Int J Clin Exp Pathol 2015;8(1):682-691
www.ijcep.com /ISSN:1936-2625/IJCEP0003423

Original Article

Correlation and prognostic significance of MMP-2 and TFPI-2 differential expression in pancreatic carcinoma

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Received October 27, 2014; Accepted December 22, 2014; Epub January 1, 2015; Published January 15, 2015

Abstract: Aberrant expression of matrix metalloproteinase (MMP)-2 and tissue factor pathway inhibitor (TFPI)-2 not only correlate with tumorigenesis, but also with tumor invasion and metastasis. This study aims to investigate the correlation and prognostic significance of MMP-2 and TFPI-2 differential expression in pancreatic carcinoma. Immunohistochemistry was used to evaluate MMP-2 and TFPI-2 expression in tumor tissues and corresponding non-tumor tissues from 122 patients with pancreatic carcinoma. The results showed that the expression of MMP-2 was significantly ($P < 0.05$) higher in tumor tissues (78.7%) than in adjacent non-tumor tissues (27.9%), whereas the expression of TFPI-2 was significantly ($P < 0.001$) lower in tumor tissues (27.9%) than in adjacent non-tumor tissues (79.5%). Spearman's rank correlation test showed a negative correlation between MMP-2 and TFPI-2 expression ($r = -0.346$, $P < 0.001$). Kaplan-Meier survival analysis showed that high MMP-2 expression was significantly correlated with decreased disease-free survival (DFS) ($P < 0.001$) and overall survival (OS) ($P < 0.001$), while high TFPI-2 expression was significantly associated with increased DFS ($P < 0.001$) and OS ($P < 0.001$) of the patients. Multivariate analysis showed that high MMP-2 expression can act as an independent predictive factor for poor DFS ($P = 0.01$); and low TFPI-2 expression as an independent prognostic factor for poor DFS ($P < 0.001$) and OS ($P < 0.001$). In conclusion, our findings suggested that the differential expression of MMP-2 and TFPI-2 have a negative correlation in pancreatic carcinoma tissues; they may be considered as valuable biomarkers for prognosis of pancreatic carcinoma.

Keywords: Pancreatic carcinoma, MMP-2, TFPI-2, biomarkers, prognosis

Introduction

Pancreatic carcinoma is one of the most lethal solid tumors; which represents the 9th most frequent malignancy and the 4th leading cause of carcinoma death in the United States [1]. The patients with pancreatic carcinoma have a dismal prognosis; if not take any measures to treat patients with the disease, the median 5-year survival is only about 4% [2]. The unfavorable prognosis is primarily attributed to the tumor aggressive biological characteristics, nonspecificity of symptoms, advanced stage at the time of diagnosis and lack of effective therapy. The only means for long-term survival is currently offered by radical resection of localized tumor, either because of early diagnosis or after neoadjuvant multimodality treatment. Although there have been an improvement in the management of patients with pancreatic carcinoma, the 5-year survival only up to 25-35% after effective treatment [3]. Local invasion and distant metastasis are the important biologic characters of pancreatic carcinoma, occurring in early stage of the disease, causing the reduction of surgery chance and death of the patients. Tumor infiltration and metastasis is a complex mechanism involved in a variety of cellular multi-step processes, among which the proteolytic degradation of extracellular matrix (ECM) is an essential event [4]. The ECM is a crucial player in carcinoma infiltration and metastasis; which can prevent carcinoma cells into the adjacent tissues via interacting with tumor cells. Extensive studies have shown that matrix degradation can be enhanced by the imbalance between matrix metalloproteinases (MMPs) and their inhibitors, degrading

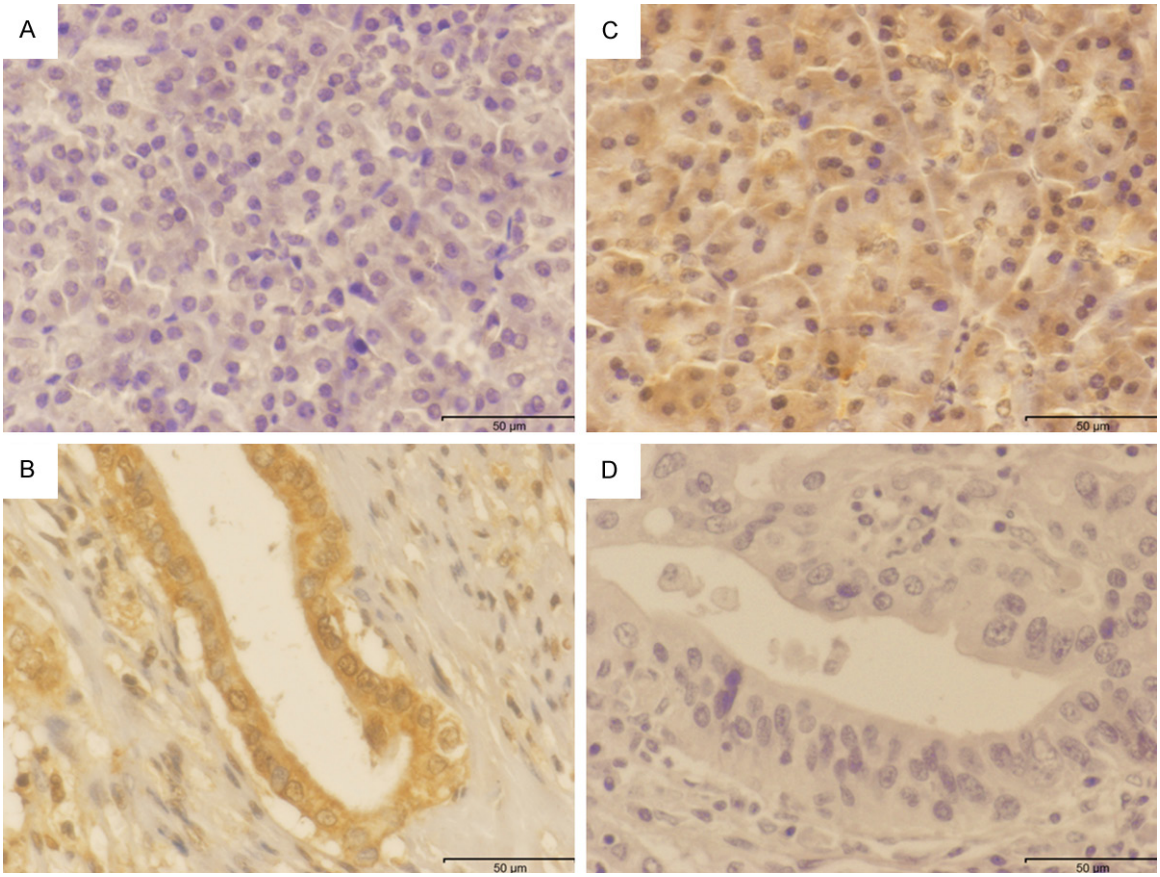

Figure 1. Immunohistochemical staining for MMP-2 and TFPI-2. The MMP-2 and TFPI-2 were principally localized in cytoplasm of cells. A: Showing the low expression of MMP-2 in para-carcinoma tissues. B: Showing the high expression of MMP-2 in pancreatic carcinoma tissues. C: Showing the high expression of TFPI-2 in para-carcinoma tissues. D: Showing the low expression of TFPI-2 in pancreatic carcinoma tissues. All images were taken at 400× magnification.

the ECM and promoting tumor invasion and metastasis [5-7].

Matrix metalloproteinase (MMP)-2 is a member of MMPs family which is zinc-dependent endopeptidases that degrade all components of ECM and vascular basal membrane. They play an important part in the development of numerous neoplastic diseases and connective tissue diseases [8]. MMPs are closely involved in tumor invasion and metastasis [9], and high expression of MMP-2 in pancreatic carcinoma has been previously elucidated [10]. Tissue factor pathway inhibitor (TFPI)-2, also known as placental protein-5, is a 32-kDa novel Kunitz-type serine proteinase inhibitor which is widely expressed in various normal human tissues and can direct against a variety of proteases including MMPs, plasmin, cathepsin G, trypsin, plasma kallikrein and chymotrypsin [11]. Based upon its potent and broad inhibitory actions on protease activities, TFPI-2 is considered as protect the ECM from degradation, thereby slowing or counteracting the infiltration and metastasis of tumor cells [12-15]. Previous studies have suggested that TFPI-2 is low expression in many malignant tumors, including pancreatic carcinoma [16-18]. Reduce expression of TFPI-2 may be closely related to its gene promoter methylation in pancreatic carcinoma [16].

It has been reported that there exists an opposite tendency in expression level of TFPI-2 and MMP-2. For instance, Izumi et al. [14] demonstrated that TFPI-2 is down-regulated in cells carrying an activated human ras oncogene, and restore TFPI-2 gene expression in cells resulted in decrease in the relative amount of MMP-2. Zhao et al. [19] showed that overexpressed TFPI-2 can strongly inhibit MMP-2 activity induced by oxidized low density lipoprotein (ox-LDL) in smooth muscle cell. Moreover, Gessler

Table 1. Differential expression of MMP-2 and TFPI-2 in pancreatic carcinoma tissues and corresponding para-carcinoma tissues (n = 122)

Tissues	MMP-2 expression			TFPI-2 expression		
	Low (%)	High (%)	*p*-value	Low (%)	High (%)	*p*-value
Carcinoma tissues	26 (21.3%)	96 (78.7%)	0.019	88 (72.1%)	34 (27.9%)	< 0.001
Para-carcinoma tissues	88 (72.1%)	34 (27.9%)		25 (20.5%)	97 (79.5%)	

MMP, matrix metalloproteinase; TFPI, tissue factor pathway inhibitor.

Table 2. Correlation between MMP-2 and TFPI-2 expression

Immunoreactivity	TFPI-2 expression			
	Low	High	*r*-value	*p*-value
MMP-2 expression				
Low	11	15	-0.346	< 0.001
High	77	19		

MMP, matrix metalloproteinase; TFPI, tissue factor pathway inhibitor.

al. [20] suggested that the anti-invasive properties of TFPI-2 is associated with inhibition of MMP-2, knockdown of TFPI-2 can promote migration and invasion of glioma cells. These all reveal that the MMP-2 and TFPI-2 may play opposite roles in tumor invasion and metastasis, according to their biological functions and their status in expression level in tumors. However, there is no study has been aimed to elucidate the association of MMP-2 and TFPI-2 expression, and their relationships with invasive, metastasis and prognosis in pancreatic carcinoma. In this study, we hypothesized that the MMP-2 and TFPI-2 expression not only negatively correlate, but also with aggressive features and survival in pancreatic carcinoma. Consequently, in order to confirm our assumptions, we detected the expression of MMP-2 and TFPI-2 in carcinoma tissues and para-carcinoma tissues from the 122 patients with pancreatic carcinoma by immunohistochemical staining, analyzed the correlation of MMP-2 and TFPI-2 expression status, and explored their relationships with clinicopathologic features and survival time of the patients.

Materials and methods

Patients and samples

This work was approved by the Human Scientific Ethics Committee of Anhui Medical University (Hefei, China), and written informed consent was obtained from all patients. Tissue samples including tumor tissues and adjacent non-tumorous tissues were obtained from a total of 122 patients who had undergone curative resection and were pathologically diagnosed with pancreatic carcinoma between 2008 and 2011 at the Affiliated Provincial Hospital of Anhui Medical University (Hefei, China). All patients had not accepted any anticarcinoma treatment in this study.

The clinicopathological parameters were collected from medical records, including age, gender, tumor diameter, tumor location, preoperative serum carbohydrate antigen 19-9 (CA19-9) concentrations, histological grade, perineural invasion, lymph node metastasis (LNM), distant metastasis and tumor-node-metastasis (TNM) stage. Sixty-five were male and fifty-seven were female, with a mean age of 56 ± 10 years. Tumors were histologically classified according to the WHO classification and TNM staging system was according to the seventh edition of Carcinoma Staging Manual of the American Joint Committee on Carcinoma (AJCC) [21]. The disease-free survival (DFS) and overall survival (OS) were investigated to evaluate MMP-2 and TFPI-2 influence on prognosis of patients with pancreatic carcinoma. Follow-up data were available for all patients with pancreatic carcinoma. Median follow-up was 16 months (range 5-28 months).

Immunohistochemical staining for MMP-2 and TFPI-2

Immunohistochemistry was performed using a two-step protocol according to the instructions of manufacturer. Sections (4-μm thick) obtained from pancreatic carcinoma tissues and their corresponding para-carcinomatous pancreatic tissues were dewaxed through xylene, rehydrated in a graded series of alcohol (100%, 95%, 75%, respectively), and washed with phosphate buffered saline (PBS). Antigen retrieval was implemented applying microwave heating method in 0.01 mol/L citrate buffer (pH 6.0) at

Table 3. Relationships between expression of MMP-2 and TFPI-2 and clinicopathological parameters

Parameters		NO. of cases	MMP-2 expression			TFPI-2 expression		
			Low	High	*p*-value	Low	High	*p*-value
Age (years)	< 60	57	12	45	0.948	45	12	0.116
	≥ 60	65	14	51		43	22	
Gender	Male	65	11	54	0.206	49	16	0.392
	Female	57	15	42		39	18	
Tumor diameter	< 20 mm	58	14	44	0.468	43	15	0.638
	≥ 20 mm	64	12	52		45	19	
Tumor location	Head	60	12	48	0.728	44	16	0.771
	Body/tail	62	14	48		44	18	
Serum CA19-9	≤ 37 U/ml	39	14	25	0.007	17	22	< 0.001
	> 37 U/ml	83	12	71		71	12	
Histological grade	Mod-poor	70	10	60	0.028	61	9	< 0.001
	Well	52	16	36		27	25	
Perineural invasion	Absent	38	22	16	< 0.001	17	21	< 0.001
	Present	84	4	80		71	13	
LNM	Absent	46	20	26	< 0.001	24	22	< 0.001
	Present	76	6	70		64	12	
Distant metastasis	Absent	45	23	22	< 0.001	25	20	0.002
	Present	77	3	74		63	14	
TNM stage	I-II	31	19	12	< 0.001	15	16	0.001
	III-IV	91	7	84		73	18	

MMP, matrix metalloproteinase; TFPI, tissue factor pathway inhibitor; CA19-9, carbohydrate antigen19-9; LNM, lymph node metastasis; TNM, tumor-node-metastasis.

80°C for 20 minutes. Then, endogenous peroxidase activity was quenched in 3% hydrogen peroxide. Subsequently, the sections were respectively incubated overnight with polyclonal rabbit anti-MMP-2 (Santa Cruz Biotechnology, Santa Cruz, CA, USA), anti-TFPI-2 (Beijing Biosynthesis Biotechnology, Beijing, China) antibody at 4°C. The sections were then incubated with biotinylated secondary mouse antibody for 30 minutes at 37°C. Immunostaining visualization was performed using 3,3-diaminobenzidine substrate. Finally, the sections were counterstained with hematoxylin followed by dehydration and mounting. In addition, for negative control groups, the primary antibodies were replaced with PBS at the same conditions.

The expressions of MMP-2 and TFPI-2 were semi-quantitatively evaluated according to percentage and intensity of staining cells [22]. The percentages of staining cells were divided into different scores, as follows: 0 for no staining; 1 point for < 10%; 2 points for 10-30%; 3 points for > 30% of staining cells. The intensity of staining was ranged as following: 0, absent; 1, weak; 2, moderate; 3, strong. The final total score was the product of the points for the percentage and intensity of staining. A final total score < 3 was considered to be low expression, and > 3 was defined as high expression. All sections were analyzed independently by two experienced pathologists who without knowing results of each other. A consensus was reached by joint views for all differences.

Statistical analysis

All statistical analyses were performed with the SPSS 17.0 software (SPSS, Inc., Chicago, IL, USA). Statistically significant differences among groups were evaluated using the X^2 test, based on the final total scores in the staining status. Correlation between MMP-2 and TFPI-2 expression was analyzed applying the X^2 test and Spearman's correlation test. Relationships between expression of MMP-2 and TFPI-2 and clinicopathological data were assessed using Fisher's exact test or X^2 test. Survival curves were plotted employing the Kaplan-Meier method, and the differences in survival period were compared applying log-rank test. Multivariate survival analysis was implemented by Cox proportional hazards regression model to ascertain the independent prognostic factors that were significant in univariate analysis. All tests were two-sided and $P < 0.05$ was considered statistically significant.

Results

Expression of MMP-2 and TFPI-2 in pancreatic carcinoma tissues and para-carcinoma tissues

Immunohistochemistry showed that MMP-2 and TFPI-2 were mainly located in the cyto-

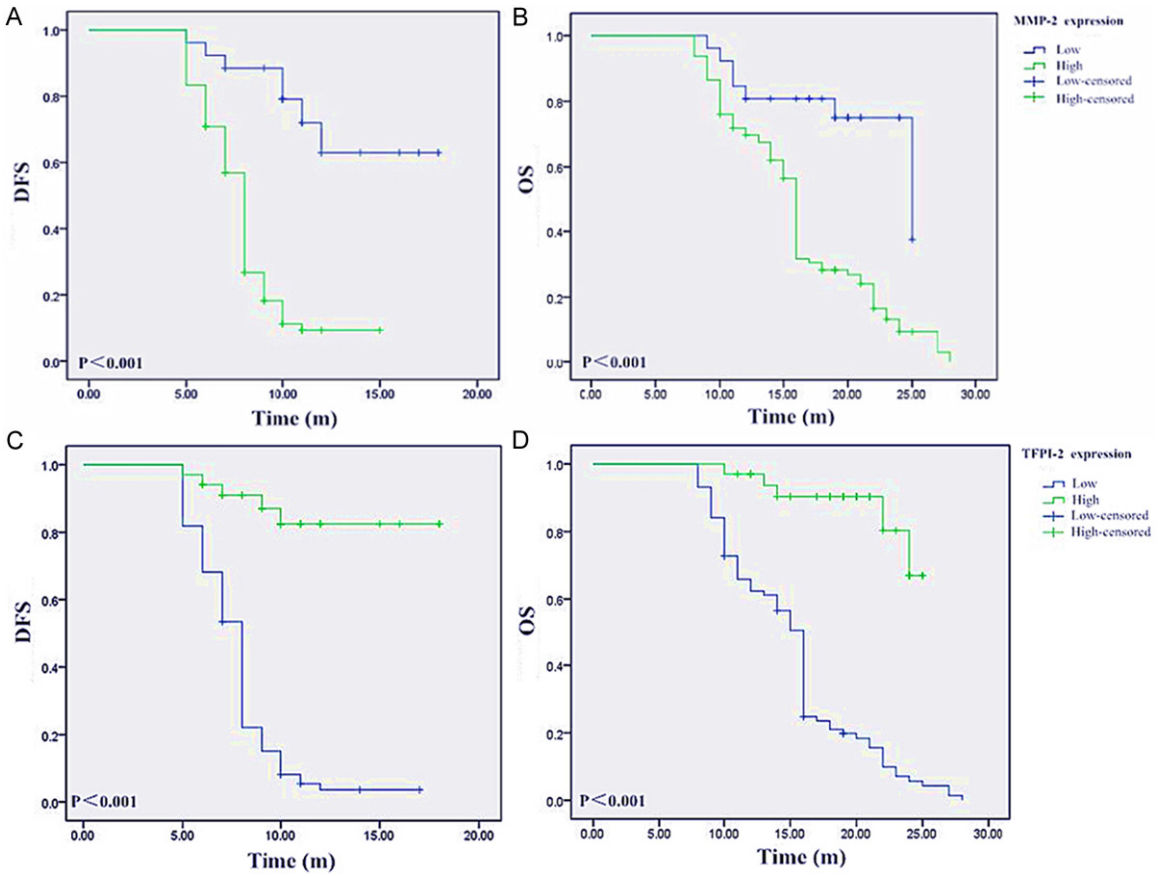

Figure 2. Kaplan-Meier analysis show that high expression level of MMP-2 (A, B) was significantly associated with worse disease-free survival (DFS) and overall survival (OS) of patients with pancreatic carcinoma, while high expression level of TFPI-2 (C, D) was significantly correlated with better DFS and OS (n = 122; $P < 0.001$; log rank test).

plasm of cells. The representative photomicrographs were shown in **Figure 1**. As predicted, the results showed that the expression of MMP-2 was significantly increased in pancreatic carcinoma tissues relative to para-carcinoma tissues ($P < 0.05$; **Table 1**). On the contrary, the expression level of TFPI-2 was significantly decreased in carcinoma tissues compared to para-carcinoma tissues ($P < 0.001$; **Table 1**). Moreover, Spearman's rank correlation test further revealed that the expression of MMP-2 was significantly and negatively correlated with the expression of TFPI-2 in pancreatic carcinoma tissues ($r = -0.346$, $P < 0.001$; **Table 2**).

Relationships between expression of MMP-2 and TFPI-2 and clinicopathological data in pancreatic carcinoma

The expression of MMP-2 was significantly higher in pancreatic carcinomas with higher preoperative serum CA19-9 ($P = 0.007$) levels, poor histological grade ($P = 0.028$), perineural invasion ($P < 0.001$), LNM ($P < 0.001$), distant metastasis ($P < 0.001$), advanced stage ($P < 0.001$). In addition, the expression of TFPI-2 showed a lower level in pancreatic carcinomas with higher preoperative serum CA19-9 ($P < 0.001$) levels, poor histological grade ($P < 0.001$), perineural invasion ($P < 0.001$), LNM ($P < 0.001$), distant metastasis ($P = 0.002$), advanced stage ($P = 0.001$) than in those without. However, the results indicated that there was no significant association between the expressions of MMP-2 and TFPI-2 and the other clinicopathological parameters, including age, gender, tumor diameter, tumor location ($P > 0.05$). The results were shown as followed in **Table 3**.

Survival analysis

Kaplan-Meier analysis showed that high MMP-2 expression (median DFS 8.0 months, median

Table 4. Univariate analysis of factors associated with OS and DFS

Variables		OS		DFS	
		Median survival time	*p*-value	Median survival time	*p*-value
MMP-2 expression	Low	25	< 0.001	10	< 0.001
	High	16		8	
TFPI-2 expression	Low	16	< 0.001	8	< 0.001
	High	19		9.5	
Age (years)	< 60	16	0.126	8	0.872
	≥ 60	16		8	
Gender	Male	16	0.534	8	0.425
	Female	16		8	
Tumor diameter	< 20 mm	16	0.601	8	0.781
	≥ 20 mm	16		8	
Tumor location	Head	16	0.317	8	0.301
	Body/tail	16		8	
Serum CA19-9	≤ 37 U/ml	22	0.005	10	0.018
	> 37 U/ml	16		8	
Histological grade	Mod-poor	14	< 0.001	7	< 0.001
	Well	22		8	
Perineural invasion	Absent	25	< 0.001	12	< 0.001
	Present	16		8	
LNM	Absent	25	0.001	11	< 0.001
	Present	16		8	
Distant metastasis	Absent	23	< 0.001	11	< 0.001
	Present	16		8	
TNM stage	I-II	23	< 0.001	10	< 0.001
	III-IV	16		8	

MMP, matrix metalloproteinase; TFPI, tissue factor pathway inhibitor; CA19-9, carbohydrate antigen19-9; LNM, lymph node metastasis; TNM, tumor-node-metastasis; OS, overall survival; DFS, disease-free survival.

OS 16.0 months) had a significantly ($P < 0.001$ for DFS and OS; **Figure 2A**, **2B**) shorter survival time compared with low MMP-2 expression (median DFS 10.0 months, median OS 25.0 months) in patients with pancreatic carcinoma. Conversely, the survival time of high TFPI-2 expression was significantly ($P < 0.001$ for DFS and OS; **Figure 2C**, **2D**) longer than low TFPI-2 expression in patients with pancreatic carcinoma. Median DFS was 9.5 months for high TFPI-2 expression, and 8.0 months for low TFPI-2 expression; median OS was 19.0 months for high TFPI-2 expression, and 16.0 months for low TFPI-2 expression.

Univariate analysis indicated that differential expression of MMP-2 and TFPI-2, serum CA19-9, histological grade, perineural invasion, LNM, distant metastasis, and TNM stage had significant effects on prognosis (**Table 4**). Multivariate analysis (**Table 5**) further revealed that the high MMP-2 expression was an independent prognostic biomarker for poor DFS [hazard ratio (HR) = 3.392; 95% CI 1.339-8.590; $P = 0.010$]. In particular, the low TFPI-2 expression served as an independent predictor for poor DFS (HR = 0.103; 95% CI 0.040-0.262; $P < 0.001$) and OS (HR = 0.161; 95% CI 0.064-0.406; $P < 0.001$). Additionally, histological grade, distant metastasis, and TNM stage were also independent predictive factors for DFS or OS (**Table 5**).

Discussion

Searching specific tumor markers apply to predict prognosis of patients with pancreatic carcinoma could make a significant and valuable contribution to management in the clinic. In the present study, we investigated the expression level of MMP-2 and TFPI-2, analyzed the correlation of MMP-2 and TFPI-2 expression status, and explored their relationships with clinicopathologic features and prognosis of the patients with pancreatic carcinoma. We found that the expression level of MMP-2 was higher in pancreatic carcinoma tissues than that in para-carcinoma tissues by immunohistochemical staining; which validated the previous results that the MMP-2 expression was significantly increased in pancreatic carcinoma tissues [10]. Besides, we also revealed that the expression level of TFPI-2 was significantly decreased in pancreatic carcinoma tissues relative to para-carcinoma tissues; the findings were consistent with previous results that the TFPI-2 expression was significantly down-regulated in pancreatic carcinoma tissues [16-18]. Interestingly, the results suggested that the level of MMP-2 expression had a significantly negative correlation with TFPI-2 expression in pancreatic carcinoma tissues, indicating the

Table 5. Multivariate analysis of factors associated with OS and DFS

Variables	OS			DFS		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
MMP-2 expression (low vs. high)	1.337	0.532-3.362	0.537	3.392	1.339-8.590	0.010
TFPI-2 expression (low vs. high)	0.161	0.064-0.406	< 0.001	0.103	0.040-0.262	< 0.001
Histological grade (mod-poor vs. well)	0.355	0.215-0.586	< 0.001	0.672	0.421-1.072	0.095
Distant metastasis (absent vs. present)	1.065	0.569-1.993	0.843	1.87	1.053-3.320	0.033
TNM stage (I-II vs. III-IV)	3.629	1.881-7.000	< 0.001	1.64	0.781-3.444	0.191

MMP, matrix metalloproteinase; TFPI, tissue factor pathway inhibitor; TNM, tumor-node-metastasis; OS, overall survival; DFS, disease-free survival.

MMP-2 is closely related to the TFPI-2 in the progression of pancreatic carcinoma. Therefore, our results combine with previous findings [14, 19, 20] revealed that they may have contrary effects on invasion and metastasis of pancreatic carcinoma.

There is increasing evidence to indicate that MMP-2 has a critical role in tumor invasion and metastasis [23-25]. Möniget et al. [23] suggested that MMP-2 expression is strongly correlated with LNM and progression, may be useful as a predictor of tumor progression in gastric carcinoma. Similarly, Zheng et al. [24] showed that MMP-2, MMP-9 and VEGF contribute largely to the angiogenesis and progression of gastric cancer. Besides, Ghosh et al. [25] reported that with the development of cervical cancer, MMP-2 has a gradual increase in expression level. TFPI-2 is considered to be an important protector which counteracting the invasion and metastasis of malignancies [12-15]. A number of studies have demonstrated that the low TFPI-2 expression is significantly associated with tumor progression [26-28]. For example, Zhu et al. [26] revealed that down-regulated TFPI-2 can contribute to invasion of hepatocellular carcinoma via alteration in the expression of metastasis-associated genes. Wang et al. [27] demonstrated that the low expression of TFPI-2 may be correlated with tumor invasion and metastasis in gastric stromal tumors. Lai et al. [28] suggested that TFPI-2 is a tumor suppressor; the down-regulation of TFPI-2 is a vital event in metastasis of oral squamous cell carcinoma. In addition, the role of TFPI-2 in the invasion and metastasis of pancreatic carcinoma has also been shown [17, 18]. Expectedly, consistent with previous reports, our data showed that high MMP-2 expression and low TFPI-2 expression were significantly associated with aggressive clinical and pathological features such as higher preoperative serum CA19-9 levels, poor histological grade, perineural invasion, LNM, distant metastasis, advanced stage. These findings indicated that the abnormal expression of MMP-2 and TFPI-2 played vital roles in the tumorigenesis, invasion and metastasis of pancreatic carcinoma, and thereby lead to significant unfavorable prognosis.

Some reports have shown that the prognostic significance of MMP-2 expression in several types of tumors [29-35]. For instance, Sier et al. [29] suggested that high carcinomatous MMP-2 value is of prognostic significance for a poor OS of patients with gastric cancer. Likewise, Davidson et al. [30, 31] revealed that MMP-2 has a pivotal role in extracellular matrix invasion and is correlated with poor survival in cervical carcinoma. Vasala et al. [32] demonstrated that MMP-2 protein overexpression is significantly associated with a reduced survival rate and may be as an independent prognostic marker for bladder cancer progression. Wu et al. [33] showed that MMP-2 expression has significant correlation with tumor differentiation, invasion and LNM, and may be an important biological property and significant prognostic maker of gastric carcinoma. Dragutinović et al. [34] reported that overexpression of MMP-2 is significant correlated with tumor progression and might be useful to predict tumor recurrence in patients with colorectal adenocarcinoma. Besides, Aparna et al. [35] showed that a higher MMP-2 expression is associated with local recurrence, distant metastasis and shorter survival, may serve as an indicator of poor prognosis in the early stages of tongue squamous cell carcinoma. With respect to the significance of TFPI-2 expression for prognosis, Wu et al. [36] suggested that hypermethylation of TFPI-2 gene is an independent marker for a poor prognosis in patients with non-small cell

lung cancer. Vaitkienė et al. [37] demonstrated that the epigenetic inactivation of TFPI-2 via promoter methylation is a frequently tumor-specific event, and TFPI-2 promoter hypermethylation might be identified as a prognostic factor in glioblastoma. Xu et al. [38] revealed that negative or low expression of TFPI-2 is associated with cancer progression, cancer recurrence and poor outcome in breast cancer patients after surgery. Additionally, low TFPI-2 expression is also determined to be an important and independent prognostic factor for unfavorable prognosis in pancreatic carcinoma patients [17]. Our results were consistent with previous studies. The present study suggested that the aberrant expression of MMP-2 and TFPI-2 were significantly correlated with prognosis of postoperative patients with pancreatic carcinoma. Univariate analysis showed that high MMP-2 expression had a reduced survival time including OS and DFS, compare with low MMP-2; high TFPI-2 expression had a relative increased survival time compare to low TFPI-2. What is more, multivariate survival analysis revealed that high MMP-2 expression was an independent prognostic factor for poor DFS; especially low TFPI-2 expression as an independent predictive factor for poor DFS and OS. High MMP-2 expression and low TFPI-2 expression had adverse effects on prognosis, which indirectly shows their genes may play opposite roles in the progression of pancreatic carcinoma.

In conclusion, our findings suggested that the differential expression of MMP-2 and TFPI-2 have a negative correlation in pancreatic carcinoma tissues, may play opposite roles in the progression of pancreatic carcinoma. The abnormal expression of MMP-2 and TFPI-2 are significantly associated with prognosis of patients with pancreatic carcinoma. Furthermore, high MMP-2 and low TFPI-2 expression serve as independent prognostic factors for poor prognosis in patients with pancreatic carcinoma after surgical operation. Thus, the differential expression of MMP-2 and TFPI-2 may have an important clinical reference value in assessing the severity and prognosis of pancreatic carcinoma. These data contribute to provide a strategy for the treatment of pancreatic carcinoma and thereby further improve the prognosis of patients with pancreatic carcinoma. Currently, there is only few data are available about the prognostic effect of MMP-2 and TFPI-2 expression in postoperative patients with pancreatic carcinoma. More studies with large population-based cohort and long-term follow-up are thus needed to support our findings.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (No. 81272740).

Disclosure of conflict of interest

None.

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