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Assessment value of quantitative indexes of pancreatic CT perfusion scanning for malignant degree of pancreatic cancer

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ABSTRACT

Objective: To analyze the assessment value of the quantitative indexes of pancreatic CT perfusion scanning for malignant degree of pancreatic cancer. **Methods:** A total of 58 patients with space-occupying pancreatic lesions were divided into 20 patients with pancreatic cancer and 38 patients with benign pancreatic lesions after pancreatic CT perfusion. Patients with pancreatic cancer received palliative surgery, and the cancer tissue and para-carcinoma tissue specimens were collected during operation. The differences in pancreatic CT perfusion scanning parameter values and serum tumor marker levels were compared between patients with pancreatic cancer and patients with benign pancreatic lesions, mRNA expression levels of malignant molecules in pancreatic cancer tissue and para-carcinoma tissue were further determined, and the correlation between pancreatic CT perfusion scanning parameter values and malignant degree of pancreatic cancer was analyzed. **Results:** CT perfusion scanning BF, BV and Per values of patients with pancreatic cancer were lower than those of patients with benign pancreatic lesions; serum CA19-9, CEA, CA125 and CA242 levels were higher than those of patients with benign pancreatic lesions (P<0.05); mRNA expression levels of *Bcl-2*, *Bcl-xL* and *survivin* in pancreatic cancer tissue samples were higher than those in para-carcinoma tissue samples, and mRNA expression levels of *P53* and *Bax* were lower than those in para-carcinoma tissue samples (P<0.05); CT perfusion scanning parameters BF, BV and Per values of patients with pancreatic cancer were negatively correlated with CA19-9, CEA, CA125 and CA242 levels in serum as well as mRNA expression levels of *Bcl-2*, *Bcl-xL* and *survivin* in pancreatic cancer tissue, and positively correlated with mRNA expression levels of *P53* and *Bax* in pancreatic cancer tissue (P<0.05). **Conclusions:** Pancreatic CT perfusion scanning is a reliable way to judge the malignant degree of pancreatic cancer and plays a positive role in guiding clinical treatment, forecasting treatment outcome and other aspects.

1. Introduction

Pancreatic cancer is the tumor with the highest malignant degree in the whole body, early tumor volume is small and cannot be accurately captured by CT and diagnosed, so its early diagnostic rate is not high and the mortality rate 1 year after diagnosis is extremely high. How to early diagnose pancreatic cancer and judge tumor malignancy is the key to take proper treatment measures and prolong patients' survival[1,2]. In view of the defects of conventional CT in the diagnosis of pancreatic cancer, clinical scholars have pointed out that CT perfusion scanning is a more reasonable and reliable way for pancreatic cancer screening. Pancreatic CT perfusion scanning forms time-density curve based on the pancreatic perfusion state and vascular features, the typical CT perfusion parameters such as blood flow (BF), blood volume (BV) and permeability (per) can reflect the tumor blood supply and are not restricted by tumor size, so they have unique advantages in differentiating benign and malignant tumor, forecasting the specific tumor malignancy and other aspects[3,4]. In the study, CT perfusion scanning was applied in patients with pancreatic cancer, and the evaluation value of the inspection way for the malignant degree of pancreatic cancer was

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mainly elaborated.

2. Materials and methods

2.1. General information

All 58 patients with space-occupying pancreatic lesions who were treated in our hospital from May 2012 to may 2015 received pancreatic CT perfusion scanning and were divided into 20 patients with pancreatic cancer and 38 patients with benign pancreatic lesions (acute or chronic pancreatitis) according to the results. The inclusion criteria for above research subjects: 1) ultrasound showed obvious pancreatic space occupying; 2) with patients' informed consent; 3) with complete clinical data. Exclusion criteria: 1) with serious liver and kidney dysfunction; 2) allergic to contrast agent; 3) pregnant or breast-feeding women. 20 patients with pancreatic cancer included 11 male cases and 9 female cases, they were 41-76 years old, the average age was (62.17±7.05) years, TNM stage was: 0 case with Ⅰ stage, 3 cases with Ⅱ stage, 10 cases with Ⅲ stage and 7 cases with Ⅳ stage; 6 cases were with tumor diameter <2 cm and 14 cases were with tumor diameter 2 cm; 12 cases were without distant metastasis and 8 cases were without distant metastasis. 38 patients with benign pancreatic lesions included 20 male cases and 18 female cases, they were 39-73 years old and the average age was (61.52±8.34) years. The two groups were not statistically different in gender and age distribution (P>0.05).

2.2. Pancreatic CT perfusion scanning

Fifteen min after routine three-phase enhancement scanning, the largest lesion slice or suspicious lesion slice in regular enhancement images was selected for CT perfusion scanning. Nonionic contrast medium (300 mg/mL) 50 mL + saline 50 mL were injected in turn with high pressure injector, and after 5 s, the selected slices were dynamically scanned. The images from CT perfusion scanning were uploaded to Siemens workstation and analyzed with Body-PCT software. The pancreatic tissue in region of interest (ROI) was selected as much as possible (automatically correcting breathing and movement deviation between slices), aorta abdominalis was selected as input artery and the 256-color perfusion image of ROC was generated. Values of CT perfusion scanning parameters were obtained at last: blood flow (BF), blood volume (BV) and permeability (per).

2.3. Serum tumor markers

A total of 5 mL of fasting peripheral venous blood was collected from patients with pancreatic cancer and patients with benign pancreatic lesions before treatment, let stand at room temperature for 1 h and then centrifuged at high speed to get serum, and chemiluminescence method was used to determine serum levels of tumor markers such as CA19-9, CEA, CA125 and CA242.

2.4. Malignant molecules in pancreatic tissue

A total of 20 patients with pancreatic cancer received surgery, and the pancreatic cancer tissue and normal pancreatic tissue 5cm from cancer were collected during operation. The obtained tissue samples were taken, homogenized and then centrifuged to get supernatant. It was centrifuged after chloroform and isopropyl alcohol were added in turn to obtain target RNA plaque. Reverse transcription kits (Beijing Mingyangkehua Bio Technology Co., Ltd.) were used to reverse-transcribe it into cDNA, and fluorescence quantitative PCR kits (NanJing SunShine Biotechnology Co., LTD.) were used to amplify the target genes *Bcl-2, Bcl-xL, P53, survivin* and *Bax*. Reaction procedures: 95 ℃, 15 s, specific annealing temperature, 20 s, 72 ℃ 25 s, repeating for 40 cycles. Internal reference β*-actin* was used to standardize data, and the levels of *Bcl-2, Bcl-xL, P53, survivin* and *Bax* were calculated.

2.5. Statistical methods

Data obtained in the study was input in SPSS23.0 and analyzed, measurement data was in terms of mean±sd, comparison between groups was performed by t test, correlation analysis was by Pearson test, confidential interval was 95% and P<0.05 indicated statistical significant differences.

3. Results

3.1. Pancreatic CT perfusion scanning

BF value and Per value of patients with pancreatic cancer were significantly lower than those of patients with benign pancreatic lesions. Differences in pancreatic CT perfusion scanning parameters BF, BV and Per values of two groups were statistically significant (P<0.05) (Table 1).

3.2. Serum tumor markers

Serum CA19-9, CEA, CA125 and CA242 levels of patients with pancreatic cancer were significantly higher than those of patients with benign pancreatic lesions, and differences in serum CA19-9, CEA, CA125 and CA242 levels of two groups were statistically significant (P<0.05), shown in Table 2.

3.3. Expression levels of apoptosis-related molecules in pancreatic tissue

mRNA expression levels of *Bcl-2, Bcl-xL* and *survivin* in pancreatic

cancer tissue samples were significantly higher than those in para-carcinoma tissue samples; mRNA expression levels of *P53* and *Bax* in pancreatic cancer tissue samples were significantly lower than those in para-carcinoma tissue samples, and differences in mRNA expression levels of *Bcl-2, Bcl-xL, surviving, P53* and *Bax* in pancreatic cancer tissue and para-carcinoma tissue were statistically significant ($P<0.05$), shown in Table 3.

3.4. Correlation between pancreatic CT perfusion scanning parameters and malignant degree of pancreatic cancer

CT perfusion scanning parameters BF, BV and Per values of patients with pancreatic cancer were negatively correlated with CA19-9, CEA, CA125 and CA242 levels in serum as well as mRNA expression levels of *Bcl-2, Bcl-xL* and *survivin* in pancreatic cancer tissue, and positively correlated with mRNA expression levels of *P53* and *Bax* in pancreatic cancer tissue ($P<0.05$) (Table 4).

Table 4

Correlation between pancreatic CT perfusion scanning parameters and malignant degree of pancreatic cancer.

Indexes	BF		BV		Per	
	Determination coefficient *r*	*P*	Determination coefficient *r*	*P*	Determination coefficient *r*	*P*
CA19-9	-0.684	<0.05	-0.704	<0.05	-0.687	<0.05
CEA	-0.712	<0.05	-0.688	<0.05	-0.721	<0.05
CA125	-0.674	<0.05	-0.699	<0.05	-0.709	<0.05
CA242	-0.728	<0.05	-0.716	<0.05	-0.684	<0.05
Bcl-2	-0.649	<0.05	-0.679	<0.05	-0.715	<0.05
Bcl-xL	-0.652	<0.05	-0.726	<0.05	-0.728	<0.05
P53	0.718	<0.05	0.732	<0.05	0.689	<0.05
survivin	-0.694	<0.05	-0.708	<0.05	-0.702	<0.05
Bax	0.726	<0.05	0.649	<0.05	0.723	<0.05

4. Discussion

Pancreatic cancer is the tumor disease with highest clinical malignant degree, the mortality rate 1 year after diagnosis is above 80%, and early diagnosis is the key to prolong patients′ survival time[5,6]. CT is the most common examination means for patients with pancreatic cancer, but for early pancreatic cancer that is with smaller tumor diameter and hasn′t caused pancreatic contour and texture change, the sensitivity of CT examination is low. CT perfusion scanning is considered as the reliable means for early diagnosis of pancreatic cancer, which obtains time-density curve according to the radioindicator dilution principle, central volume principle and so on, uses different mathematical models to calculate perfusion parameters, and visually displays blood perfusion and physiological function changes in pancreatic tissue as well as blood flow characteristics and vascular features in tumor[7,8]. It was found in the study that CT perfusion scanning BF, BV and Per values of patients with pancreatic cancer were lower than those of patients with benign pancreatic lesions, which are basically consistent with the results of previous literature reports, and indicate that the pancreatic cancer tissue is in a relatively blood supply-insufficient state[9]. CT perfusion scanning, as a noninvasive way, is thought to be able to replace conventional CT and become a reliable method to judge the malignant degree of pancreas, and its relationship with the malignant molecule expression in pancreatic serum and tumor tissue is still not clear.

Serum tumor markers CA19-9, CEA, CA125 and CA242 are the markers for current diagnosis of pancreatic cancer and evaluation of disease severity, and they are produced or released into the

Table 1

Pancreatic CT perfusion scanning parameter values.

Groups	Case No.	BF (mL/100 mL/min)	BV (mL/100 mL)	Per (0.5 mL/100 mL/min)
Pancreatic cancer	20	72.55±8.02	94.37±10.25	63.17±7.24
Benign pancreatic lesions	38	121.64±15.09	176.26±20.31	99.42±8.69
t		8.394	11.283	9.345
P		<0.05	<0.05	<0.05

Table 2

Serum tumor marker levels.

Groups	Case No.	CA19-9 (kU/L)	CEA (μg/L)	CA125 (kU/L)	CA242 (kU/L)
Pancreatic cancer	20	251.66±28.94	9.53±0.87	51.75±5.89	93.26±10.15
Benign pancreatic lesions	38	43.28±5.07	2.16±0.31	17.36±2.04	17.27±2.51
t		13.284	7.283	8.394	11.273
P		<0.05	<0.05	<0.05	<0.05

Table 3

mRNA expression levels of apoptosis-related molecules in pancreatic cancer and para-carcinoma tissue.

Groups	Case No.	Anti-apoptotic molecules			Pro-apoptotic molecules	
		Bcl-2	*Bcl-xL*	*survivin*	*Bax*	*P53*
Pancreatic cancer tissue	20	189.63±20.54	176.39±19.62	212.37±24.38	51.27±5.89	34.28±4.11
Para-carcinoma tissue	20	100±9.34	100±8.74	100±8.39	100±10.23	100±9.39
t		8.394	7.283	13.274	8.293	11.293
P		<0.05	<0.05	<0.05	<0.05	<0.05

blood in the process of tumor cell proliferation and are detected. Though the specificity and sensitivity of a single serum tumor marker for diagnosis of malignant tumor are low, the combined detection of multiple tumor markers can still provide the basis for the diagnosis of malignant tumor. In addition, serum tumor marker levels have good consistency with the degree malignant tumor load, and the higher the serum CA19-9, CEA, CA125 and CA242 levels, the more vigorous the growth of pancreatic cancer[10,11]. Joint detection of four indicators in the study showed that serum CA19-9, CEA, CA125 and CA242 levels of patients with pancreatic cancer significantly increased and were negatively correlated with pancreatic CT perfusion parameters BF, BV and Per. This means that the parameters measured by pancreatic perfusion CT are correlated with the change of serum tumor marker levels, and can be used to assess pancreatic cancer tumor load and the vitality of cancer cell growth.

In the occurrence and development of pancreatic cancer, the expression levels of a variety of malignant molecules in local tissue were significantly abnormal. In the study, fluorescence quantitative PCR detection of the mRNA expression levels of malignant molecules in pancreatic cancer tissue showed that mRNA expression levels of *Bcl-2*, *Bcl-xL* and *survivin* in tumor tissue of patients with pancreatic cancer were higher and negatively correlated with pancreatic CT perfusion parameters BF, BV and Per, and mRNA expression levels of *P53* and *Bax* were lower and positively correlated with pancreatic CT perfusion parameters BF, BV and Per. *Bcl-2* and *Bcl-xL* are the apoptosis-inhibiting genes with similar functions, and have been confirmed to be massively expressed in a variety of malignant tumors[12]; *survivin* gene is the strongest apoptosis-inhibiting factor discovered at present, and it is found in rat models that applied siRNA to silence survivin expression that tumor cell apoptosis rate increases significantly; *P53* is the upstream signal of mitochondrial apoptosis pathway, and can up-regulate Bax expression and cause apoptosis[13-15]. The above results indicate that the expression of pro-apoptotic molecules and anti-apoptotic molecules in pancreatic cancer tissue is significantly abnormal and pancreatic CT perfusion parameters can assess the expression of apoptosis-related molecules.

Based on above discussion, it is believed that pancreatic CT perfusion inspection can be a reliable way for early diagnosis of pancreatic cancer, and the analysis of specific CT perfusion parameter values can accurately judge the malignant degree of pancreatic cancer and provide guide for clinical treatment and prognosis judgment.

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