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Research Article

HSP70 and CA 19-9 Serum Expression Correlation with Radiotherapy Sensitivity in Patients with Pancreatic Cancer

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Abstract

Objective: To study the serum expression level of heat shock proteins 70 (HSP70) and its relationship with radiotherapy sensitivity in pancreatic carcinoma. **Methods:** 168 patients with pancreatic cancer were enrolled between January 2019 and March 2021 from Southern Medical University Ping Xiang Hospital. Serum HSP70 and CA 19-9 levels were analyzed before, during, and post-radiotherapy. The receiver operating characteristic curve (ROC) was used for obtaining the predictive value of serum HSP70 level with radiotherapy sensitivity. **Results:** Serum levels of HSP70 were positively correlated with tumor diameter, stage, and lymph node metastasis but negatively correlated with the tumor grade. The concentration trend of HSP70 and CA 19-9 before treatment were: normal control group < complete response (CR) group < partial response (PR) group < stable disease (SD) group < progressive disease (PD) group. The concentrations of HSP70 in the CR, PR, and SD groups decreased after radiotherapy, while the concentrations of HSP70 in the PD group increased after the radiotherapy. The reduction percentage of HSP70 in the CR, PR, and SD groups was positively correlated with the reduction percentage of tumor diameter and CA 19-9. In contrast, the increase percentage of HSP70 in the PD group was positively correlated with the increase percentage in tumor diameter and CA 19-9. **Conclusion:** Serum HSP70 and CA 19-9 were positively correlated and closely related to the radiotherapy sensitivity of pancreatic cancer. Moreover, HSP70 and CA 19-9 can be used as biomarkers to predict radiotherapy sensitivity of pancreatic carcinoma. However, a combined diagnosis is better for sensitivity and specificity.

Keywords: Pancreatic cancer; HSP70; CA 19-9; Radiosensitivity

Introduction

Pancreatic cancer is one of the most aggressive and highly malignant tumors ranking the fourth most common cause of cancer-associated death with a five-year survival rate as low as 9% globally [1]. Pancreaticoduodenectomy is considered the only potential treatment; however, less than 10% of patients are fit for the surgery, with a 5-year survival ratio of only 24.6% [2]. Radiotherapy is a treatment of choice for postoperative and unresectable pancreatic cancer [3]. To improve the effect of radiotherapy on patients with pancreatic cancer, it is important to elucidate the biological mechanisms contributing to the tumor refractoriness to radiotherapy. Furthermore, it is vital to identify an effective predictive prognosis model and biomarkers to guide the individualized systemic treatment, which contributes to identifying the newer therapeutics to treat this fatal disease [4]. When the patient receives radiotherapy, the radioactive rays change the body's homeostasis, stimulating HSP building [5]. Among them, HSP70 is the easiest to induce, with multiple biological functions and a key role in carcinogenesis [6]. Elevated HSP70 expression in cancer cells may lead to cancer genesis and progression by providing resistance to radiotherapy [7]. Classically CA 19-9 has been proven a tumor marker for pancreatic cancer [8]. This present study examined the serum levels of HSP70 and CA 19-9 and their relationship with radiotherapy sensitivity in pancreatic cancer patients.

Materials and Methods

Patient selection

From January 2019 and March 2021, 168 patients diagnosed with pancreatic cancer in Southern Medical Pingxiang Hospital were randomly enrolled in this study. 20 healthy adult people (12 male/8 female) were enrolled as controls. The study protocol was approved by the Human Ethics Committee of Southern Medical University Pingxing Hospital (N0: 2010A170-KS01; date, 12/8/2010; Pingxiang, China). The study was conducted according to the principles of the Declaration of Helsinki. Before participation, written informed consent was obtained from all participants to use their tissues and blood. Inclusion criteria: (1) diagnosed by endoscopic ultrasound-guided fine-needle aspiration tissue biopsy pathology; (2) not received prior radiotherapy, chemotherapy, surgery, targeted drugs, and other treatments before enrollment; (3) complete clinical data and good treatment compliance; (4) physical condition with an estimated survival time of at least 1 year. Exclusion criteria: (1) secondary tumors; (2) abnormal liver, kidney, and cardiovascular functions; (3) pregnant or lactating women; (4) patients with radiotherapy intolerance or contraindications.

Radiotherapy methods

After being confirmed and monitored by pre-treatment and intrafraction cone-beam CT scans, the enrolled patients were aligned with the spine and then moved to baseline alignment. All treatments were carried out on an Elekta linear accelerator unit (Elekta, Stockholm, Sweden). Thinly sliced CT scans with intravenous contrast were performed and used for the therapy plan. Target volumes and tissues or organs at risk were delineated using the Pinnacle treatment planning system (Phillips Radiation Oncology Systems, Fitchburg, WI). The planning target volume (PTV) was identified by adding a 2-5 mm isotropic margin to the CTV in breath-hold cases or ITV in breath-free cases. Radiotherapy dose was prescribed to about 70-90% isodose line. Images technology such as CT, MRI, or PET-CT was used to identify the gross tumor volume (GTV). The motion ranges of the GTV and normal organs were evaluated by inspecting all CT images from other phases. A respiratory gating scheme was utilized to decrease the internal motion margins. After enough gating window round the end-expiratory phase (30-70% in most cases) was determined, the maximum intensity projection (MIP) images were generated from the CT sets according to the gating window, which was executed to contour the internal target volume (ITV). Full-phase MIP images were registered onto the end-expiratory phase CT images to evaluate marker movement during simulation to delineate marker trajectory. The planning target volume (PTV) was identified using 3-mm isotropic margins to the ITV to account for set-up errors except for the margin resulting in an expansion into the stomach or duodenum. The metastatic regional lymph nodes were also involved in the target volume. The prescribed dose was utilized in the isodose line to cover the PTV. The total dose was calculated according to general dosage guidelines after identifying the dose administered to the normal organs. Stereotactic body radiation therapy was performed. The radiotherapy doses for the organ were maximal point dose to the small bowel duodenum or stomach < 30 Gy, ≥ 700 cm^3 volume of normal liver < 15 Gy, 75% volume of combined kidneys < 12 Gy, spinal cord < 20 Gy. Efficacy of solid tumors was evaluated according to WHO solid tumors, which were divided into (1) CR: existing lesions disappeared, and no occurrence of new lesions; (2) PR: lesions decreased more than 50%, and no new lesions recurred within 4 weeks; (3) SD: the lesion increased but not up to 20% or the lesion decreased less than 50%; (4) PD: new lesions or lesion area increased more than 20%.

Identification of serum HSP70 and CA 19-9 level

Pre-radiotherapy, during-radiotherapy (1 week after radiotherapy beginning), and post-radiotherapy (1 month after radiotherapy completment), 5ml of posterior elbow venous blood was collected from patients with pancreatic cancer. Soluble HSP70 levels were identified using an ELISA kit (R&D Systems,

Minneapolis, MN, USA, Catalogue No. DYC1663E). After being coated with mouse anti-human HSP70 antibody (100µl; 2µg/ml) in carbonate buffer (pH 9.5) overnight at 4 °C, the 96-well microtitre plates were washed thrice with phosphate-buffered saline (PBS) containing 0.1 % Tween-20. After being washed, 100µl of the standard (recombinant human HSP70, 0-10µg/ ml) or samples (1:1) were added to the plates and incubated for 2 h at room temperature. Next, the plates were washed, and HSP70 binding was identified using a biotinylated rabbit anti-human antibody (100µl; 0.5µg/ml) in PBS gelatine. After being placed at room temperature for 1.5 h, the plates were washed again and incubated with streptavidin–horseradish–peroxidase (1:200) in PBS gelatine at room temperature for 20 minutes. After the plates were washed, 100µl of o-phenylene-diamine (Sigma, St Louis, MO, USA) in citrate buffer was added to all wells. The optical density was measured at λ=490 nm (reference at λ=620 nm). The level of CA 19-9 in the serum sample was calculated using a solid-phase radioimmunoassay (Centocor, Malvern, PA). All samples were identified in duplicate according to the guideline of the manufacturer's protocol. The quantity of CA 19-9 was demonstrated in arbitrary units (U/ml). One unit activity was equal to 0.8 ng of purified antigenic protein for CA 19-9 in a solid phase radioimmunoassay.

Statistical analysis

Statistical analysis was carried out using SPSS 22.0 (SPSS Inc., Chicago, IL) software and GraphPad Prism 6.01 (GraphPad Software Inc., San Diego, CA). The patient characteristics and response rates were analyzed using descriptive statistics. Data were listed as mean±standard deviation (mean±SD), median with interquartile ranges, or frequencies. A χ^2 test was used to compare ratios and frequencies. One-way analysis of variance and Student's t-test were used to analyze normally distributed variables, whereas the Mann-Whitney's U test was used for non-normal distributed variables. Correlations between the variables were demonstrated using the non-parametric Spearman's correlation coefficients. The correlation between HSP70 concentration and patient survival was analyzed using Cox regression. Survival analysis was performed using the Kaplan-Meier method. Receiver operating characteristic (ROC) curves analysis was used to determine the optimal cut-off value and were compared to analyze the statistical significance using log-rank testing. All tests were two-tailed. A P value of < 0.05 was considered statistically significant.

Results

Relationship between serum HSP70, CA 19-9 and clinicopathological features of pancreatic cancer patients

The expression profile of serum HSP70 and CA 19-9 in different stages of TNM and tumor grade were: stage I < stage II < stage III < stage IV, high differentiation < medium differentiation < low differentiation (Table 1). The serum HSP70 and CA 19-9 levels in patients with lymph node metastasis were significantly up-regulated compared to patients without metastasis. The serum HSP70 in pancreatic cancer patients was significantly up-regulated compared to the healthy control (Figure 1A). The serum CA 19-9 level in pancreatic cancer patients was up-regulated significantly from the healthy people (Figure 1B). In pancreatic cancer patients, the serum HSP70 was positively correlated with serum CA 19-9 (Figure 1C). The serum HSP70 was positively correlated to the diameter of the tumor in pancreatic cancer patients (Figure 1D). The serum CA 19-9 was positively correlated to the diameter of the tumor in pancreatic cancer patients (Figure 1E). The ROC curve analysis showed that the serum level of HSP70 and Ca19-9 were effective; however, the combination of HSP70 and CA19-9 more efficiently distinguished the patients with pancreatic cancer from controls (Figure 1F). At the cutoff value of 1.92 ng/ml for HSP70, the area under the ROC curve (AUC) of serum HSP70 for predicting pancreatic cancer patients was 0.799, with a 95% CI of 0.699 to 0.900, and Youden index J of 0.754. The sensitivity and specificity for predicting radiotherapy sensitivity were 67.7% and 87.5%, respectively. At the cutoff value of 67.3U/ml for CA 19-9, the AUC of serum CA 19-9 for predicting radiotherapy sensitivity of pancreatic cancer was 0.929, with a 95% CI of 0.874 to 0.984, and Youden index J of 0.749. The sensitivity and specificity for predicting radiotherapy sensitivity were 88.7% and 87.5%, respectively. AUC of the combination of serum HSP70 and serum CA 19-9 in predicting radiotherapy sensitivity of pancreatic cancer patients was 0.966, with a 95% CI of 0.930 to 1.000, and Youden index J of 0.876. The sensitivity and specificity for predicting pancreatic cancer were 83.9% and 99.0%, respectively (Table 2).

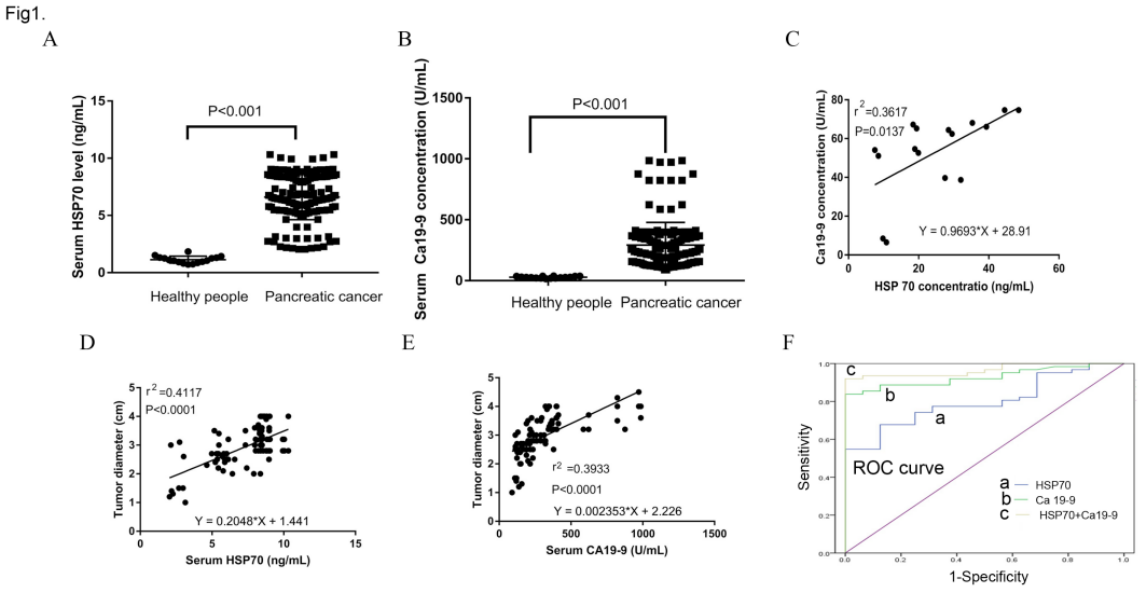

Figure 1: Relationship between serum HSP70, CA 19-9 and clinicopathological features of pancreatic cancer patients. (A) Serum HSP70 in pancreatic cancer patients and healthy people. (B) Serum CA19-9 in pancreatic cancer patients and the healthy people. (C) Correlation of serum HSP70 and CA19-9 in pancreatic cancer patients. (D) Correlation of serum HSP70 and diameter of tumor. (E) Correlation of Serum CA 19-9 and diameter of tumor. (F) ROC for serum level of HSP70 and CA19-9 for the diagnosis of patients with pancreatic cancer.

Characteristic		n	sHSP70 (ng/mL)	F/t	P	sCA199 (U/mL)	F/t	P
Sex	Male	92	6.52±2.00	-1.154	0.122	184.78±19.26	-1.139	2.256
	Female	76	6.67±1.87			187.28±21.48		
Age	<60	87	6.45±2.02	-8.989	0.370	186.37±19.98	-4.559	0.654
	≥60	81	6.72±1.85			186.69±20.74		
TNM stage	I	20	3.14±1.37	77.007	<0.001	124.74±19.96	32.237	<0.001
	II	24	5.69±0.80			167.66±38.25		
	III	70	6.37±1.18			233.37±53.93		
	IV	54	10.34±8.62			486.56±211.73		
Lymph node metastasis	N_0	94	5.28±1.53	107.084	<0.001	187.53±60.69	82.727	<0.001
	$N_{1/2}$	74	8.28±1.04			425.68±207.35		
Differentiation grade	High	44	4.55±1.67	121.876	<0.001	148.12±56.14	30.346	<0.001
	Medium	50	5.96±0.96			222.18±56.12		
	Low	74	8.28±1.03			425.68±207.38		

Table 1: Serum HSP70 and CA19-9 with TNM stage, lymph node metastasis and tumor grade

Parameters	Cut-off Value	AUC	95% CI	Youden index J	Sensitivity (%)	Specificity (%)
HSP70	1.92 ng/ml	0.799	0.699, 0.900	0.754	67.7	87.5
Ca 19-9	67.3U/ml	0.929	0.784,0.984	0.749	88.7	87.5
Combination	-	0.966	0.930,1.000	0.876	83.9	99.0

Table 2: Predictive value of HS70 and Ca 19-9 in the diagnosis of pancreatic cancer

Serum HSP70 and CA 199 expression trend in pancreatic cancer patients' pre-radiotherapy, during-radiotherapy, and post-radiotherapy

Before treatment, the HSP70 concentration profile in each group was: CR < PR < SD < PD. The HSP70 concentration trend in each group during treatment was: CR < PR < SD < PD. After treatment, the HSP70 concentration trend for each group was: CR < PR < SD < PD. The decrease percentage trend of serum HSP70 was: CR > PR > SD (Table 3). The intra-group comparison of CR group was: post-treatment < pre-treatment < during-treatment (Figure 2A). The intra-group comparison of HSP70 concentration of PR was: post-treatment < pre-treatment < during-treatment (Figure 2B). The intra-group comparison of HSP70 concentration in SD group was: post-treatment < pre-treatment < during-treatment (Figure 2C). The intra-group comparison of HSP70 concentration in PD group was: pre-treatment < post-treatment < during-treatment (Figure 2D). Before treatment, tumor diameter trend was: CR < PR <SD < PD group; after treatment tumor diameter trend was: CR < PR < SD < PD; decrease percentage of trend was: CR > PR > SD. Intra-group comparison of CR group was: post-treatment< pre-treatment; Intra-group comparison of PR group: post-treatment < pre-treatment; Intra-group comparison of SD group: post-treatment< pre-treatment. Intra-group comparison of disease progression group: post-treatment> pre-treatment (Table 4). Before treatment, the CA19-9 concentration profile in each group was: CR < PR < SD < PD. The CA19-9 concentration trend in each group during treatment was: CR < PR < SD < PD. After treatment, the CA19-9 concentration trend for each group was: CR < PR < SD < PD. The decrease percentage trend of serum CA19-9 was: CR > PR > SD (Table 5).

Groups	n	Pre-treatment	During-treatment	Post-treatment	Decrease percentage	Increase percentage
CR	13	2.53±0.40	5.48±0.74^{a}	1.91±0.32^{ab}	23.48±4.24	-
PR	104	5.73±0.89*	12.40±2.47^{*a}	3.49±0.77^{*ab}	38.45±7.17*	-
SD	24	6.67±1.01$^{*\#}$	15.33±2.36$^{*\#a}$	5.48±0.83$^{*\#ab}$	17.39±1.48$^{*\#}$	-
PD	27	8.64±0.81$^{*\#\Delta}$	20.74±6.03$^{*\#\Delta a}$	14.06±0.34$^{*\#\Delta ab}$	-	63.77±3.04

Table 3: Comparison of serum HSP70 expression levels in patients with pancreatic cancer before, during and after treatment. **CR**: Complete response, **PR**: partial response, **SD**: stable disease, **PD**: progressive disease, ***:** compared with CR group, P<0.05, #: compared with PR group, P<0.05, ∆: compared with SD group, P<0.05, ^{a}: compared with before treatment, P<0.05, ^{b}: compared with during-group comparison, P<0.05.

Fig.2

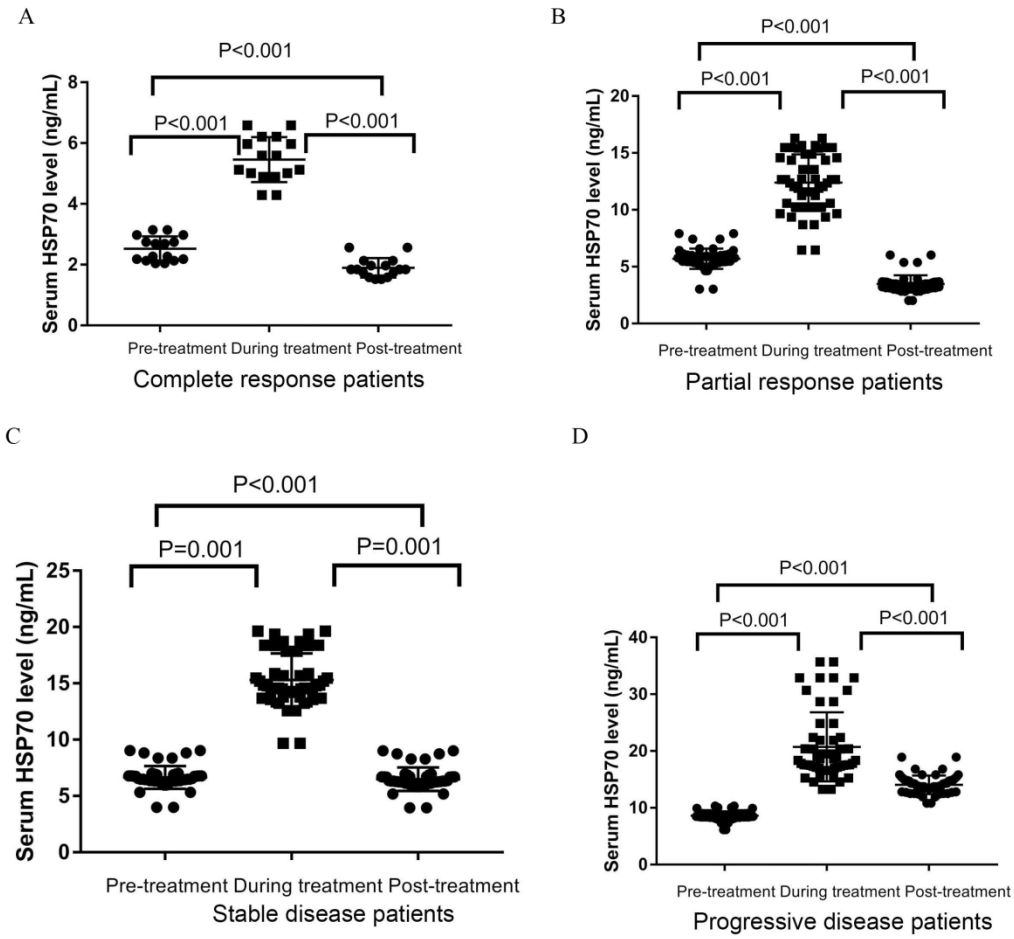

Figure 2: Serum HSP70 expression trend in pancreatic cancer patients' pre-radiotherapy, during-radiotherapy and post-radiotherapy. (A) Serum HSP70 expression trend in complete response patients. (B) Serum HSP70 expression trend in partial response patients. (C) Serum HSP70 expression trend in stable disease patients. (D) Serum HSP70 expression trend in progressive disease patients.

Groups	Pre-treament(cm)	Post-treatment(cm)	Decrease percentage (%)	Increase percentage (%)
CR	0.58 ± 0.08	0	100	-
PR	1.17 ± 0.16*	0.49 ± 0.08*	58.78 ± 47.87*	-
SD	2.18 ± 0.38$^{*\#}$	1.42 ± 0.28$^{*\#a}$	35.17 ± 7.48$^{*\#}$	-
PD	2.99 ± 0.22$^{*\#\Delta}$	3.76 ± 0.24$^{*\#\Delta a}$	-	25.86 ± 35.46

Table 4: Comparison of tumor diameter between patients before and after treatment. **CR**: Complete response, **PR**: partial response, **SD**: stable disease, **PD**: progressive disease, *****: compared with CR group, P<0.05, **#**: compared with PR group, P<0.05, **Δ**: compared with SD group, P<0.05, **[a]**: compared with before treatment, P<0.05.

Group	Pre-treament	During-treament	Post-treament	Decrease percentage	Increase percentage
CR	121.69 ± 20.19	223.36±40.38^{a}	49.36±13.27^{ab}	58.97±11.14	-
PR	169.54± 37.87*	319.08±75.67^{*a}	113.08±25.35^{*ab}	24.37±8.46*	-
SD	258.94±38.96$^{*\#}$	487.87±76.76$^{*\#a}$	207.17±30.68$^{*\#ab}$	16.06±0.57$^{*\#}$	-
PD	462.19±199.66$^{*\#\Delta}$	785.17±285.18$^{*\#\Delta a}$	695.08±297.11$^{*\#\Delta ab}$	-	52.86±38.21

Table 5: Comparison of CA19-9 expression levels in patients with pancreatic cancer before and after treatment (U/mL) **CR**: Complete response, **PR**: partial response, **SD**: stable disease, **PD**: progressive disease, *: compared with CR group, P<0.05, #: compared with PR group, P<0.05, Δ: compared with SD group, P<0.05, ^{a}: compared with before treatment, P<0.05, ^{b}: compared with during-group comparison, P<0.05.

Correlation of serum HSP70 and radiosensitivity of the patients with pancreatic cancer

The decrease percentage of HSP70 was correlated at the horizontal line with the decrease percentage of tumor diameter in patients with CR (Figure 3A). The decrease percentage of HSP70 was positively correlated with the decrease percentage of tumor diameter in patients with PR (Figure 3B). The decrease percentage of HSP70 was positively correlated with the decrease percentage of tumor diameter in patients with SD (Figure 3C). The increase percentage of HSP70 was positively correlated with the increase percentage of tumor diameter in patients with PD (Figure 3D). The ROC curve showed that the serum levels of HSP70 and CA19-9 were useful biomarkers for distinguishing radiosensitivity in patients with pancreatic cancer (Figure 3E). At the cutoff value of 23.6 ng/ml for HSP70, the area under the AUC of serum HSP70 for predicting radiotherapy sensitivity of pancreatic cancer patients was 0.604, with a 95% CI of 0.512 to 0.695, and Youden index J of 0.651. The sensitivity and specificity for predicting radiotherapy sensitivity were 52.9% and 95.7%, respectively. At the cutoff value of 162.8 ng/ml for CA 19-9, the AUC of serum CA 19-9 for predicting radiotherapy sensitivity of pancreatic cancer was 0.903, with a 95% CI of 0.853 to 0.953, and Youden index J of 0.645. The sensitivity and specificity for predicting radiotherapy sensitivity were 86.3% and 73.8%, respectively. AUC of the combination of serum HSP70 and serum CA 19-9 in predicting radiotherapy sensitivity of pancreatic cancer patients was 0.971, with a 95% CI of 0.948 to 0.955, and Youden index J of 0.824. The sensitivity and specificity for predicting radiotherapy sensitivity were 87.3% and 70.0%, respectively (Table 6).

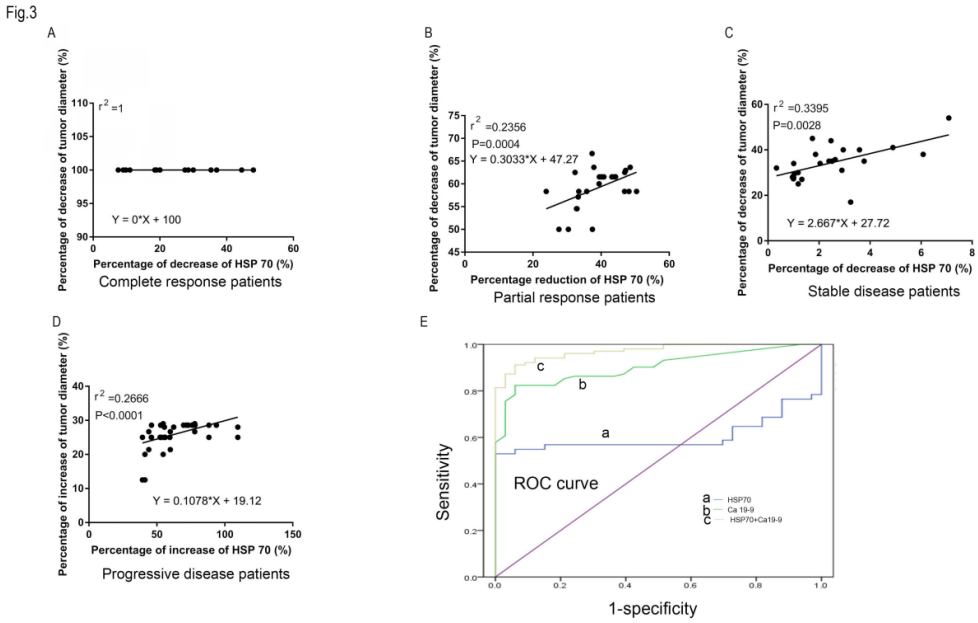

Figure 3: Correlation of serum HSP70 decrease percentage with the decrease percentage of tumor diameter in patients with pancreatic cancer

(A) Correlation of serum HSP70 decrease percentage with the decrease percentage of tumor diameter in complete response patients

(B) Correlation of serum HSP70 decrease percentage with the decrease percentage of tumor diameter in partial response patients

(C) Correlation of serum HSP70 decrease percentage with the decrease percentage of tumor diameter in stable disease patients

(D) Correlation of serum HSP70 decrease percentage with the decrease percentage of tumor diameter in progressive disease patients

(E) ROC of serum level of HSP70 and Ca19-9 for the radiosensitivity of patients with pancreatic cancer.

Parameters	Cut-off Value	AUC	95% CI	Youden index J	Sensitivity (%)	Specificity (%)
HSP70	23.6 ng/ml	0.604	0.512, 0.695	0.651	52.9	75.7
Ca 19-9	162.8 U/ml	0.903	0.853, 0.953	0.645	86.3	73.8
Combination	-	0.971	0.948, 0.955	0.824	87.4	80.0

Table 6: Predictive value of HS70 and Ca 19-9 in sensitivity to radiotherapy for pancreatic cancer

Discussion

Pancreatic cancer, a malignant tumor, is a fatal disease with difficult treatment choices and high mortality rates [9]. Surgical resection is the only choice for radical therapy. However, due to the early metastasis, only a small section of patients are suitable for surgical intervention [10]. Radiotherapy is an ideal treatment option for patients with locally advanced unresectable diseases. However, some patients are intrinsically resistant or have developed acquired resistance to radiotherapy. Early diagnosis and treatment of pancreatic cancer are significant hurdles in modern medicine. Thus, there is an urgent need to find new diagnostic, prognostic biomarkers and therapeutic targets [11]. However, studies assessing outcomes after radiation therapy have demonstrated conflicting results [12]. Therefore, it is vital to find specific markers for radiotherapy sensitivity. Moreover, early prediction of patients radiotherapy sensitivity is also important to develop a reasonable clinical treatment plan [13].

HSP70 is a molecular chaperone with many functions, including protein folding, transportation, repair, and degradation of damaged proteins [14]. HSP70 can inhibit non-specific protein aggregation and help protein obtain normal structure, besides anti-apoptotic properties, tumor cell proliferation, invasion, metastasis, and death [15].

CA 19-9 is classically considered a biomarker of pancreatic disease [16]. However, recent studies found that CA 19-9 is not simply a "bystander" but a promoter of pancreatitis and pancreatic cancer. In addition, CA 19-9 plays a crucial role in the pathophysiology of cancer, including (1) over-activation of epidermal growth factor receptor (EGFR) signals; (2) synergistic invasion with KrasG12D oncogene; (3) modification of stromal cell protein fibulin-3 increases its interaction with EGFR [17].

This present study found that serum HSP70 was positively correlated with tumor diameter, stage, and lymph node metastasis while negatively correlated with tumor grade. The concentration trends of HSP70 and CA 19-9 pre-treatment were: normal control group < CR group < PR group < SD group < PD group. The concentrations of HSP70 in the CR, PR, and SD groups decreased after radiotherapy, while the concentrations of HSP70 in the PD group increased after radiotherapy. The decrease percentage of HSP70 in the CR, PR, and SD groups was positively correlated with the decrease percentage of tumor diameter and CA 19-9, while the increase percentage of HSP70 in the PD group was positively correlated with the increase percentage of tumor diameter and CA 19-9. Additionally, this study showed that the changes in HSP70 and CA 19-9 levels were consistent before, during, and after radiotherapy with pancreatic cancer. Their expressions were positively correlated, indicating a synergistic effect between HSP70 and CA 19-9. Thus, both can be used as biomarkers to predict radiotherapy sensitivity of pancreatic carcinoma and can be used in combination to diagnose better sensitivity and specificity to the radiotherapy. The possible mechanism is as follows: (1) Under the action of carcinogens and radiotherapy, the PI3K-Akt signaling pathway and transcription factors such as NF-κB and AP-1 can be activated, which eventually promote the expression of HSP70 and CA 19-9 proteins [18-21], (2) HSP70 affects the formation and activity of protein complexes through EGFR signal transduction, resulting in cell cycle disorders, changing adhesion structure between epithelial cells, cell polarity, and cytoskeleton, etc., which promotes the expression of CA 19-9 on the cell surface [22].

In conclusion, serum HSP70 and CA 19-9 were positively correlated and closely related to the radiotherapy sensitivity of pancreatic cancer. Therefore, both can be used as biomarkers to predict the radiotherapy sensitivity of pancreatic carcinoma. Moreover, combined use of these biomarkers can result in better sensitivity and specificity of the disease diagnosis.

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