

Basic Study

Increased tensin 4 expression is related to the histological type of gastric cancer

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Abstract

BACKGROUND

Gastric cancer (GC) is one of the most common malignant tumors worldwide. Tensin 4 (TNS4) is an adhesive protein belonging to the tensin family. This protein is located in focal adhesion sites. The *TNS4* gene is considered an oncogene in numerous cancers. This protein plays an important role in adhesion, migration and proliferation of cells.

AIM

To evaluate expression of TNS4 protein in GC tissues and analysis of the clinical and histopathological parameters as well as the overall survival rate of patients.

METHODS

The expression of TNS4 was assessed in 89 patients using immunohistochemistry.

RESULTS

Positive expression of TNS4 was observed in 49 of 89 patients (55.06%). Higher TNS4 expression was more common in GC tumors with a diameter ≥ 5 cm ($P = 0.040$). We demonstrated that an increase in TNS4 expression was more frequent in tumors of the histological type without mucinous components than in tumors from mucosal cancers ($P = 0.023$). Furthermore, TNS4 expression was higher in moderately differentiated tumors than in poorly differentiated and non-differentiated tumors ($P = 0.002$). Increased TNS4 expression was also noted in the intestinal type of GC according to Lauren's classification ($P = 0.020$). No statistically significant correlation was found between the expression of TNS4 and the

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overall survival rate of patients.

CONCLUSION

TNS4 expression was significantly higher in tumors with a diameter ≥ 5 cm of the moderately differentiated intestinal type (according to Lauren's classification) of GC without a mucinous component. Therefore, increased TNS4 expression is related to the histological type of GC with a better prognosis.

Key Words: Gastric cancer; Tensin 4; Adhesion proteins; Immunohistochemistry

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Core Tip: Tensin 4 (TNS4) is an adhesive protein belonging to the tensin family that plays an important role in cell adhesion, migration, and proliferation. These processes are important in cancer development and may limit cancer cell growth and improve patient survival. By applying immunohistochemistry, we investigated TNS4 expression in gastric cancer (GC) tissues and discovered that TNS4 expression was significantly higher in tumors with a diameter greater than 5 cm, in tumors of the moderately differentiated intestinal type (according to Lauren's classification) and in GC without a mucinous component. We concluded that enhanced TNS4 expression was associated with the histological type of GC with a better prognosis.

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INTRODUCTION

In 2018, more than one million people were diagnosed with gastric cancer (GC), accounting for 5.7% of all malignant cancers worldwide; this cancer is ranked 5th in terms of incidence. Moreover, 8.2% of patients with GC died, which reveals the aggressive nature of this disease. GC was diagnosed twice as often in men than in women[1]. The development of this cancer is a multistage process, and there are numerous environmental and genetic factors that contribute to its progression, including infection with *Helicobacter pylori* (*H. pylori*) bacteria and Epstein-Barr virus, consumption of excess salt and alcohol or smoking[2]. An alarming phenomenon is the incidence of this type of cancer in young people under 40 years of age, most often as a result of a genetic predisposition. A previous report showed that 30% of patients under 30 had GC in their family history[3]. The diagnosis of this cancer at early stages of its progression is of key importance. Preoperative chemotherapy followed by surgical removal of the tumor mass in early cancer results in a 90% 5-year survival rate [4]. Therefore, it is crucial to search for molecular and biochemical changes typical of early stages of cancer development to inhibit tumor progression and increase the survival rate of patients with this type of cancer.

Tensin 4 (TNS4), also known as C-terminal tensin-like protein, belongs to the tensin family, which also includes tensins 1-3. The *TNS4* gene is located on the long arm of chromosome 17q12-21. The TNS4 protein has a molecular weight of 77 kDa. In terms of structure, TNS4 is composed of the Src homology 2 domain (SH2) and the phosphotyrosine-binding domain (PTB). The SH2 domain allows the TNS4 protein to participate in the transmission of intracellular signals, while the PTB domain binds to membrane integrator receptors. Unlike tensins 1-3, TNS4 does not have an actin-binding domain[5]. Intracellularly, TNS4 is located in focal adhesion sites, where it enables signaling between the extracellular matrix and the cell interior. From a physiological perspective, the expression of TNS4 has been detected in the prostate and placenta[6]. Pathologically increased TNS4 expression appears in cancerous tumors. *TNS4* was originally classified as a suppressor gene in prostate cancer[6], but as research on tensins progressed, its role as an oncogene was demonstrated in

colorectal, breast, colon, esophagus, and lung cancers and thymoma, where this protein was overexpressed[7-15]. TNS4 plays an important role in biological processes connected with carcinogenesis, such as proliferation, migration, cell adhesion and invasiveness[16].

The aim of our study was to evaluate the IHC expression of TNS4 protein in GC (stages I-IV) as well as to assess the relationship between protein expression and selected clinical and pathological parameters and the overall survival rate of patients.

MATERIALS AND METHODS

Study group

The study was conducted on a group of 89 patients diagnosed with GC who were treated surgically in the 2nd Clinical Department of General and Gastroenterological Surgery of the Medical University of Białystok in the years 2005–2015. The tissue material was obtained from the archives of the Academic Center for Pathomorphological and Genetic-Molecular Diagnostics in Białystok. The inclusion criterion was diagnosed adenocarcinoma at any stage of its progression; the exclusion criteria were diagnosed squamous cell carcinoma and other non-epithelial cancers, metastases of other cancers to the stomach and the lack of complete medical records. The normal mucous membrane was used as the control tissue. The research was approved by the Bioethics Committee of the Medical University of Białystok, permission No. R-I-002/29/2019. The study was conducted in accordance with the World Medical Association Declaration of Helsinki for ethical principles for medical research involving human subjects. The characteristics of the study group are presented in Table 1.

Tissue preparations

Tissues collected during the operation were fixed in 4% buffered formalin and embedded in paraffin. Paraffin blocks were then cut on a microtome into approximately 4-μm-thick sections and stained with hematoxylin and eosin. A routine histopathological examination included the assessment of the histological type of cancer, malignancy grade (G), anatomoclinical stage (pT) and presence of lymph node metastases (pN), infiltration of blood and lymphatic vessels, perineural infiltration, peritumoral inflammation and degree of desmoplasia. Moreover, *H. pylori* infection was assessed by Giemsa staining. The following information was selected from the records with histopathological diagnosis: age and sex of patients, diameter and location of the tumor, presence of distant metastases and the type of cancer according to Lauren's classification.

Immunohistochemistry

Immunohistochemical (IHC) staining was performed on 89 GC tissues. Paraffin blocks were cut on a microtome into approximately 4-μm-thick sections and mounted onto silanized slides. The microscopic sections were incubated overnight at 60 °C and then deparaffinized in xylene solutions and hydrated in a series of alcohol solutions of decreasing concentration (2 × 99.9%, 96%, 70%). The next step was blocking endogenous peroxidase activity by using 3% hydrogen peroxide solution (10 min) as well as nonspecific antibody binding by means of horse serum (anti-mouse/rabbit serum produced in horse, Vector Laboratories, Germany) (20 min). In the following step, the sections were incubated with polyclonal anti-TNS4 antibody at a dilution of 1:75 (Biorbyt, orb186458 produced in rabbit) for 30 min at room temperature. The antibody binding sites were visualized with an ImmPress Universal Antibody Polymer Reagent kit (Vector Laboratories, Germany) and ImmPACT DAB chromogen (Vector Laboratories, Germany). Cell nuclei were stained with hematoxylin. The preparations were then dehydrated in a series of alcohol solutions of increasing concentration and overexposed in xylene solutions.

Validation of TNS4 expression detection

We particularly focused on obtaining reliable results of TNS4 IHC staining. To optimize the TNS4 staining procedure, we used positive and negative controls, and selected primary antibody dilutions (1:50, 1:75, 1:100, 1:200) and incubation times (30 min, 60 min, 120 min) were tested. For the control, antigen retrieval was also performed in buffers with pH = 6.0 and pH = 9.0.

Table 1 The characteristics of study group

Parameter	Number of cases
Age	
< 60	29 (32.58%)
≥ 60	60 (67.42%)
Gender	
Female	29 (32.58%)
Male	60 (67.42%)
Tumor diameter	
< 5 cm	18 (20.22%)
≥ 5 cm	71 (79.78%)
Tumor localization	
Upper 1/3	17 (19.10%)
Middle 1/3	33 (37.08%)
Lower 1/3	16 (17.98%)
Whole stomach	23 (25.84%)
Histological type	
Adenocarcinoma	54 (60.67%)
Adenocarcinoma mucinosum	35 (39.33%)
Histological differentiation	
Moderately differentiated	25 (28.09%)
Poorly differentiated	35 (39.33%)
Non differentiated	29 (32.58%)
Depth of invasion	
T1	6 (6.74%)
T2	7 (7.87%)
T3	66 (74.16%)
T4	10 (11.23%)
Lymph node metastasis	
Absent	17 (19.10%)
Present	72 (80.90%)
Distant metastasis	
Absent	61 (68.54%)
Present	28 (31.46%)
Blood vessel infiltration	
Absent	48 (84.21%)
Present	9 (15.79%)
Lymphatic vessel infiltration	
Absent	21 (31.82%)
Present	45 (68.18%)
Perineural infiltration	
Absent	28 (34.15%)
Present	54 (65.85%)

Peritumoral inflammation	
Absent	42 (50.00%)
Present	42 (50.00%)
Desmoplasia	
Small	55 (66.27%)
Large	28 (33.73%)
<i>Helicobacter pylori</i> infection	
Absent	61 (73.49%)
Present	22 (26.51%)
Lauren's classification	
Intestinal	44 (55.00%)
Diffuse	36 (45.00%)

Microscopic evaluation

The preparations were examined under an Olympus BX41 light microscope by two independent pathomorphologists. TNS4 protein expression was evaluated under 400× magnification in 10 representative fields of view. In each field of view, 100 or more cancer cells were assessed. Protein expression was observed in both the cell membrane and the cytoplasm. The presence of TNS4 protein in $\geq 20\%$ of neoplastic cells was considered positive expression.

Statistical analysis

The comparison of TNS4 expression with the selected clinicopathological parameters was carried out by the Mann-Whitney U test for two groups and the Kruskal-Wallis test for 3 or more groups. Dunn's multiple comparison post hoc tests were conducted for the Kruskal-Wallis test. A value of $P < 0.05$ was considered statistically significant. The overall survival analysis was based on the Kaplan-Meier test. The program Statistica 13 (Statsoft, Krakow, Poland) was used for the analysis. Missing data were removed in pairs.

RESULTS

TNS4 expression in GC samples

TNS4 protein expression was tested immunohistochemically in 89 GC samples and 20 normal stomach tissues. Statistical analysis demonstrated that positive TNS4 expression in cancer cells occurred in 49 of 89 patients (55%). In neoplastic cells, the expression of TNS4 was observed in the cell membrane and cytoplasm (Figure 1)

Analysis of the correlation of TNS4 expression with clinical and pathological parameters of GC

The statistical analysis did not show any significant relationships between TNS4 protein expression and the age and sex of patients, tumor location, anatomoclinical stage-pT, presence of lymph node and distant metastases, blood and lymphatic vessel infiltration, perineural infiltration, peritumoral inflammation, desmoplasia or *H. pylori* infection. However, a significant correlation was found between TNS4 expression and tumor diameter. Tumors with a diameter of < 5 cm were present in 20.22% of the patients, while tumors with a diameter of ≥ 5 cm were found in 79.78% of the patients. Positive expression of the TNS4 protein was more frequent in gastric tumors with a diameter of ≥ 5 cm (60.56% of the patients with positive expression) than in tumors < 5 cm in diameter (33.33% of the patients) ($P = 0.040$) (Figure 2A). Furthermore, a significant correlation with the histological type of tumor was demonstrated. Cancers without mucinous components were diagnosed in 60.67% of the patients, and mucosal tumors were diagnosed in 39.33% of the patients. A positive reaction to the TNS4 protein was considerably more frequent in the histological type without a mucinous component (64.81% of patients) than in mucinous adenocarcinomas (40.00% of patients) ($P = 0.023$) (Figure 2B). Statistical analysis also showed a significant

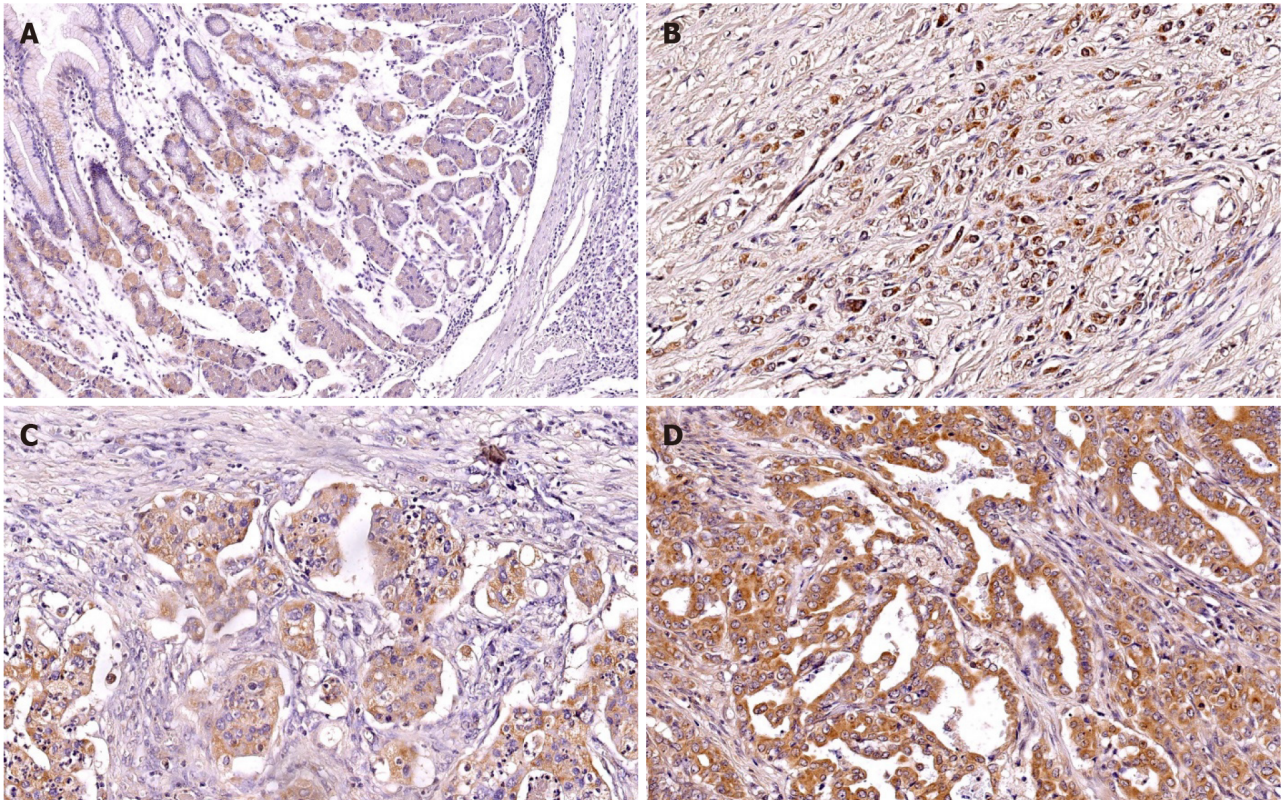


Figure 1 Tensin 4 expression in normal gastric mucosa. A: 100× magnification and gastric cancer samples; B and C: Poorly differentiated gastric cancer (GC); D: Moderately differentiated GC (magnification 200×).

correlation with the malignancy grade. In the study group, there were 28.09% moderately differentiated, 39.32% poorly differentiated and 32.59% non-differentiated tumors. The TNS4 protein occurred much more frequently in moderately differentiated cancers (80.00% of the patients) than in poorly differentiated (57.14%) and non-differentiated (31.03%) tumors ($P = 0.002$) (Figure 2C). It was also proven that TNS4 protein expression correlates with the type of tumor according to Lauren's classification. The intestinal type was present in 55% of the patients, while 45% of the patients suffered from the diffuse type of GC. The presence of TNS4 was more frequently observed in intestinal-type tumors (70.45%) than in diffuse-type tumors (44.44%) ($P = 0.020$) (Figure 2D).

Table 2 presents a summary of the correlation between clinicopathological parameters and TNS4 protein expression found in our study.

Analysis of the correlation of TNS4 protein expression with the overall survival rate

Statistical analysis did not reveal a significant correlation between TNS4 protein expression and overall patient survival ($P = 0.25$) (Figure 3).

DISCUSSION

In our study, we performed an IHC assessment of the expression of the TNS4 protein in GC patients diagnosed with stage I to IV disease. We observed that TNS4 expression was higher in tumor cells than in normal tissue, which is consistent with the results presented by Qi *et al*[17]. Sawazaki *et al*[18] evaluated the clinical significance of *TNS4* mRNA expression in GC and demonstrated that its expression is significantly higher in tumor tissue, as confirmed by Sakashita *et al*[19]. Based on these observations, it can be concluded that changes in the expression of the *TNS4* gene occur in tumor cells compared to normal gastric mucosa cells. This change is reflected in increased expression of TNS4 protein in GC.

In our research, we demonstrated that positive expression of TNS4 protein occurs twice as often in GC tumors with a diameter of ≥ 5 cm than in tumors with a diameter smaller than 5 cm. Similar observations were reported by other authors who noted that TNS4 protein expression increases with the size of breast tumors and hepatocellular

Table 2 Correlation between clinical pathological parameters and tensin 4 protein expression

Parameter	Expression of tensin 4 protein		P value
	Negative	Positive	
Age			0.666
< 60	14 (48.28%)	15 (51.72%)	
≥ 60	26 (43.33%)	34 (56.67%)	
Gender			0.182
Female	16 (55.17%)	13 (44.83%)	
Male	24 (40.00%)	36 (60.00%)	
Tumor diameter			0.040
< 5 cm	12 (66.67%)	6 (33.33%)	
≥ 5 cm	28 (39.44%)	43 (60.56%)	
Tumor localization			0.081
Upper 1/3	10 (58.82%)	7 (41.18%)	
Middle 1/3	9 (27.27%)	24 (72.73%)	
Lower 1/3	9 (56.25%)	7 (43.75%)	
Whole stomach	12 (52.17%)	11 (47.83%)	
Histological type			0.023
Adenocarcinoma	19 (35.19%)	35 (64.81%)	
Adenocarcinoma mucinosum	21 (60.00%)	14 (40.00%)	
Histological differentiation			0.002 (< 0.001)
Moderately differentiated	5 (20.00%)	20 (80.00%)	
Poorly differentiated	15 (42.86%)	20 (57.14%)	
Non differentiated	20 (68.97%)	9 (31.03%)	
Depth of invasion			0.208
T1	5 (83.33%)	1 (16.67%)	
T2	2 (28.57%)	5 (71.43%)	
T3	28 (42.42%)	38 (57.58%)	
T4	5 (50.00%)	5 (50.00%)	
Lymph node metastasis			0.071
Absent	11 (64.71%)	6 (35.29%)	
Present	29 (40.28%)	43 (59.72%)	
Distant metastasis			0.794
Absent	28 (45.90%)	33 (54.10%)	
Present	12 (42.86%)	16 (57.14%)	
Blood vessel infiltration			0.980
Absent	21 (43.75%)	27 (56.25%)	
Present	4 (44.44%)	5 (55.56%)	
Lymphatic vessel infiltration			0.358
Absent	10 (47.62%)	11 (52.38%)	
Present	16 (35.56%)	29 (64.44%)	
Perineural infiltration			0.628
Absent	13 (46.43%)	15 (53.57%)	

Present	22 (40.74%)	32 (59.26%)	
Peritumoral inflammation			0.453
Absent	19 (46.34%)	22 (53.66%)	
Present	16 (38.10%)	26 (61.90%)	
Desmoplasia			0.710
Small	24 (43.64%)	31 (56.36%)	
Large	11 (39.29%)	17 (60.71%)	
<i>Helicobacter pylori</i> infection			0.824
Absent	26 (42.62%)	35 (57.38%)	
Present	10 (45.45%)	12 (54.55%)	
Lauren's classification			0.020
Intestinal	13 (29.55%)	31 (70.45%)	
Diffuse	20 (55.56%)	16 (44.44%)	

^aIn bracket is *P* value before Dunn's multiple comparison post hoc test.

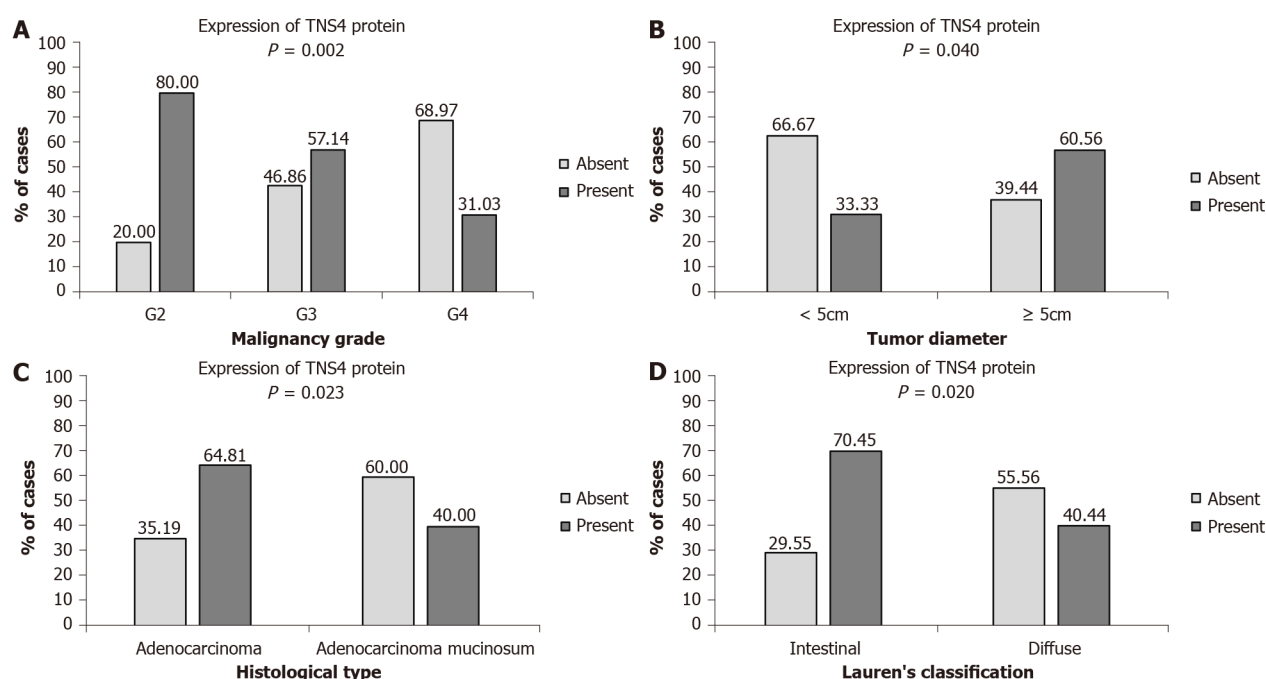


Figure 2 Tensin 4 expression with clinical and pathological parameters of gastric cancer. A: Comparison of tensin 4 (TNS4) expression and (A) malignancy grade, G2 vs G4, statistically significant at $P = 0.002$; B: Tumor diameter; C: Histological type; D: Lauren's classification. The comparison of TNS4 expression with the selected clinicopathological parameters was conducted using the Mann-Whitney U test for two groups and the Kruskal-Wallis test for three groups. Dunn's multiple comparison post hoc tests were implemented for the Kruskal-Wallis test. A value of $P < 0.05$ was considered significant. ^a $P < 0.05$ G2 vs G4 TNS4 expression level in gastric cancer. G2: Moderately differentiated gastric cancer (GC); G3: Poorly differentiated GC; G4: non-differentiated GC.

carcinoma tumors[11,20]. This finding indicates a correlation between TNS4 expression and the progression of the tumor and may be associated with the activation of signaling pathways, including PI3/AKT and Ras/MAPK, the stimulation of which intensifies the processes of cell proliferation and migration[13]. During the activation of these pathways, TNS4 expression is increased under the influence of epidermal growth factor at the levels of mRNA transcription and protein translation. Increased TNS4 expression leads to enhanced migration and proliferative potential of cancer cells.

We observed significant correlations between the expression of TNS4 and malignancy grade, histological type and type of tumor according to Lauren's classification. TNS4 protein was much more frequently present in moderately differentiated

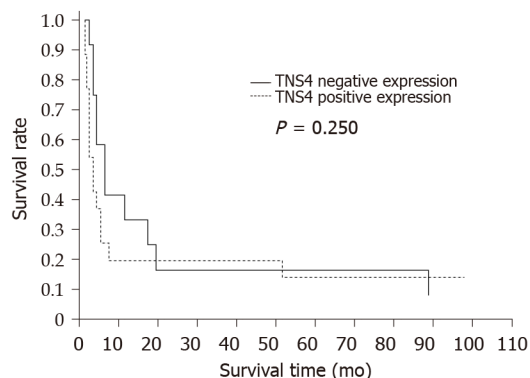


Figure 3 Analysis of the correlation of tensin 4 protein expression with the overall survival rate.

tumors than in poorly differentiated and non-differentiated tumors, in adenocarcinomas without mucinous components and in the intestinal type of GC. The classification of GC based on the degree of glandular cell differentiation is a prognostic factor. The more differentiated the gastric adenocarcinoma, the better the prognosis is for a patient. Poorly and non-differentiated adenocarcinoma cells differ phenotypically from each other, forming clusters without visibly formed glands[21]. There are no reports in the literature suggesting a significant relationship between TNS4 protein expression and the grade of tumor malignancy, which indicates the uniqueness of our study. In contrast, Sakashita *et al*[19] evaluated the *TNS4* mRNA expression and observed that patients with moderately or poorly differentiated GC had higher levels of *TNS4* expression. The differences in the results obtained by these researchers and us may be due to numerous mutations in the *TNS4* gene in tumor cells, entailing changes in the structure of this protein. We demonstrated higher expression of this protein in moderately differentiated gastric adenocarcinoma, which suggests that TNS4 overexpression is associated with a better prognosis of the tumor.

Poorly differentiated GCs are characterized by weak or no developed glandular tubules. Under normal conditions, TNS4 is involved in glandular duct morphogenesis. This phenomenon was described by Wu *et al*[22] after their study on a 3D model of RWPE-1 cells of the prostate. These researchers demonstrated that a decrease in protein expression does not affect the phenotype of the newly formed glands, although their number decreased. The authors suggested that lowering TNS4 expression inhibits the proliferation of normal epithelial cells of the prostate by stopping the cell cycle. However, increased expression of TNS4 leads to disturbances in the formation of glandular ducts through β_1 -integrin/FAK pathway induction. Albasri *et al*[8] identified a link between TNS4 and the morphology of colorectal cancer cells. By means of confocal microscopy, these researchers demonstrated that induced expression of TNS4 affects the shape of cancer cells. Under the conditions of TNS4 overexpression, HCT116 cells assume a spindle shape compared to cells with physiologically low expression of TNS4.

In our research, we demonstrated significant differences in TNS4 expression between the two histological types of GC. We noted that positive expression of TNS4 protein was more frequent in GCs without mucinous components than in mucinous adenocarcinomas. Gastric mucosal adenocarcinomas have been linked to poorer prognosis, lower sensitivity to oncological treatment and increased risk of acquiring resistance to chemotherapy[23]. Currently, there are no data available to indicate a link between TNS4 expression and gastric adenocarcinomas without a mucinous component. Phenotypically, GC with a mucinous component is characterized by a considerable amount of mucin in the extracellular space (> 50%)[24].

In our study, we correlated the expression of TNS4 protein with the cancer type according to Lauren's classification. Statistical analysis showed that positive TNS4 staining correlates with the intestinal type of tumor. The presence of this protein was more often observed in adenocarcinomas of the intestinal than diffuse type. The results presented by Chen *et al*[25] indicate that the intestinal type correlates with better prognosis and better clinical and pathological parameters than the diffuse type. From a histological point of view, intestinal-type GC is phenotypically characterized by cells forming glandular ducts in the lumen of which the cancer grows. Usually, these cells do not secrete mucus, but if it is produced, it remains in the lumen of the glands[26]. In the literature, we did not find any studies assessing TNS4 expression in relation to the histological type of GC according to Lauren's classification. The positive

correlation between the expression of TNS4 and the intestinal type of cancer suggests further directions of research as well as the need to investigate the role of this protein in the histogenesis of GC.

Our study did not show any correlation between the level of TNS4 protein expression and tumor progression (pT, pN, pM status), although the literature shows that TNS4 is located in focal adhesion sites and participates in cell migration, thus increasing the metastatic potential of tumor cells. Qi *et al*[17] observed a significant correlation between TNS4 expression and the tumor stage. Their results indicated a correlation between TNS4 expression and deeper infiltrating tumors as well as lymph node and distant metastases. We did not observe similar significant relationships in our study. Other researchers have shown that stimulated TNS4 expression results in an increased ability of cells to migrate, infiltrate into adjacent tissues and metastasize. TNS4 was shown to play an important role in epithelial-mesenchymal transition by stimulating several signaling pathways, including E-cadherin, Akt, Src, TGF- β /Smad and Snail[8,17,27-29]. Other signaling pathways that are stimulated under TNS4 overexpression are PI3K/Akt and Ras/MAPK. Their activation may intensify cell proliferation and migration[13]. Furthermore, *in vitro* studies revealed that TNS4 may promote colony formation, as demonstrated in a study on pancreatic cancer cells[30]. Another important signaling protein in cancer development is MET, which is stabilized by TNS4 and acts as a mediator in carcinogenesis[31]. The exact mechanisms regulating TNS4, *e.g.*, a mutation that stabilizes this protein or amplifies the *TNS4* gene, have not been discovered thus far. Thorpe *et al*[32] reported that TNS4 can be regulated by the EGFR/KRAS and STAT3 pathways. Other studies have indicated that the expression of this protein may be modulated by growth factors and cytokines, *e.g.*, FGF2, PDGF, IGF-1, TGF- β , IL-6 and IL-13[33]. Other literature reports suggest that TNS4 may be engaged in tubulogenesis[34] as one of the stages of angiogenesis. The formation of blood vessel networks by tumor cells is the way in which the tumor microenvironment acquires nutrients and oxygen needed for tumor growth. Various publications have presented evidence for the oncogenic role of TNS4. In our research, we did not confirm the procancer role of the TNS4 protein. Our results prove that TNS4 may be related to the formation of a certain type of cancer, as observed in prostate cancer[35].

Moreover, we did not demonstrate any significant correlations between TNS4 expression level and the patients' overall survival rate. According to the works of Qi *et al*[17] and Sakashita *et al*[19], TNS4 overexpression correlates with shorter survival time and worse prognosis for patients with GC. In our study, the lack of this correlation may result from a small number of evaluated patients and the lack of data on the survival of many of these patients, which is a limitation of our research and does not allow us to draw broader conclusions about the participation of TNS4 in GC carcinogenesis. Additionally, it is possible that differences between the mRNA level in the study by Sakashita *et al*[19] and the protein expression level in our research are because the regulation of TNS4 transcription depends on the type of cells or tissues as well as on potential mutations in the *TNS4* gene in GC cells. Thus, the expression level of this protein in different tissues is different. The control of this gene expression may also result from epigenetic modifications[36].

CONCLUSION

The expression of TNS4 was significantly higher in tumors with a diameter of ≥ 5 cm, of a moderately differentiated type of GC without a mucinous component, and of the intestinal type according to Lauren's classification. Increased levels of TNS4 expression are linked to the histological type of GC with a better prognosis.

ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) is still one of the most common malignant neoplasms worldwide in terms of incidence and cancer motility. The development of GC is a multistage process. Tensin 4 (TNS4) belongs to the tensin family. This protein can participate in the transmission of intracellular signals. TNS4 plays an important role in biological processes connected with carcinogenesis, such as proliferation, migration, cell adhesion and invasiveness. It is very important to search for new biomarkers that

could help to diagnose GC at the early stages of its development.

Research motivation

We wanted to evaluate the role of the TNS4 protein in the development of GC. This protein may be a promising biomarker in the diagnosis of GC at the early stages of its development.

Research objectives

The study objective was to show the expression of TNS4 in GC tissues and assess the relationship between protein expression and clinical and pathological parameters and the overall survival rate of patients.

Research methods

In our study, we used immunohistochemistry to evaluate the expression of the TNS4 protein. The research was conducted on a group of 89 patients.

Research results

We observed that higher TNS4 expression was more often observed in GCs with a larger diameter ($P = 0.040$). Our results also showed that an increase in TNS4 expression was more frequently observed in tumors without mucinous components than in tumors from mucosal cancers ($P = 0.023$). Furthermore, higher TNS4 expression was demonstrated in moderately differentiated tumors ($P = 0.002$). Increased TNS4 expression was also noted in the intestinal type of GC according to Lauren's classification ($P = 0.020$). No significant correlation was found between the expression of TNS4 and the overall survival rate of patients.

Research conclusions

The expression of TNS4 was significantly higher in tumors with a diameter of ≥ 5 cm, of a moderately differentiated type of GC without a mucinous component, and of the intestinal type according to Lauren's classification. Increased levels of TNS4 expression are linked to the histological type of GC with a better prognosis.

Research perspectives

It is possible to develop this study with cell line methods. It will be possible to investigate the potential role of TNS4 in GC cell proliferation.

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