

Follow-up

Telephone follow-up was done for patients until April 1st, 2015. The survival time was from the first time of tumor markers detection after patients was confirmed to patients' death or the time of final follow-up.

Statistical data analysis

SPSS15.0 software package was applied for data analysis. The measurement data was presented as mean±standard deviation ($\bar{x}\pm s$), and the comparison of levels of tumor markers among groups were analyzed by t test. The comparison of the rate among groups was analyzed using χ^2 test. The influence of age, gender, location of tumor, tumor size, CA19-9, CEA, CA125 and CA242 on survival of patients was analyzed by using Kaplan-Meier method. Cox Proportional Hazard Model was used for analyzing the hazard ratio (HR) and 95% confidential interval (CI) for survival time. A value of $P<0.05$ was considered statistically significant.

Results

Levels of serum CA19-9, CEA, CA125 and CA242 in different groups

As shown in Table 1, the levels of serum CA19-9, CEA, CA125 and CA242 in patients with pancreatic

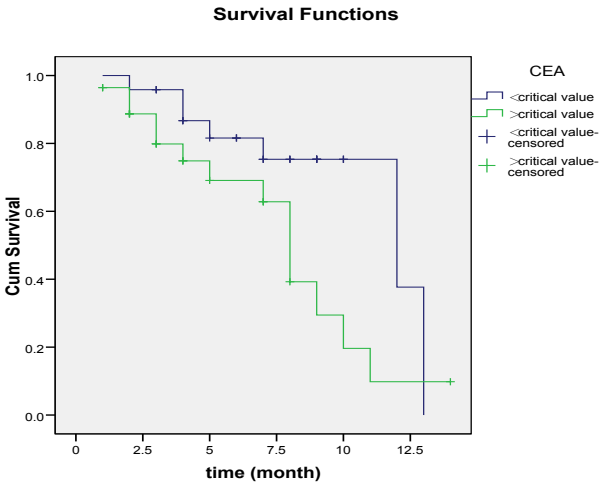

Figure 3. The Influence of Level of CEA on Survival Time of Pancreatic Cancer. Patients with the increasing level of serum CA had shorter survival time than patients with normal level of serum CEA, P=0.043, HR=1.023 (95% CI 0.975~3.208)

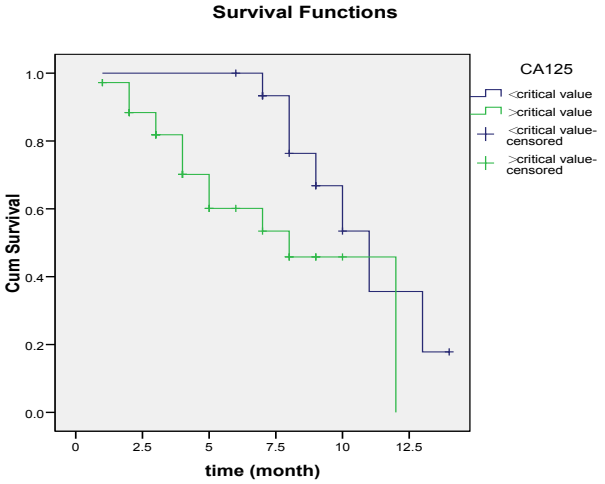

Figure 4. The Influence of Level of CA125 on Survival Time of Pancreatic Cancer. Patients with the increasing level of serum CA125 had shorter survival time than patients with normal level of serum CA 125, P=0.041, HR=2.998 (95% CI 1.684~4.867)

Table 3. Analysis of Different Influencing Factors on Survival Time of Pancreatic Cancer

	Cases	Median survival time (95% CI, month)	Wald	P	HR(95% CI)
Gender					
Male	29	10.0 (7.355~12.645)	0.222	0.638	0.724 (0.457~5.063)
Female	23	11.0 (7.229~14.771)			
Age (years)					
≤55	20	8.0 (5.853~10.147)	0.544	0.461	0.852 (0.546~1.506)
>55	32	10.0(7.858~12.142)			
Location of tumor					
Head	32	11.0 (8.864~13.136)	18.517	0.000	1.603 (0.487~1.563)
Body and tail	15	5.0 (1.465~8.535)			
Whole pancreas	5	3.0 (1.040~4.960)			
Tumor size (cm)					
≤5	15	12.0 (6.055~17.945)	3.609	0.057	1.034 (0.842~1.865)
>5	37	10.0 (4.340~15.660)			
CA19-9					
<critical value	9	11.0 (9.480~12.520)	3.962	0.047	3.540 (1.035~9.402)
>critical value	43	8.0 (5.913~10.087)			
CEA					
<critical value	24	12.0 (4.954~19.046)	4.084	0.043	1.023 (0.975~3.208)
>critical value	28	8.0 (6.941~9.059)			
CA125					
<critical value	16	11.0 (8.718~13.282)	4.165	0.041	2.998 (1.684~4.867)
>critical value	36	8.0 (5.349~10.651)			
CA242					
<critical value	12	11.0 (8.818~13.182)	4.760	0.029	4.603 (2.105~5.124)
>critical value	40	8.0 (7.389~12.611)			

Table 4. Multivariate Analysis of Survival Time of Pancreatic Cancer

	B	SE	Wald	df	P	Exp(B)	95%CI
Gender	-0.661	0.555	1.421	1	0.233	0.516	0.174~1.531
Age	-1.602	0.667	5.764	1	0.727	0.810	0.249~2.637
Location of tumor	1.216	0.303	8.108	1	0.053	2.373	1.531~7.430
Tumor size	0.793	0.640	1.532	1	0.216	2.209	0.630~7.752
CA19-9	2.298	0.687	11.197	1	0.001	9.954	2.591~38.243
CEA	1.669	1.008	2.741	1	0.098	5.305	0.736~38.251
CA125	0.528	0.784	0.454	1	0.501	1.696	0.365~7.892
CA242	1.426	1.044	1.865	1	0.172	4.162	0.538~32.221

cancer were significantly higher than those in patients with benign pancreatic diseases and healthy people (P<0.001). Compared with normal control group, the levels of those four markers in patients with benign pancreatic diseases were higher (P<0.01).

Value of single or joint detection of serum CA19-9, CEA, CA125, CA242 in diagnosis of pancreatic cancer

In the single detection of tumor markers, the sensitivity of CA19-9 was the highest one among them, followed by CA242, CA125 and CEA. The specificity of CA242 is the highest, followed by CA125, CEA and CA19-9. The sensitivity and specificity of joint detection of serum CA19-9, CEA, CA125and CA242 were 90.4% and 93.8%, obviously higher than single detection of those markers in diagnosis of pancreatic cancer, showing that joint detection of those tumor markets was more sensitive to pancreatic cancer, with higher detectable rate. The diagnostic accuracy of joint detection of 4 tumor markets was higher than the single detection of them in diagnosis of pancreatic cancer. (Table 2)

Prognostic value of serum CA19-9, CEA, CA125, CA242 in pancreatic cancer

All patients were followed up until April 1st, 2015. The median survival time of 52 patients with pancreatic cancer was 10 months (95% CI 7.389~12.611). The survival time of pancreatic head cancer was longer than that of pancreatic body and tail carcinoma and the whole pancreatic cancer (P=0.000) (Figure1). Patients with the increasing level of serum CA19-9, CEA, CA125, CA242 had shorter survival time (P=0.047. 0.043, 0.0041, 0.029) (Figure 2, 3, 4 and 5). However, the survival time of patients had no relationships with age, gender and tumor size (P=0.05). The detailed data were showed in Table 3.

COX regression analysis showed that CA19-9 was an independent prognostic factor for patients with pancreatic cancer (P=0.001, 95%CI 2.591~38.243). When the level of serum CA19-9 exceeds the critical value, the mortality risk increased. However, the others had no obvious influence on the survival of patients. (Table 4).

Discussion

Pancreatic cancer is a kind of digestive tract tumor of high malignant degree. Patients have no obvious clinical symptom at an early stage, but they have been at an advanced stage and had multiple metastatic sites when diagnosed and lost the best chance of surgery. Therefore, how to improve the early detection for pancreatic cancer and achieve the goal of early treatment is the key to the prognosis (Jiang et al., 2004; Chen et al., 2012). In recent years, due to the constant depth of basic and clinical research, and advance in laboratory, endoscope, imaging techniques and equipments, especially the development of molecular biological techniques, the early detection level of malignant tumors in the digestive system have been improved greatly and more than 10 kinds of serum tumor markers for pancreatic cancer have been widely applied in clinic such as CA19-9, CEA, CA125, CA242, etc. (Liu et al., 2014). However, there exist limitations such as low sensitivity, and poor specificity (Duraker et al., 2007).

CA19-9 is a sort of sialic acid derivative which is a marker for pancreatic cancer. CA19-9 also elevated in other digestive tract tumors such as gallbladder carcinoma, gastric cancer, liver cancer, to different degrees. Research was found that the increased CA 19-9 in serum was directly related to the size and metastasis of tumor and the prognosis of the patients (Jamieson et al., 2011). CA242 often exists in pancreas and colon cancer. The immunofluorescent staining for CA242 was stronger than that in normal adjacent pancreatic cells. Another research reported that CA242 is more valuable that CA19-9 for judging the prognosis of pancreatic cancer (Zhou et al., 2012) and its specificity is higher than 19-9 (Li et al., 2014). CEA, a kind of acidoglycoprotein, is first used as tumor marker for the diagnosis of pancreatic cancer. It is also a kind of the most widely used tumor markers presently and expressed in multiple tumors, but with poor specificity. CA125 is glycoprotein on cytomembrane of primary epithelial ovarian cancer, which has high specificity to epithelioma, but low specificity to pancreatic cancer.

The finding of the present study showed that the levels of serum CA19-9, CEA, CA125 and CA242 in patients with pancreatic cancer were significantly higher than those in patients with benign pancreatic diseases and healthy people (P<0.001), which was consistent with the results of Mu et al's study (Mu et al., 2011) and Wu et al's study (Wu et al., 2011). The results of single or joint detection of serum CA19-9, CEA, CA125, CA242 in diagnosis of pancreatic cancer showed that the sensitivity of CA19-9 was 82.7%, the highest one among them, followed by CA242 (76.9%), CA125 (69.2%) and CEA (53.8%). The specificity of CA242 is 90.0%, followed by CA125 (67.5%), CEA (56.3%) and CA19-9 (58.6%). The sensitivity and specificity of joint detection of serum CA19-9, CEA, CA125and CA242 were 90.4% and 93.8%,

obviously higher than single detection of those markers in diagnosis of pancreatic cancer, and the diagnostic accuracy of joint detection of tumor markers was 92.4%, higher than the single detection of them in diagnosis of pancreatic cancer, which were conductive to differential diagnosis for pancreatic cancer and pancreatic benign diseases.

The survival time for pancreatic cancer is closely associated with tumor staging, location and markers. Humphris et al (Humphris et al., 2012) reported that CA19-9 is of significance to the diagnosis and prognosis of pancreatic cancer. Li et al (Li et al., 2014) suggested that CA19-9 and CA242 are independent prognostic factors for assessing the prognosis of pancreatic carcinoma. However, researches about the influence of CEA and CA125 on survival time of pancreatic cancer are rarely reported at home and abroad. In present study, patients with the increasing level of serum CA19-9, CEA, CA125, CA242 had shorter survival time (P=0.047. 0.043, 0.0041, 0.029), with poor prognosis. However, the survival time of patients had no relationships with age, gender and tumor size. Moreover, COX regression analysis showed that the high level of CA19-9 is an independent prognostic factor for evaluating the pancreatic cancer, which was consistent with the part of the results of previous study (Reitz et al., 2015).

In conclusion, the occurrence of pancreatic cancer is related to multiple factors and the early diagnosis and early treatment is the key to improving the survival time. In present study, the detection of serum tumor markers (CA19-9, CEA, CA125 and CA242) is conductive to the early diagnosis of pancreatic cancer and the joint detection of tumor markers helps improve the diagnostic efficiency. Moreover, CA19-9 was an independent prognostic factor for patients with pancreatic cancer, which is very conductive to the prognosis assessment of patients with pancreatic cancer.

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