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Research article

Bioinformatics analysis on the expression of GPX family in gastric cancer and its correlation with the prognosis of gastric cancer

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ABSTRACT

Background: Gastric cancer (GC) is one of the most common cancers of the digestive tract, with the fifth-highest incidence and third highest mortality rate in the world.
Methods: In this study, the Kaplan-Meier Plotter database was used to analyze the correlation between the expression of the glutathione peroxidase (GPX) family and the clinical prognosis of gastric cancer (GC). The prognostic value of increased GPX family mRNA expression in GC patients in different clinical stages, with different differentiation degrees, in different genders and human epidermal growth factor receptor-2 (HER2) status, and treated with different therapeutic regimens was also studied.
Results: The results showed that with the increase of GPX1 and GPX2 mRNA low expression levels, the overall survival (OS) of gastric cancer patients was longer. However, when the high expression levels of GPX3, GPX5 and GPX6 mRNA increased, gastric cancer patients presented good OS, while the increase of GPX4 mRNA expression level had no significant correlation with OS in gastric cancer patients.
Conclusion: The results of this study are expected to provide a reliable basis for the clinical treatment of GC and lay a foundation for the development of a novel GC treatment approach.

Introduction

GC is a common malignant tumor in the world, which is also the most prevalent malignant tumor of the upper gastrointestinal tract in China [1]. According to the global cancer statistics in 2018, the mortality of GC ranks third among all tumors, accounting for 8.2% of all cancer deaths. Currently, the primary treatment for gastric cancer is surgery, which is often combined with multidisciplinary comprehensive and individualized therapies such as chemotherapy and radiotherapy [2]. GC occurs mainly in Asia, especially in some Southeast Asian countries such as China, Korea, and Japan, with the highest incidence rate in the world, bringing a heavy burden on the global health economy. With the change of the era of science and technology, more and more people pay attention to the quality of life but cancers may be so hidden that they cannot be found, so it is particularly important to find some molecular markers conducive to the early diagnosis of GC [3].

GPX is an important enzyme with antioxidant function, and its moderate expression is crucial for maintaining the normal metabolism in the body [4]. Several studies in recent years have shown that the GPX family is abnormally expressed in various tumor tissues, including human lung cancer, esophageal cancer, colorectal cancer, and liver cancer, and that it is closely related to the occurrence, development, and treatment of a variety of tumors [5]. Some scholars believe that GPX1 is involved in the protective autophagy and the regulation of the tumor microenvironment in pancreatic ductal adenocarcinoma [6]. With the increase of tumor volume, tumor cells are limited in obtaining nutrients to varying degrees. Since GPX2 can affect tumor cell apoptosis by regulating the concentration of reactive oxygen species in them, it has been suggested that GPX2 might be a potential biomarker or therapeutic target for bladder cancer [7]. GPX3, similar to GPX1 in structure, is the main scavenger of reactive oxygen species in plasma, and the down-regulation of GPX3 expression may inhibit the clonal formation and survival of tumor cells in ovarian cancer

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Table 1. ID of GPX family genes in Kaplan-Meier Plotte

Name of genes	ID
GPX1	200736_s_at
GPX2	202831_at
GPX3	201348_at
GPX4	201106_at
GPX5	214648_at
GPX6	213170_at

[8]. In addition, GPX3 has redox regulation and can inhibit the growth of cancer cells. GPX4 is widely expressed in a variety of human tissues [9], but there are few studies on its correlation with tumors. It has been confirmed that GPX4 can affect the occurrence and progression of liver cancer by inhibiting angiogenesis and tumor cell proliferation of tumor cells [10]. Rusoloet al. [11] found low GPX5 expression in breast cancer and proved that breast cancer cells can change the expression of these genes, the role of GPX5 in other tumors remains to be further studied. At present, there are few studies on GPX6 in tumors. Studies have found that the polymorphism of the GPX6 gene is closely related to the occurrence and classification of ovarian cancer and GPX6 may play an important role in the formation of tumors [12]. GPX7 is a newly discovered non-selenium member of the GPX family in recent years [13]. Currently, most studies indicate that GPX7 can inhibit cancer and protect against oxidative stress in cancer cells. GPX8 is the last discovered member of the GPX family, and there are few studies on it in tumors. However, this was recently demonstrated that GPX8 plays a variety of important physiological functions in cervical cancer HeLa cells [14] and inhibits the proliferation of tumor cells [15]. According to Kaplan-Meier Plotter database query results, GPX6 and GPX7 have the same gene ID, and the GPX8 gene has not been found in gastric cancer and its key mechanism in gastric cancer cells remains to be explored. Therefore, GPX1-GPX6 was selected for this study.

The GPX family, which has an antioxidant function and is vital for human health, may not only remove hydrogen peroxide and lipid peroxide but also minimize free radical generation through its unique

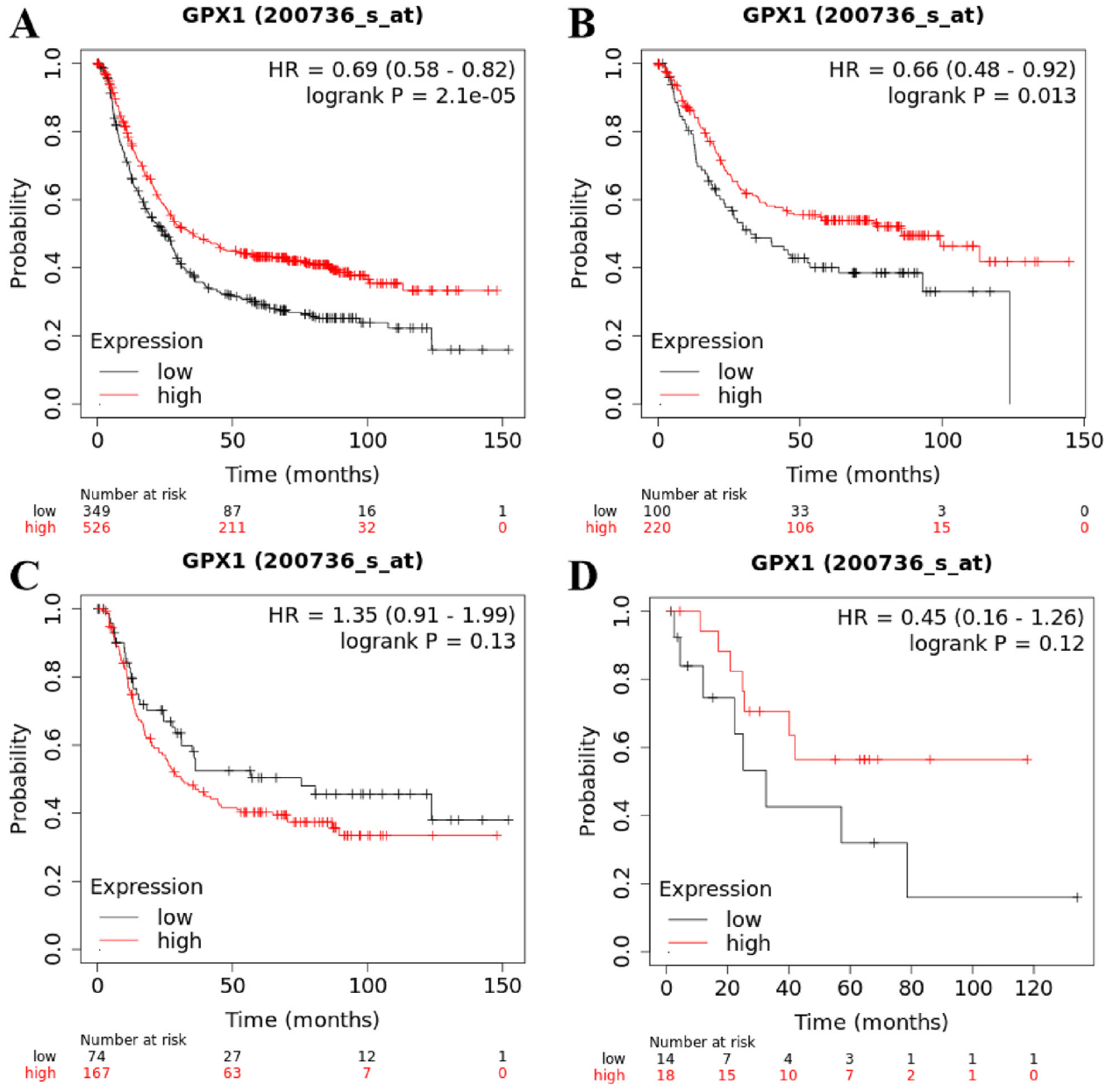

Figure 1. Prognostic value of GPX1 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

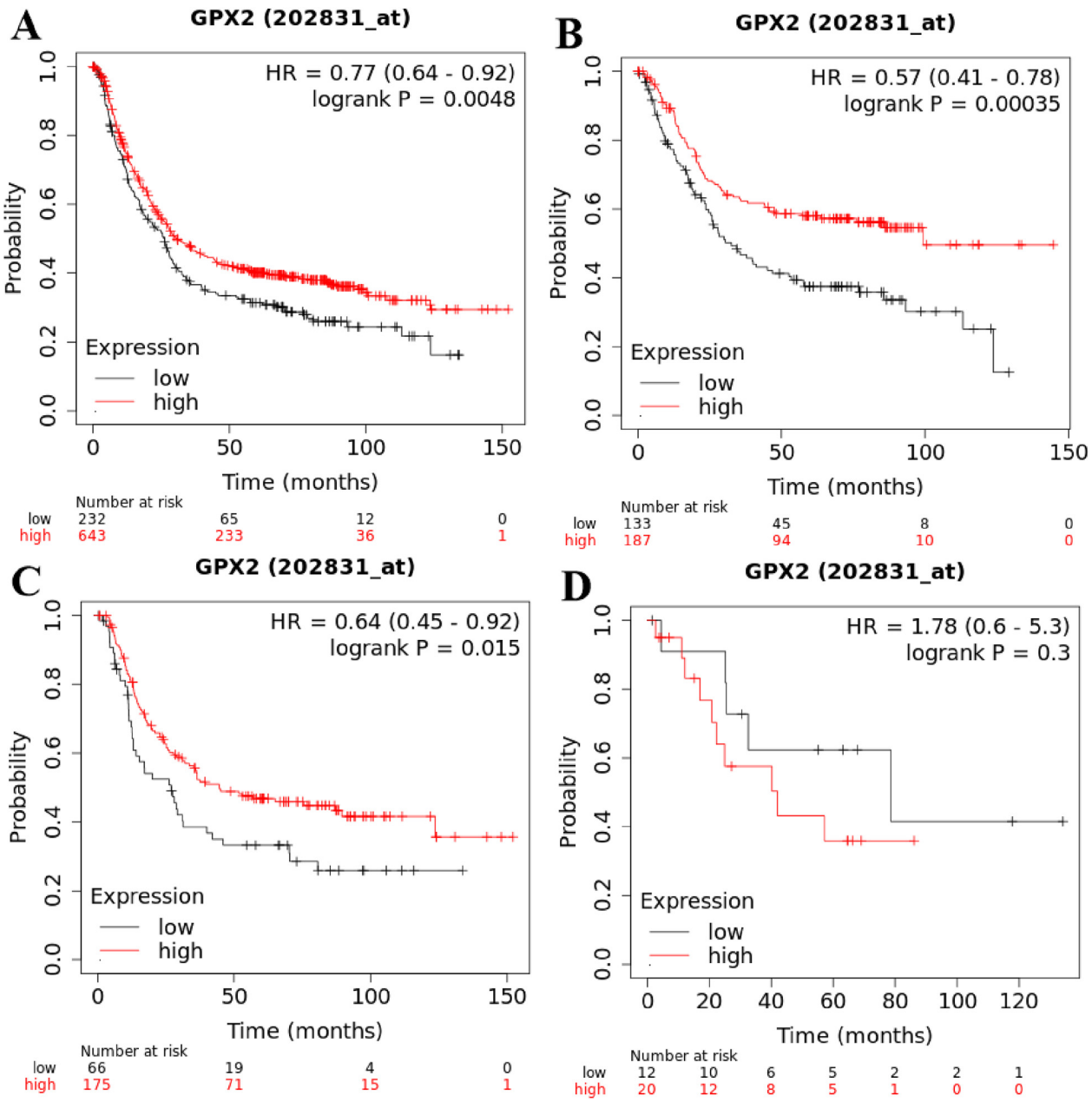

Figure 2. Prognostic value of GPX2 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

chemical reaction of reduced glutathione [16]. Due to the diversity of GPX functions and the difference of subtypes, the mechanism of GPX in tumors is complex, suggesting that GPX has a potential application value in the prevention, diagnosis, and treatment of tumors, so more studies are needed to be carried out to understand the role and regulation of GPX in cancers. The Kaplan-Meier Plotter database was used in this research to analyze the clinical manifestations of GPX1-GPX6 in gastric cancer and the prognostic value of gastric cancer patients, which is important for early tumor diagnosis, improving the patient prognosis, and clinical treatment efficacy.

1. Experimental material

1.1. GPX family gene ID

Online Kaplan-Meier Plotter database was used to find the ID code of GPX family genes on the website (Table 1).

1.2. Kaplan-Meier Plotter database

An online Kaplan-Meier Plotter (http://www.kmplot.com) database was used to evaluate the prognostic value of mRNA expression of GPX members for OS of GC patients. The database was established based on gene expression data from the survival information of Gene Expression Omnibus (GEO), European Genome-phenome Archive (EGA), and the Cancer Genome Atlas (TGGA).

2. Experimental methods

The prognostic value of GPX family members' mRNA expression in the OS was assessed using an online Kaplan-Meier Plotter (http://kmplot.com/analysis) database. In this database, the integrated GEO was used, including GSE14210, GSE22377, GSE51105, GSE15459, GSE29272, and other survival information [17, 18, 19, 20, 21]. Currently, 54675 genes related to gastric cancer, breast cancer, ovarian cancer, lung

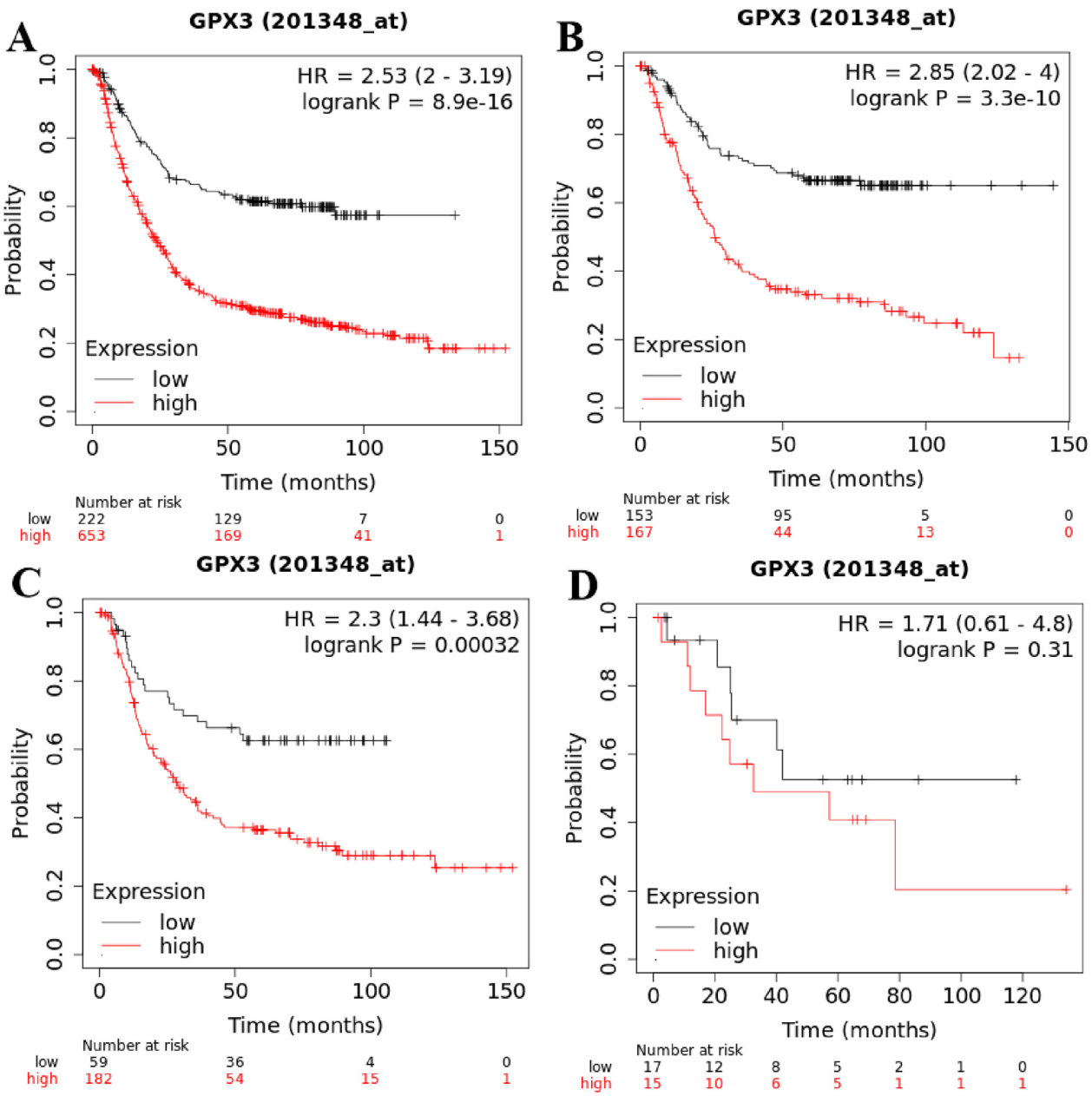

Figure 3. Prognostic value of GPX3 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

cancer, and liver cancer, as well as Lauren classification, clinical-stage, differentiation, gender, HER2 status, and treatment of gastric cancer patients, have been included in the database. In this study, six GPX family members (GPX1, GPX2, GPX3, GPX4, GPX5, and GPX6) were entered into a database to obtain the Kaplan-Meier survival plots, and the hazard ratio (HR), 95% confidence interval (CI), and Log-rank *P-values* were presented in charts using existing data sources and clinical data. A value with $P < 0.05$ was considered statistically significant.

3. Experimental results

3.1. Analysis of the expression of GPX mRNA and OS curve data in GC patients

3.1.1. Analysis of GPX1 expression results

Kaplan-Meier Plotter database results showed that increased GPX1 mRNA high expression was significantly correlated with OS in GC patients and Gastrointestinal cancer patients (Figure 1A) (Figure 1B), ($P < 0.05$), and the Lauren classification results showed that the increase of GPX1 mRNA expression had no correlation with OS and was not statistically significant in diffuse GC (Figure 1C) and mixed GC (Figure 1D) patients ($P > 0.05$).

3.1.2. Analysis of GPX2 expression results

According to the Kaplan-Meier Plotter database, increasing GPX2 mRNA high expression was significantly correlated with OS, which was statistically significant (Figure 2A) ($P < 0.05$). Lauren classification results showed that increased GPX2 mRNA high expression was correlated with a good prognosis of OS in GC patients (Figure 2B) ($P < 0.05$), while the increased expression of GPX2 mRNA was not significantly correlated with the OS in diffuse GC (Figure 2C) and mixed GC (Figure 2D) patients ($P > 0.05$).

3.1.3. Analysis of GPX3 expression results

Kaplan-Meier Plotter database results showed that with the increase of GPX3 mRNA low expression in GC patients, there was a significant

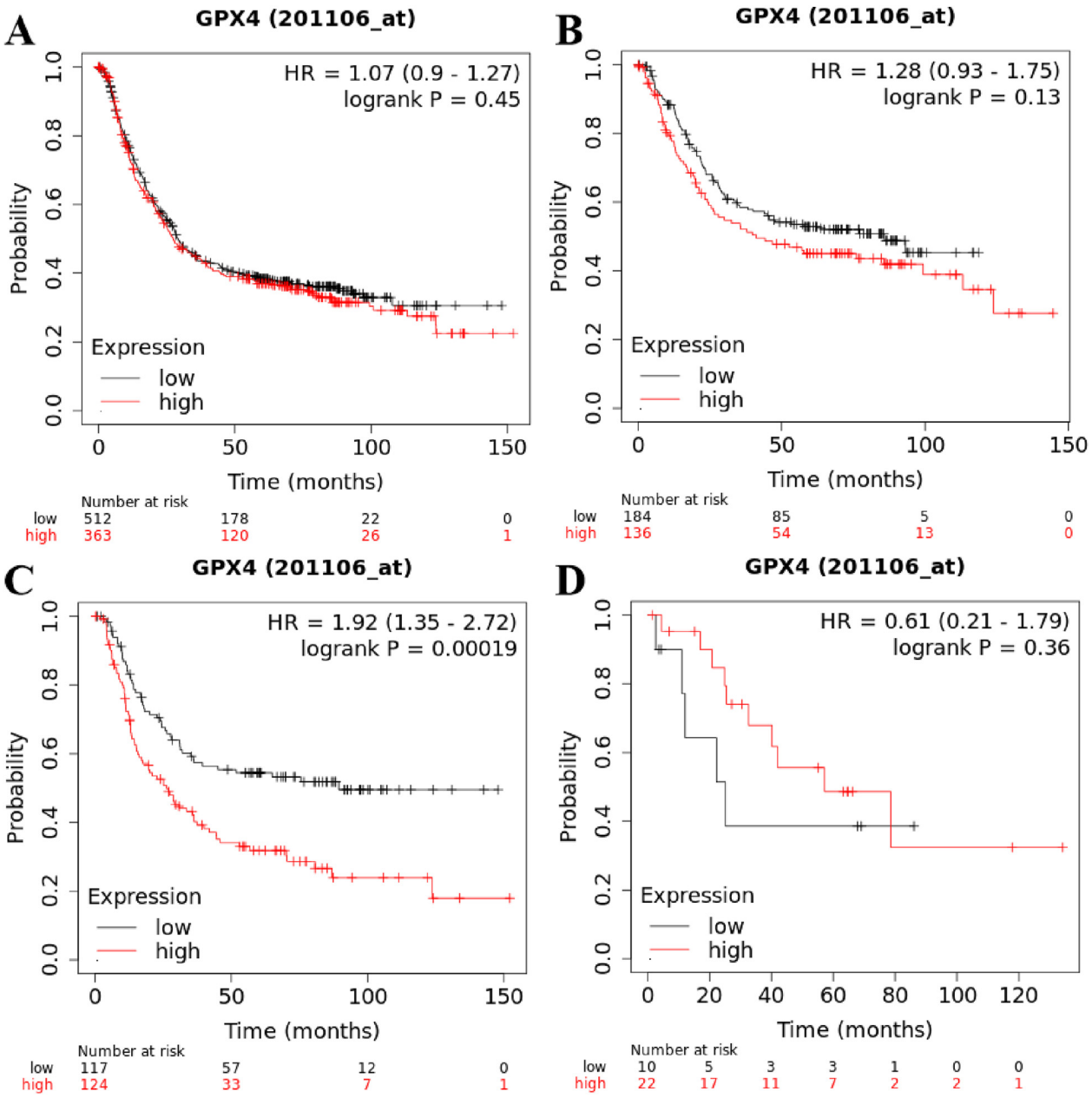

Figure 4. Prognostic value of GPX4 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

correlation with OS, which was statistically significant (Figure 3A) ($P < 0.05$), and the Lauren classification results showed that increased GPX3 mRNA low expression was also associated with OS in patients with gastrointestinal cancer (Figure 3B) and diffuse GC (Figure 3C) patient ($P < 0.05$), while the increased expression of GPX3 mRNA was not significantly correlated with the OS in mixed GC patients (Figure 3D) ($P > 0.05$).

3.1.4. Analysis of GPX4 expression results

According to the Kaplan-Meier Plotter database, increased expression of GPX4 mRNA was not significantly correlated with OS in GC patients (Figure 4A) ($P > 0.05$), and the Lauren classification results showed that the increase of GPX4 mRNA expression was not correlated with the OS in gastrointestinal cancer (Figure 4B) and mixed GC (Figure 4D) patients ($P > 0.05$), while OS showed a favorable trend with the increase of GPX4 mRNA low expression, which was statistically significant in diffuse GC patients (Figure 4C) ($P < 0.05$).

3.1.5. Analysis of GPX5 expression results

The Kaplan-Meier Plotter database results revealed that an increase in GPX5 mRNA expression in GC patients was significantly correlated with OS (Figure 5A) (P0.05), and Lauren classification results showed that an increase in GPX5 mRNA low expression in GC patients showed a favorable prognostic trend in OS. (Figure 5B) ($P < 0.05$), while the increased expression of GPX5 mRNA was not significantly correlated with the OS in diffuse GC (Figure 5C) and mixed GC (Figure 5D) patients ($P > 0.05$).

3.1.6. Analysis of GPX6 expression results

Kaplan-Meier Plotter database results showed that the increase of GPX6 mRNA expression was correlated with OS, which was statistically

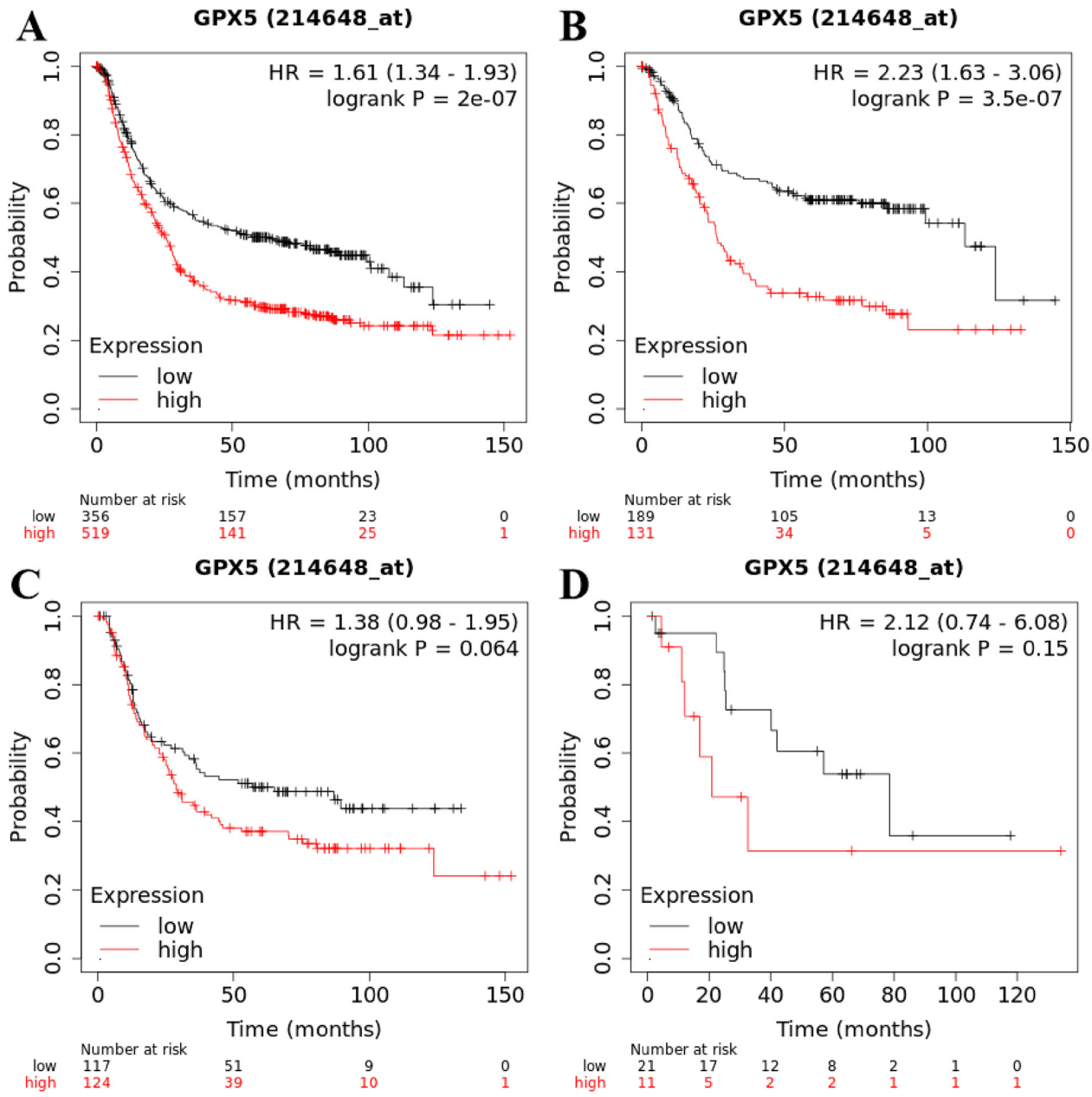

Figure 5. Prognostic value of GPX5 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

significant in GC patients (Figure 6A) ($P < 0.05$). Lauren classification results showed that OS showed a good trend with increased GPX6 mRNA low expression in patients with gastrointestinal cancer (Figure 6B), diffuse GC (Figure 6C), and mixed GC (Figure 6D) patients ($P < 0.05$).

3.2. Analysis of GPX gene expression data based on clinical stages

It was observed (Table2) that higher expression of GPX1 mRNA might induce tumor cell apoptosis, with a significant correlation with OS in clinical phase I GC patients ($P < 0.05$); the high expression of GPX3 and GPX6 mRNA was significantly correlated with the OS in all clinical stages of GC patients ($P < 0.05$); on the contrary, up-regulated GPX2 and GPX4 mRNA expression was significantly correlated with OS only after clinical stage III of GC patients ($P < 0.05$); GPX5 mRNA expression was significantly correlated with clinical STAGE I and III OS in GC patients ($P < 0.05$).

3.3. Analysis of the GPX gene expression data based onHER2 expression status

As shown in Table 3, under the conditions ofHER2 expression status (negative) and the same number of cases, the expression of GPX1-6 mRNA was significantly correlated with the OS in GC patients ($P < 0.05$), and in the positive HER2 status, GPXs mRNA expression has no correlation with prognosis of GC patients except GPX3 and GPX5 ($P > 0.05$).

3.4. Analysis of gene expression data based on therapeutic regimens

The expression of GPX1-6 mRNA was significantly correlated with the good prognosis of GC patients treated with surgery alone ($P < 0.05$), and the expression of GPX2 and GPXx3 mRNA was significantly correlated with the good prognosis of GC patients treated with 5-FU adjuvant ($P <$

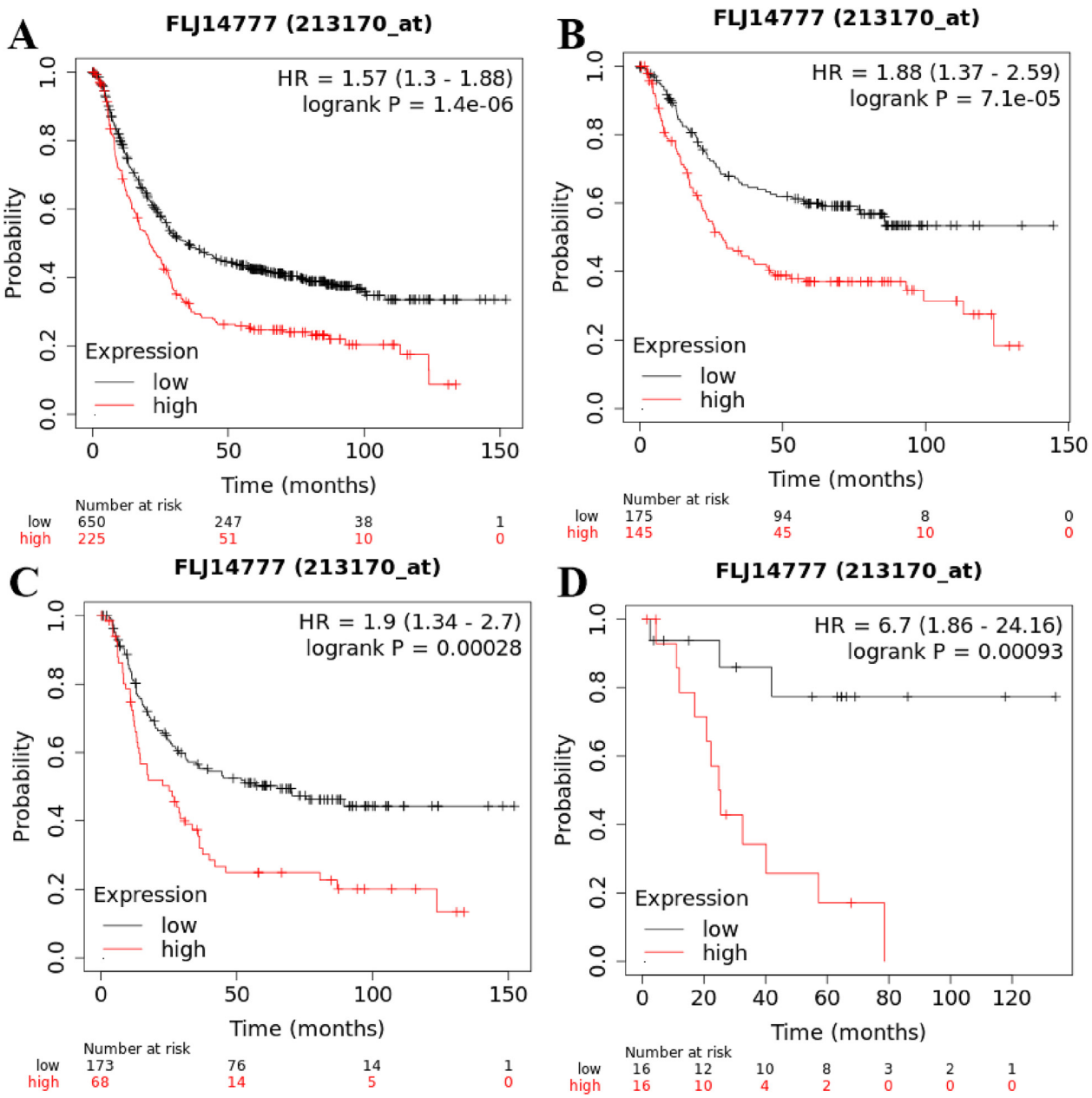

Figure 6. Prognostic value of GPX6 in patients with different tissue types of gastric cancer. A: Gastric cancer patients; B: Gastrointestinal cancer patients; C: Diffuse gastric cancer patients; D: Mixed gastric cancer patients.

0.05), as shown in Table 4. The prognosis of other adjuvant treatments showed that the mRNA expressions of GPX3 and GPX6 were significantly correlated with the OS of GC patients, which was statistically significant ($P < 0.05$).

3.5. Analysis of gene expression data based on different genders

As indicated in Table5, the expression of GPX1-6 mRNA was statistically significant ($P < 0.05$) correlated with the good prognosis of male GC patients; the expression of GPX1 and GPX4 mRNA was not significantly correlated with the OS in female GC patients ($P > 0.05$). As shown in Figure 7, the expression of GPX1-6 in gastric cancer was recorded in every million patients of different ages. The results showed that GPX3 was significantly overexpressed in normal people, suggesting that GPX3 has a certain inhibitory effect on cancer.

3.6. Analysis of gene expression data based on degrees of differentiation

The expression of GPX genes in GC patients with varying degrees of differentiation revealed that GPX2 and GPX6mRNA expression were significantly correlated with OS in GC patients with high degrees of differentiation ($P < 0.05$), Similarly, GPX2 mRNA expression was also correlated with OS in GC patients with moderate differentiation ($P < 0.05$). The mRNA expressions of GPX1, GPX3, and GPX5 at different levels of differentiation did not correlate with OS in GC patients ($P > 0.05$), as shown in Table 6.

4. Discussion

Gastric cancer is one of the most common gastrointestinal cancers worldwide. Despite recent advancements in drug therapy, the overall

Table 2. The relationship between GPX gene expression level and OS in different pathological stages.

GPXs	Clinical stage	Case load	HR (95% CI)	*P* values
GPX1	I	67	0.31 (0.12–0.83)	0.014*
	II	140	0.58 (0.31–1.09)	0.085
	III	305	0.73 (0.53–1.02)	0.067
	IV	148	0.83 (0.54–1.27)	0.39
GPX2	I	67	0.45 (0.16–1.21)	0.1
	II	140	0.7 (0.37–1.33)	0.28
	III	305	0.69 (0.52–0.92)	0.011*
	IV	148	0.7 (0.47–1.05)	0.081
GPX3	I	67	8.27 (1.08–63.51)	0.015*
	II	140	6.13 (2.18–17.19)	8.5×10^{-5}*
	III	305	2.2 (1.53–3.17)	1.4×10^{-5}*
	IV	148	1.82 (1.14–2.91)	0.011*
GPX4	I	67	0.55 (0.2–1.54)	0.25
	II	140	1.59 (0.87–2.89)	0.13
	III	305	1.42 (1–2.01)	0.046*
	IV	148	1.93 (1.31–2.86)	8×10^{-4}*
GPX5	I	67	6.58 (2.11–20.47)	0.00018*
	II	140	1.71 (0.94–3.11)	0.076
	III	305	1.59 (1.17–2.17)	0.0029*
	IV	148	0.85 (0.55–1.3)	0.45
GPX6	I	67	3.12 (1.13–8.61)	0.021*
	II	140	2.31 (1.27–4.18)	0.0046*
	III	305	1.73 (1.29–2.32)	2×10^{-4}*
	IV	148	2 (1.31–3.05)	0.0011*

Note: *: $P < 0.05$; OS: overall survival rate; CI: confidence interval; HR: hazard ratio.

survival of GC remains bleak [17]. Therefore, it is of great theoretical and clinical significance to find meaningful molecular markers and diagnostic targets for early diagnosis of GC and new targeted therapy for GC. Kaplan-Meier Plotter database was able to evaluate the effect of 54K genes (mRNA, protein, miRNA) on survival of 21 types of cancer, including breast cancer (6234 cases), gastric cancer (1440 cases), ovarian cancer (2190 cases), lung cancer (3452 cases), etc. [18, 19, 20]. The database includes clinical information such as Lauren Classification,

Table 3. Analysis on the relationship between GPX gene expression and OS in GC patients based on HER2 expression status.

GPXs	HER2 status	Case load	Low expression	High expression	HR (95%CI)	*P* values
GPX1	Negative	532	201	331	0.61 (0.49–0.77)	$1.8 \times 10–5$*
	Positive	343	101	242	0.77 (0.59–1.02)	0.069
GPX2	Negative	532	166	366	0.73 (0.57–0.92)	0.0069*
	Positive	343	114	229	0.74 (0.57–0.97)	0.03
GPX3	Negative	532	227	305	2.24 (1.75–2.86)	$4 \times 10–11$*
	Positive	343	85	258	1.6 (1.16–2.22)	0.004*
GPX4	Negative	532	317	215	1.2 (0.96–1.5)	0.04*
	Positive	343	237	106	0.75 (0.56–1.01)	0.059
GPX5	Negative	532	241	291	1.62 (1.29–2.04)	$3.5 \times 10–5$*
	Positive	343	124	219	1.57 (1.18–2.09)	0.002*
GPX6	Negative	532	387	145	1.91 (1.51–2.42)	$3.6 \times 10–8$*
	Positive	343	85	258	1.4 (1.02–1.92)	0.037

Note: *: $P < 0.05$; OS: overall survival rate; CI: confidence interval; HER2: human epidermal growth factor receptor-2; HR: hazard ratio.

Table 4. Analysis on the relationship between GPX gene expression and OS in GC patients based on therapeutic regimens.

GPXs	Treatment options	Case load	HR (95%CI)	*P* values
GPX1	Surgery alone	380	0.82 (0.59–1.14)	0.023*
	With 5-FU adjuvant	152	0.82 (0.55–1.21)	0.31
	With other adjuvants	76	3.79 (0.88–16.34)	0.055
GPX2	Surgery alone	380	0.72 (0.54–0.96)	0.023*
	With 5-FU adjuvant	152	1.54 (1.04–2.28)	0.031*
	With other adjuvants	76	2.33 (0.95–5.73)	0.057
GPX3	Surgery alone	380	2.03 (1.38–2.98)	0.00026*
	With 5-FU adjuvant	152	0.51 (0.35–0.74)	0.00037*
	With other adjuvants	76	4.13 (1.38–12.38)	0.006*
GPX4	Surgery alone	380	1.4 (1.02–1.92)	0.035*
	With 5-FU adjuvant	152	0.74 (0.52–1.06)	0.099
	With other adjuvants	76	2.17 (0.72–6.5)	0.16
GPX5	Surgery alone	380	1.58 (1.18–2.1)	0.0017*
	With 5-FU adjuvant	152	1.34 (0.92–1.97)	0.13
	With other adjuvants	76	2.68 (0.79–9.15)	0.1
GPX6	Surgery alone	380	1.72 (1.27–2.33)	0.00035*
	With 5-FU adjuvant	152	0.72 (0.51–1.02)	0.061
	With other adjuvants	76	3.71 (1.35–10.23)	0.0065*

Note: *: $P < 0.05$; OS: overall survival rate; CI: confidence interval; 5-FU: 5-fluorouracil; HR: hazard ratio.

gender, HER2 status, clinical stage, degree of differentiation, and treatment of PATIENTS with GC. The purpose of this study was to comprehensively analyze GPXs mRNA expression and prognosis in gastric cancer by Kaplan-Meier Plotter database, to provide reliable clues and theoretical basis for further research on the role of GPXs in the occurrence and development of gastric cancer.

Stage I, II, III, and IV of GC indicate its different tumor sizes and different degrees of diffusion, respectively, and a tumor at stage I and II of GC are considered one with small degrees of diffusion [21]. It was found that the lower the expression of GPX1 mRNA, the greater the expression of GPX3 and GPX6 mRNA can lead to a reduction of ROS produced by cancer cells, which then inhibits cancer cell proliferation, migration, and invasion, resulting in a high overall survival rate of GC patients at all clinical stages. While the expression of GPX2 mRNA could promote the growth of tumor cells, so the prognosis of GC patients should be poor at stage III. YAN et al. confirmed that overexpression of GPX2 can reduce oxidative stress-induced apoptosis of MCF7 cells, while RNAi knockdown of GPX2 can significantly increase the sensitivity of MCF7 cells to oxidative stress-induced apoptosis [22]. HER2 is human epidermal growth factor receptor-2, which has been shown to alter the sensitivity of tumors to hormones and chemotherapy drugs [23, 24]. It is now clear that HER2 is expressed in many tissues, including the breast,

Table 5. Analysis on the relationship between GPX gene expression and OS in GC patients based on genders.

GPXs	Gender	Case load	HR (95%CI)	*P* values
GPX1	Male	544	0.64 (0.51–0.79)	3.1×10^{-5}*
	Female	236	1.16 (0.81–1.66)	0.42
GPX2	Male	544	0.79 (0.64–0.98)	0.033*
	Female	236	0.69 (0.48–0.99)	0.04*
GPX3	Male	544	2.69 (2.05–3.54)	1.2×10^{-13}*
	Female	236	2.89 (1.73–4.83)	2.1×10^{-5}*
GPX4	Male	544	1.14 (0.92–1.42)	0.023*
	Female	236	0.7 (0.46–1.07)	0.096
GPX5	Male	544	1.83 (1.4–2.38)	5.3×10^{-6}*
	Female	236	1.83 (1.26–2.64)	0.0011*
GPX6	Male	544	1.36 (1.09–1.69)	0.0055*
	Female	236	2.22 (1.55–3.18)	8.1×10^{-6}*

Note: *: $P < 0.05$; OS: overall survival rate; CI: confidence interval; HR: hazard ratio.

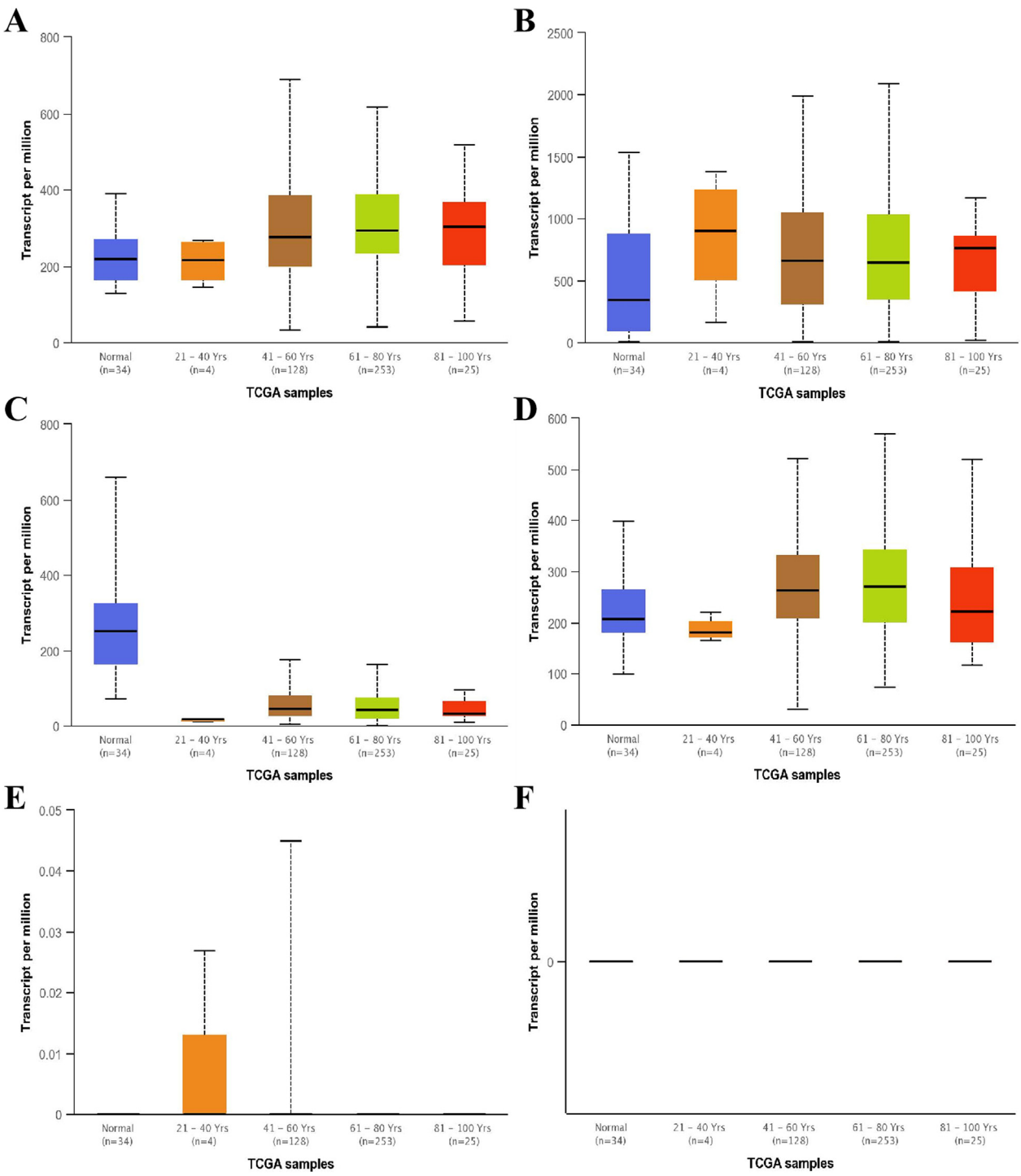

Figure 7. The expression of GPX1-6 in gastric cancer was recorded per million patients of different ages A:GPX1 B:GPX2 C:GPX3 D:GPX4 E:GPX5 F:GPX6.

gastrointestinal tract, kidney, and heart [25]. In this study, GPXs gene analysis revealed that the expression of GPX1-6 mRNA was significantly correlated with THE OS of GC patients under the condition of HER2 status (negative) and a consistent number of cases. When HER2 status was positive, in addition to GPX3 and GPX5, GPXs mRNA expression has a low overall survival rate for GC patients, and more experiments are needed to explore and prove the specific mechanism of GPXs in the development of GC disease. However, further research is needed to investigate and confirm the specific mechanism of GPXs in the advancement of GC. Surgery is the most common therapy for the treatment of GC, and 5-FU is one of the most commonly used drugs for the treatment of breast cancer, head and neck cancer, gastric cancer, colon cancer, and melanoma [26, 27, 28]. The results of this study confirmed that GPX1-6 had a higher overall survival rate in GC patients with a single surgery, while only GPX2 and GPX3 had a higher survival rate in GC patients with 5FU adjuvant treatment. Male GC patients with low GPX1-6 mRNA expression had a better prognosis, however, there was no significant correlation between OS and GPX1 and GPX4 mRNA expression in female GC patients. The results of this study showed that, according to different degrees of differentiation, the expression of GPX2 and GPX6 mRNA was significantly correlated with OS in GC patients with a high degree of differentiation, and GPX2 mRNA expression was also

Table 6. Analysis on the relationship between GPX gene expression and OS in GC patients with different degrees of differentiation.

GPXs	Differentiations	Case load	HR (95%CI)	*P* values
GPX1	Low differentiation	165	1.54 (0.99–2.37)	0.051
	Moderate differentiation	67	165 (0.86–3.17)	0.13
	High differentiation	32	0.5 (0.21–1.2)	0.11
GPX2	Low differentiation	165	1.21 (0.8–1.82)	0.37
	Moderate differentiation	67	2.48 (1.25–4.9)	0.0072*
	High differentiation	32	0.17 (0.05–0.57)	0.0014*
GPX3	Low differentiation	165	0.83 (0.55–1.26)	0.38
	Moderate differentiation	67	2.12 (0.87–5.18)	0.092
	High differentiation	32	0.61 (0.26–1.45)	0.26
GPX4	Low differentiation	165	1.44 (0.96–2.14)	0.074
	Moderate differentiation	67	0.64 (0.3–1.35)	0.23
	High differentiation	32	0.46 (0.19–1.12)	0.078
GPX5	Low differentiation	165	0.85 (0.57–1.28)	0.44
	Moderate differentiation	67	1.53 (0.8–2.92)	0.2
	High differentiation	32	3.37 (0.78–14.52)	0.084
GPX6	Low differentiation	165	0.72 (0.45–1.14)	0.16
	Moderate differentiation	67	1.56 (0.81–2.99)	0.18
	High differentiation	32	2.74 (1.14–6.6)	0.02*

Note: *: $P < 0.05$; OS: overall survival rate; CI: confidence interval; HR: hazard ratio.

correlated with OS in GC patients with a medium degree of differentiation, namely, the lower the expression, the higher the overall survival rate. The mRNA expression of GPX1, GPX3, and GPX5 at different levels of differentiation had no correlation with OS in GC patients.

GPX plays an important role in the occurrence and development of tumors, and it can achieve fine regulation of tumor cells by affecting ROS levels. Different GPX subtypes play different roles in tumors, and the mechanisms of action need to be studied further [29]. JIAO et al. confirmed that high GPXs mRNA expression was related to the overall survival of lung adenocarcinoma patients by using the online tools GEPIA and cBioPortal database analysis, but the mechanism remains to be improved [30]. The results of this study showed that the low expression of GPX1 and GPX2 was beneficial to the prognosis of GC patients. The increased low expression of GPX3, GPX5, and GPX6 was detrimental to GC prognosis. The increased expression of GPX4 has no significant effect on the prognosis of GC patients. This study provides a novel approach for the prognosis of patients with GC assessment, preliminarily identified GPXs gene expression in gastric cancer and its prognosis diagnosis value. However, due to the slow updating of case samples, there are still some limitations that need to be improved and perfected. In other words, the advancements in the era of large data, database mining tumors, have helped to shorten the research period, improved the efficiency of scientific research, enhanced the reliability of the theoretical basis of the scientific research project, and can provide a powerful basis for the clinical treatment of GC.

Ethics approval and consent to participate

All information regarding human material was managed using anonymous numerical codes, and all samples were handled in compliance with the Declaration of Helsinki.

Consent for publication

All authors agree to publication.

Declarations

Author contribution statement

Siping Ye and Rui Lin Conceived and designed the experiments and Performed the experiments; Naiyuan Guo and Jiaying Xing Performed the experiments; Xiao Guo Analyzed and interpreted the data; Keyi Liu and Wenchuang Yang Contributed reagents, materials, analysis tools or data; all authors wrote the paper.

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Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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