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Analysis of demographics and treatment outcomes for gastrointestinal leiomyosarcoma based on the SEER database

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Knowledge of patients with gastrointestinal leiomyosarcoma (GILMS) is lacking. In this study, we aimed to clarify the disease features and prognosis of GILMS based on the Surveillance, Epidemiology, and End Results database. The clinicopathological, treatment, survival, and prognostic data of GILMS from 2000–2020 were retrieved. Appropriate statistical approaches were used to evaluate demographic characteristics and survival outcomes. A total of 479 individuals with GILMS met the screening criteria. The median age of patients was 64 (15–90) years. Only 7.9% of these cases were diagnosed with lymph node metastasis. T2 or higher primary tumor extension was diagnosed in 78.1% of the patients. The 5-year cancer-specific survival (CSS) of patients who had and had not undergone surgery was 66.5% and 0%, respectively. Multivariate Cox proportional hazards analysis based on overall survival and CSS showed that female sex was a significant independent protective factor. Significant independent risk factors included age 65–79, age ≥ 80, poor differentiation, T2 and higher T stage, distant metastasis, and no surgery. Neither chemotherapy nor radiotherapy influenced survival or prognosis. This comprehensive analysis underscored the necessity of surgical excision for prolonging survival times and highlighted the urgent need to explore effective systematic treatments.

Keywords Chemotherapy, Gastrointestinal leiomyosarcomas, Radiotherapy, SEER, Surgery

Soft tissue sarcomas (STSs) are a rare subtype of malignant tumors with a low incidence rate of 0.69% in the United States in 2022[1]. Leiomyosarcoma (LMS) is a relatively common subtype of STSs, representing approximately 10% to 20% of all STSs[2]. Common sites of origin include the uterus, large blood vessels, and the retroperitoneum[3]. The clinical behavior and response to LMS therapy at different primary sites vary[4,5]. The uterus is the most vulnerable to LMS compared with other organs. Understanding the behavior of uterine LMS is feasible in large population-based studies[3]. Considering the rarity of LMS in certain sites, such as the gastrointestinal (GI) tract, related clinical studies remain critical to elucidate clinicopathological and prognostic information. Moreover, these investigations can inform clinicians of LMS in the GI tract.

Prior to discovering gene mutations in KIT (before 2000), gastrointestinal stromal tumors (GISTs) were defined as LMS[6]. GISTs are distinguished from gastrointestinal leiomyosarcoma (GILMS) according to genomic alterations (FDGFRA or KIT) and immunohistochemical indicators (CD117 and/or CD34, DOG1)[5]. This distinction is paramount, as GILMS is rarer and has different treatments and prognoses than GISTs[7]. Few retrospective studies are available, and many have small cohorts[7,8]. One study analyzed only 11 cases and reviewed the published literature on GILMS since 2000. Another study summarized the limited clinicopathological features and survival outcomes of 47 patients in a single institution between 2000 and 2020. Demographics, tumor extension, and lymph and distant metastasis rates have not been well described in the literature. Furthermore, surgical outcomes and responses to chemotherapy and radiotherapy remain poorly understood.

The Surveillance, Epidemiology, and End Result Analysis (SEER) database includes demographic, treatment, and prognostic data for approximately 28% of the American population. Using the SEER database, we aimed to clarify the clinical characteristics and survival outcomes of a large cohort of patients with GILMS and to further improve the recognition of this rare STS subtype.

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Methods

Participants

We retrieved the SEER dataset named "the Incidence – SEER Research Data, 17 Registries, Nov 2022 Sub (2000–2020)." Data were downloaded using the SEER*Stat software (version 8.4.2) acquired from the SEER official website (https://seer.cancer.gov/data-software/). Cases with a GILMS diagnosis were identified according to the specific histologic International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) codes: 8890/3, 8891/3, 8896/3 and their corresponding location: site recode ICD-O-3/World Health Organization 2008: esophagus, stomach, small intestine, and colorectum.

Variables

The clinicopathological variables analyzed included sex, year of diagnosis, ethnicity, age, and primary site (labeled, grade record, regional node positivity, metastasis positivity, surgery, radiotherapy, chemotherapy, tumor size, primary tumor extension, vital status records, and survival months). No recommended American Joint Committee on Cancer (AJCC) prognostic stage groups were used at this time; however, the definitions of primary tumor (T), regional lymph node (N), and distant metastasis (M) were used clinically. T was classified as T1 (organ-confined), T2 (tumor extension into the tissue beyond the organ), T3 (invading another organ), or T4 (multifocal involvement). The N stage was further subdivided into N0 (no lymph node involvement) and N1 (lymph node involvement). The AJCC also classifies the M as M0 (no metastasis) and M1 (metastasis present)[9].

First, 704 patients with GILMS were identified between January 1, 2000, and December 31, 2020. Twelve patients without records of surgery, survival months, or race were excluded. Finally, 479 patients were included after 213 patients with missing information on tumor size, tumor extension, lymphatic metastasis, and distant metastasis were excluded. The screening process is illustrated in Fig. 1.

Statistical analysis

Unordered variables were analyzed using the chi-square test. The ranked variables were compared using the rank-sum test. Continuous variables were compared using Student's t-test or one-way analysis of variance. Kaplan–Meier plots were used to create the survival curves. Survival was compared between different variables using the log-rank test. The Cox proportional hazards model was used to identify prognostic factors for overall survival (OS) and cancer-specific survival (CSS). To ascertain the influence of GILMS on survival, a death due to GILMS was defined as an event, and other reasons were censored observations. CSS was defined as the period from diagnosis to death caused by GILMS or until the last follow-up. One-to-one propensity score matching (PSM) analysis was used to adjust for confounding factors in chemotherapy (n = 42) and radiotherapy (n = 41). Survival differences were also analyzed using Kaplan–Meier curves and log-rank tests. All the statistical analyses were performed using version 26.0 (IBM Inc., Chicago, IL, USA). A two-tailed p-value < 0.05 indicated statistical significance.

The methods used in this study were conducted in accordance with the research guidelines published in the SEER database. This study was approved by the Institutional Review Board at the Third Affiliated Hospital of Kunming Medical University.

Results

Features of patients with GILMS

As shown in Fig. 1, 704 patients were diagnosed with GILMS between 2000 and 2020. Our line chart shows minimal variation in yearly cases over the last two decades (Fig. 2A). Disease-specific information on patients with GILMS is shown in Table 1. The male-to-female ratio was close to 1, and 50.5% of patients were male. The mean age was 63 ± 14 years, and patients aged > 50 were the major population, accounting for 82.9%. Only 3.8% of the patients had a primary site in the esophagus. A total of 78.1% of patients were diagnosed with T2 or higher primary tumor extension. The rate of lymph node metastasis was 7.9%, and 55 patients (11.5%) were diagnosed with distant organ metastasis. Regarding therapeutic measures, 8.6% of patients with GILMS received radiotherapy and 13.8% underwent chemotherapy. Most of the patients (93.9%) received surgical management. Surgery alone (77.2%) was the most common treatment regimen (Fig. 2B).

Next, we evaluated the discrepancies in demographic, pathologic, and treatment data based on T stages or sex break down as survival and prognostic differences between various T stages and sexes were apparent. A comparison of the clinicopathological information is shown in Table 2. Patients diagnosed in earlier years were more likely to be in an advanced T stage ($p = 0.007$). Patients with T3–T4 stage meant a higher proportion of lymph node metastasis (12.8%, $p = 0.031$), distant metastasis (18.3%, $p = 0.011$), and undifferentiated differentiation ($p = 0.043$). Patients with a primary site in the small intestine showed a trend toward T3–T4 (42.2%), whereas primary sites in the colorectum had a higher proportion of T1–T2 (40.0%, $p = 0.050$). Regarding treatment measures, patients with T3–T4 had a higher proportion of chemotherapy (32.1%, $p < 0.001$) and a lower possibility of surgery compared with those with T1–T2 (87.2%, $p = 0.001$). Compared with men, women usually had a younger onset age ($p = 0.005$) and a lower rate of distant metastasis (8.5%, $p = 0.039$). As shown in Table 3, the years of diagnosis ($p = 0.004$), tumor size ($p = 0.003$), tumor extension ($p = 0.032$), surgery ($p = 0.005$), and radiotherapy ($p < 0.004$) of GILMS were significantly different at various tumor sites. The proportion of patients primarily diagnosed with GILMS in the small intestine and colorectum between 2011 and 2020 increased compared with those diagnosed in 2000–2010. The GILMS tumor size in the colorectum was smaller than that at other sites. GILMS in the stomach and small intestine were diagnosed at a higher T stage than those in the esophagus and colorectum. Moreover, patients with GILMS of the esophagus had a lower proportion of surgeries (77.8%) and a higher ratio of radiotherapy (44.4%).

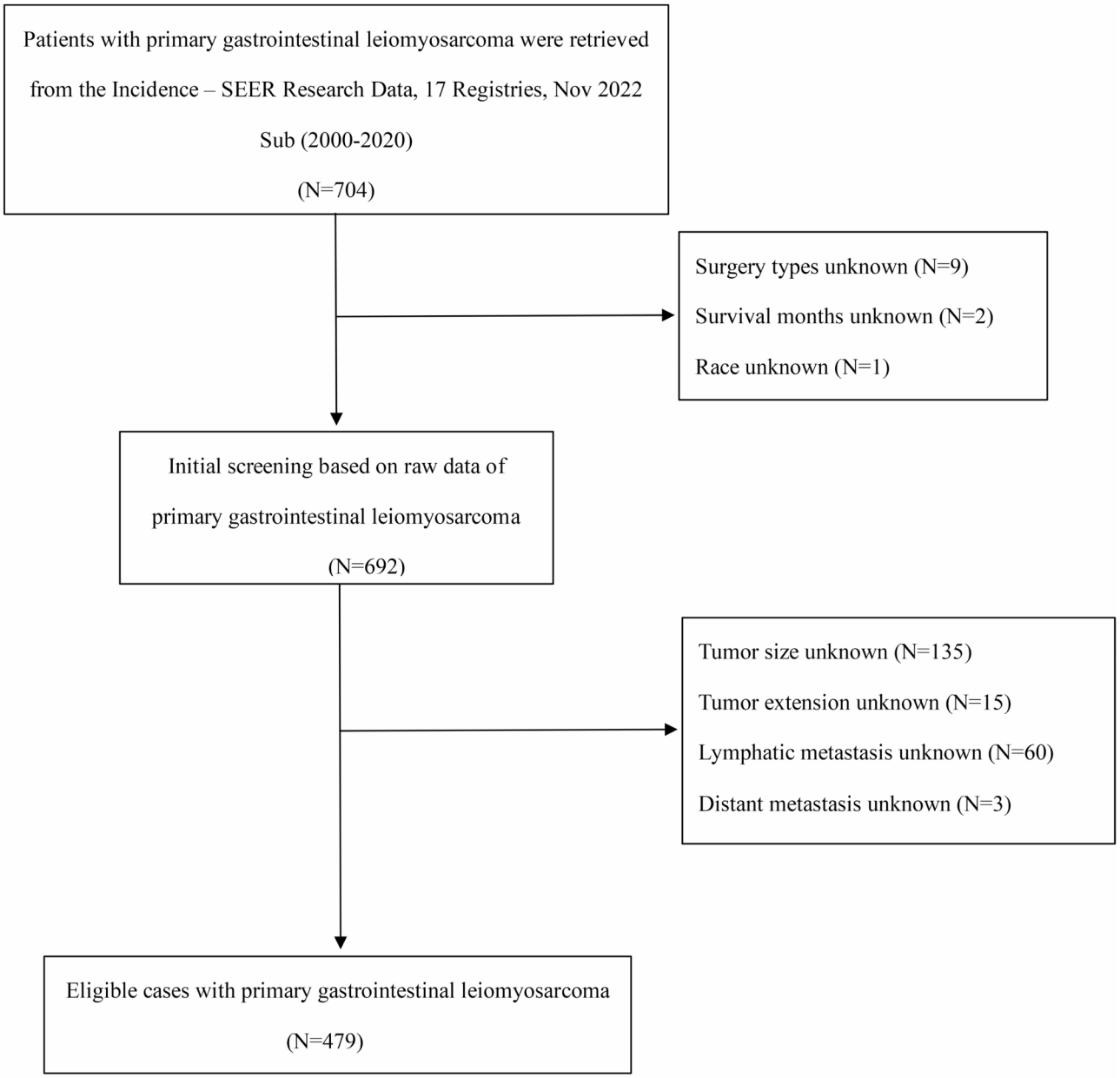

Fig. 1. Case selection process.

Survival analysis

The 1-, 3-, and 5-year OS of patients with GILMS was 84.0%, 64.9%, and 54.6%, respectively (Fig. 3A). The 1-, 3-, and 5-year CSS compared with OS were 87.7%, 72.1%, and 64.1%, respectively (Fig. 3B). Compared with men, women had better OS and CSS ($p < 0.001$) (Fig. 3C, D). Patients diagnosed with good and moderate differentiation showed significantly higher OS and CSS rates ($p < 0.001$) than those diagnosed with poor and undifferentiated types (Fig. 3E, F). Patients with early T stage had significantly longer OS and CSS than those with advanced T stage ($p < 0.001$) (Fig. 3G, H). The onset of distant metastasis was associated with poorer OS and CSS ($p < 0.001$) (Fig. 3I, J). Surgery resulted in obvious survival benefits in OS and CSS (Fig. 3K, L) ($p < 0.001$). Longitudinal analysis demonstrated a trend of improvement in OS and CSS from 2006 to 2020, although the p-value was not significant. The 5-year CSS rate of patients with GILMS between 2006 and 2010 was 59.7%, which increased to 65.2 between 2016 and 2020 (Fig. 3M, N). Patients who received radiotherapy and chemotherapy did not show a prolonged survival time and had shorter survival times than patients who did not receive chemotherapy or radiotherapy. The baseline features of patients with or without chemotherapy and radiotherapy varied greatly, which might have influenced the survival outcomes (Supplementary Table 1 and Supplementary Table 2). Thus, we used PSM to erase the baseline differences. However, neither chemotherapy nor radiotherapy benefited patients with GILMS in the PSM (Fig. 4). The 1-, 3-, and 5-year OS and CSS rates for the relevant variables are detailed in Table 4.

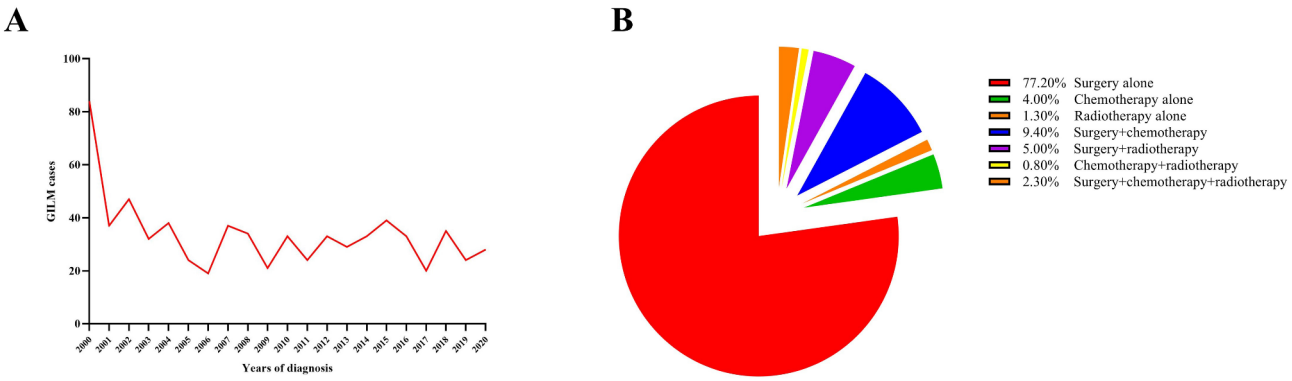

Fig. 2. (**A**) Line chart for number of diagnosed GILMS cases each year between 2000 and 2020. (**B**) Pie chart for therapeutic measures of patients with GILMS. GILMS, gastrointestinal leiomyosarcoma

Prognosis analysis

The results of the Cox proportional hazards model analysis for patients with GILMS are shown in Table 5. Prognostic analyses were performed for OS and CSS. Univariate analysis indicated that female sex, younger age, good differentiation, small tumor size, early T stage, absence of lymph nodes, and distant metastasis were protective factors for OS and CSS ($p < 0.05$). Surgery is a beneficial therapeutic measure, and chemotherapy may result in a poor prognosis ($p < 0.05$). The OS-related independent protective variable was female sex (hazard ratio [HR] = 0.711, 95% confidence interval [CI] 0.549–0.921; $p = 0.010$). Female sex was also an independent protective factor for CSS (HR = 0.657, 95% CI 0.485–0.890; $p = 0.007$). CSS-related multivariate analysis demonstrated the following as risk factors: age of 65–79 (HR = 2.107, 95% CI 1.292–3.435; $p = 0.003$), age of ≥ 80 years (HR = 3.787, 95% CI 2.198–6.526; $p < 0.001$), poor differentiation (HR = 2.507, 95% CI 1.215–5.175; $p = 0.013$), T2 (HR = 1.659, 95% CI 1.005–2.740; $p = 0.048$), T3 (HR = 2.706, 95% CI 1.474–4.967; $p = 0.001$), T4 (HR = 2.465, 95% CI 1.340–4.534; $p = 0.004$), distant metastasis (HR = 1.875, 95% CI 1.226–52.867; $p = 0.004$), and no surgery (HR = 3.436, 95% CI 2.048–5.765; $p < 0.001$). Independent prognostic analysis based on OS also revealed another risk factor, tumor size > 10 cm (HR = 1.771, 95% CI 1.247–2.515; $p = 0.001$), in addition to the variables mentioned in the CSS-related independent factor analysis above.

Discussion

GILMS is rare. To date, only a few cohort studies have focused on GILMS because of its rarity. A series of 11 patients with GILMS was published by The American University of Beirut Medical Centre in 2016[8]. The relatively small sample size limited the analysis of histopathological features, adjuvant therapy, and outcomes, although this study had the largest number of patients at that time. In 2021, a larger case study included 46 patients at The Royal Marsden Hospital in the United Kingdom[7]. This study lacked information on therapeutic efficiency, survival months, and prognosis. Some clinicopathological data require a larger, population-based study to validate these findings. Data mining of rare malignant tumors is convenient in the SEER database because of the large population size. Also in 2021, the prognostic factors of 523 patients with GILMS from the SEER Program 18 registry between 2001 and 2016 were reported. However, this study had its limitations as the sample size was smaller than that in our study, and information on tumor size, T and N stages, and treatment information, including radiotherapy and chemotherapy, was lacking[10]. This study did not include information about the epidemiology and treatment outcomes that were comprehensively discussed in our study. We identified 704 patients with GILMS over the past two decades from the SEER database. This is the largest study to clarify the clinicopathological characteristics, survival, and prognostic factors, thereby addressing the knowledge gaps on the behavior of this rare STS subtype. Our study covered 20 years, starting in 2000, and distinguished the molecular subtype of LMS from GISTs. The diagnosis of this disease was steady and rare over this period, illustrating the difficulty in validating its etiology.

As with LMS, the incidence generally peaks in the seventh decade and the overall incidence rate increases with age[11]. Our study suggests that 68.9% of the patients with GILMS were diagnosed at an older age (50–79 years). The median age of GILMS onset in this cohort was 64 years, which was older than the age of patients (56 years) with GILMS in previous studies[8,12,13]. Older age is a risk factor for developing GILMS. We indicate that females (49.5%) had a similar proportion to males (50.5%). These results are inconsistent with the outcomes of a retrospective study conducted by Alpert et al. on 407 individuals with GI smooth muscle tumors. They found that the number of females was higher than in males[13]. Although GI smooth muscle tumors include benign smooth muscle tumors except for GILMS, 407 cases were valuable for GILMS recognition. In contrast to previous reports, our study indicated that there were fewer patients with esophageal LMS (18 cases) than gastric LMS.

The mean tumor size was 7.7 cm, which is consistent with the findings of a previous study. A relatively large tumor size often implies an increased proportion of high tumor extension. Localized tumors (T1) only accounted for 21.9% of GILMS cases. These data are extremely low compared with those of prior studies. Complete excision with negative margins (R0 resection) remains the cornerstone treatment, offering the best option for a cure[14].

Characteristics	GILMS	
	N	%
All	479	100
Gender		
Male	242	50.5
Female	237	49.5
Age at diagnosis (years old)		
Median	64 years old	
Mean	63 ± 14 years old	
< 50	82	17.1
50–64	164	34.2
65–79	166	34.7
≥ 80	67	14.0
Years of diagnosis		
2000–2005	159	33.2
2006–2010	80	16.7
2011–2015	111	23.2
2016–2020	129	26.9
Ethnicity		
Caucasian	382	79.7
African-American	60	12.5
Asian	37	7.7
Primary sites		
Esophagus	18	3.8
Stomach	121	25.3
Small intestine	163	34.0
Colorectum	177	37.0
Pathological differentiation		
Well	33	6.9
Moderate	67	14.0
Poor	61	12.7
Undifferentiated	111	23.2
Unknown	207	43.2
Tumor size (cm)		
Median	6.0 cm	
Mean	7.7 ± 5.5 cm	
0–5 cm	179	37.4
5–10 cm	195	40.7
> 10 cm	105	21.9
Tumor extension		
T1	105	21.9
T2	265	55.3
T3	60	12.5
T4	49	10.2
Lymphatic metastasis		
Yes	38	7.9
No	441	92.1
Distant metastasis		
Yes	55	11.5
No	424	88.5
Surgery		
Yes	450	93.9
No	29	6.1
Radiotherapy		
Yes	41	8.6
No	438	91.4
Chemotherapy		
Continued		

Characteristics	GILMS	
	N	%
Yes	66	13.8
No	413	86.2
Treatment regimens		
Surgery alone	370	77.2
Chemotherapy alone	19	4.0
Radiotherapy alone	6	1.3
Surgery + chemotherapy	45	9.4
Surgery + radiotherapy	24	5.0
Chemotherapy + radiotherapy	4	0.8
Surgery + chemotherapy + radiotherapy	11	2.3

Table 1. Characteristics of patients with GILMS (N = 479).

The survival benefits of surgery reported in our cohort are essential in supporting this treatment. A total of 93.9% of patients with GILMS had surgery, although 78.1% of them were diagnosed with a high T stage. GILMS with large tumor size and high extension may achieve a higher rate of surgical R0 resection than in extraperitoneal LMS, such as the retroperitoneum (65%), as a result of anatomic convenience[15].

A total of 11.5% of patients with GILMS had synchronous metastasis at diagnosis. This was lower than in large retrospective cohorts across STS subtypes (14–26.5%)[16]. The occurrence of synchronous metastasis meant extremely low survival times (14.8% 5-year OS and 25.8% 5-year CSS). Studies have indicated a low likelihood of nodal metastasis[17]. Our analysis aligns with this conclusion, as a 7.9% nodal metastasis rate was observed in our cohort. Positive lymphatic metastasis suggested worse survival outcomes (40.0% 5-year OS and 55.6% 5-year CSS).

Sixty-six individuals received chemotherapy in this series, which is the largest number for the analysis of chemotherapy in clinical studies. Our data show that chemotherapy did not improve patient survival rates. Furthermore, patients who underwent chemotherapy had a shorter survival time (5-year OS: 37.2% vs. 57.0%; 5-year CSS: 43.9 vs. 67.1%). This outcome was partly due to a large proportion of high tumor extension in chemotherapy (32.1% vs. 8.4%). Some studies suggest that contemporary chemotherapy protocols (doxorubicin-based or gemcitabine-based) have no real benefits on survival[18,19]. No established first-line chemotherapeutic treatments currently exist. We attempted to eliminate variable differentiation using PSM. The PSM results showed no significant difference in survival between the two groups, which is consistent with previous studies. Only 8.6% of patients received radiotherapy, which showed a similar lack of survival difference with chemotherapy. In addition, radiation exposure may be considered a putative trigger for developing GILMS[20]. No effective radiotherapeutic treatments currently exist. Moreover, the small sample size (66 patients received chemotherapy and 41 patients received radiotherapy) may be the decisive factor that resulted in no survival benefits for the two types of therapy. A larger cohort is needed from a statistical perspective to determine whether there is any survival benefit for either treatment.

Pathological differentiation grade, tumor size, and extent of tumor invasion are the three common prognostic factors for STS[21,22]. This is the first study to show that sex, age, synchronous metastasis, and surgery are significant independent prognostic factors. Females usually have a better prognosis than males. However, the potential mechanisms underlying these results require further exploration. Older age indicates a poor prognosis, which may be caused by difficulties in physical recovery and severe complications.

Our study has some limitations. First, the signs and symptoms that may reflect the invasive range of GILMS were not recorded in the SEER database. Most of the patients with GILMS (96%) had specific symptoms, such as abdominal pain, bleeding, intussusception, and bowel obstruction[7]. The presentation of these symptoms was high compared with iliocaval LMS and GISTs (77–81%)[23–25]. Discovering common GILMS symptoms is essential for diagnosing this sarcoma and improving survival outcomes. However, establishing a summary of symptoms is difficult, given their variable presentation and rarity. Second, the GILMS recurrence rate after therapy was lacking in the SEER database. The recurrence rate after therapy is critical for evaluating the efficacy of various treatment regimens and survival outcomes. Half of the patients with GILMS experience recurrence even after complete oncologic resection[7]. The high rate of distant metastasis with surgery supports the notion that systematic therapy may be the cornerstone for this anatomical LMS variant. Third, R0 status, representing negative surgical margins after surgery, is pivotal for patient survival outcomes. However, in the current study, we only had information on whether patients underwent surgery, and R0 status was not included in the SEER database. Lastly, the names of chemotherapeutics, chemotherapy protocols, combination therapy regimens, and treatment orders for surgery and chemoradiotherapy were missing in the SEER database.

Conclusion

This study included the largest cohort of patients with GILMS. First, we systematically described the clinicopathological characteristics, survival, and prognostic factors of patients with GILMS. GILMS was frequently diagnosed in older patients with low rates of nodal and distant metastases. However, most GILMS cases had a large tumor size and a high extent of tumor invasion. Surgical excision was a unique and effective

Characteristics	T1-2		T3-4		*p* value	Male		Female		*p* value
	N	%	N	%		N	%	N	%	
All	370	100	109	100		242	100	237	100	
Gender					0.839	–	–	–	–	
Male	186	50.3	56	51.4		–	–	–	–	
Female	184	49.7	53	48.6						
Age at diagnosis (years)					0.396					**0.005**
< 50	64	17.3	18	16.5		32	13.2	50	21.1	
50–64	124	33.5	40	36.7		79	32.6	85	35.9	
65–79	125	33.8	41	37.6		101	41.7	65	27.4	
≥ 80	57	15.4	10	9.2		30	12.4	37	15.6	
Years of diagnosis					**0.007**					0.140
2000–2005	110	29.7	49	45.0		73	30.2	86	36.3	
2006–2010	59	15.9	21	19.3		49	20.2	31	13.1	
2011–2015	93	25.1	18	16.5		53	21.9	58	24.5	
2016–2020	108	29.2	21	19.3		67	27.7	62	26.2	
Ethnicity					0.981					0.184
Caucasian	295	79.7	87	79.8		201	83.1	181	76.4	
African-American	46	12.4	14	12.8		26	10.7	34	14.3	
Asian	29	7.8	8	7.3		15	6.2	22	9.3	
Primary sites					**0.050**					0.137
Esophagus	15	4.1	3	2.8		13	5.4	5	2.1	
Stomach	90	24.3	31	28.4		61	25.2	60	25.3	
Small intestine	117	31.6	46	42.2		87	36.0	76	32.1	
Colorectum	148	40.0	29	26.6		81	33.5	96	40.5	
Pathological differentiation					**0.043**					0.077
Well	30	8.1	3	2.8		11	4.5	22	9.3	
Moderate	53	14.3	14	12.8		31	12.8	36	15.2	
Poor	52	14.1	9	8.3		29	12.0	32	13.5	
Undifferentiated	77	20.8	34	31.2		53	21.9	58	24.5	
Unknown	158	42.7	49	45.0		118	48.8	89	37.6	
Tumor size (cm)					**< 0.001**					0.450
0–5 cm	159	43.0	20	18.3		85	35.1	94	39.7	
5–10 cm	144	38.9	51	46.8		99	40.9	96	40.5	
> 10 cm	67	18.1	38	34.9		58	24.0	47	19.8	
Tumor extension										0.907
T1-2	–	–	–	–		186	76.9	184	77.6	
T3-4	–	–	–	–		56	23.1	53	22.4	
Lymphatic metastasis					**0.031**					0.343
Yes	24	6.5	14	12.8		220	90.9	221	93.2	
No	346	93.5	95	87.2		22	9.1	16	6.8	
Distant metastasis					**0.011**					**0.039**
Yes	35	9.5	20	18.3		35	14.5	20	8.4	
No	335	90.5	89	81.7		207	85.5	217	91.6	
Surgery					**0.001**					0.605
Yes	355	95.9	95	87.2		226	93.4	224	94.5	
No	15	4.1	14	12.8		16	6.6	13	5.5	
Radiotherapy					0.515					0.375
Yes	30	8.1	11	10.1		18	7.4	23	9.7	
No	340	91.9	98	89.9		224	92.6	214	90.3	
Chemotherapy					**< 0.001**					0.078
Yes	31	8.4	35	32.1		40	16.5	26	11.0	
No	339	91.6	74	67.9		202	83.5	211	89.0	

Table 2. Characteristics of GILMS patients classified by tumor extension and gender respectively. Significant values are in bold.

Characteristics	Esophagus		Stomach		Small intestine		Colorectum		*p* value
	N	%	N	%	N	%	N	%	
All	18	100	121	100	163	100	177	100	
Gender									0.130
Male	13	72.2	61	50.4	87	53.4	81	45.8	
Female	5	27.8	60	49.6	76	46.6	96	54.2	
Age at diagnosis (years)									0.076
< 50	1	5.6	29	24.0	26	16.0	26	14.7	
50–64	9	50.0	28	23.1	60	36.8	67	37.9	
65–79	7	38.9	49	40.5	51	31.3	59	33.3	
≥ 80	1	5.6	15	12.4	26	16.0	25	14.1	
Years of diagnosis									**0.004**
2000–2005	9	50.0	58	47.9	48	29.4	44	24.9	
2006–2010	3	16.7	16	13.2	31	19.0	30	16.9	
2011–2015	4	22.2	25	20.7	34	20.9	48	27.1	
2016–2020	2	11.1	22	18.2	50	30.7	55	31.1	
Ethnicity									0.493
Caucasian	12	66.7	94	77.7	131	80.4	145	81.9	
African-American	4	22.2	18	14.9	22	13.5	16	9.0	
Asian	2	11.1	9	7.4	10	6.1	16	9.0	
Pathological differentiation									
Well	0	0	10	8.3	12	7.4	11	6.2	0.880
Moderate	4	22.2	18	14.9	27	16.6	18	10.2	
Poor	4	22.2	11	9.1	19	11.7	27	15.3	
Undifferentiated	3	16.7	22	18.2	41	25.2	45	25.4	
Unknown	7	38.9	60	49.6	64	39.3	76	42.9	
Tumor size (cm)									**0.003**
0–5 cm	6	33.3	34	28.1	51	31.3	88	49.7	
5–10 cm	9	50.0	53	43.8	73	44.8	60	33.9	
> 10 cm	3	16.7	34	28.1	39	23.9	29	16.4	
Tumor extension									**0.032**
T1-2	15	83.3	90	74.4	117	71.8	148	83.6	
T3-4	3	16.7	31	25.6	46	28.2	29	16.4	
Lymphatic metastasis									0.051
Yes	0	0	5	4.1	12	7.4	21	11.9	
No	18	100	116	95.9	151	92.6	156	88.1	
Distant metastasis									0.560
Yes	1	5.6	11	9.1	19	11.7	24	13.6	
No	17	94.4	110	90.9	144	88.3	153	86.4	
Surgery									**0.005**
Yes	14	77.8	110	90.9	155	95.1	171	96.6	
No	4	22.2	11	9.1	8	4.9	6	3.4	
Radiotherapy									**< 0.001**
Yes	8	44.4	10	8.3	3	1.8	20	11.3	
No	10	55.6	111	91.7	160	98.2	157	88.7	
Chemotherapy									0.810
Yes	3	16.7	14	11.6	25	15.3	24	13.6	
No	15	83.3	107	88.4	138	84.7	153	86.4	

Table 3. Characteristics of GILM patients classified by different origins. Significant values are in bold.

approach to prolong survival. Chemotherapy and radiotherapy had no benefit on the prognosis, highlighting the urgent need for better systematic treatment to improve the survival outcomes of patients with GILMS.

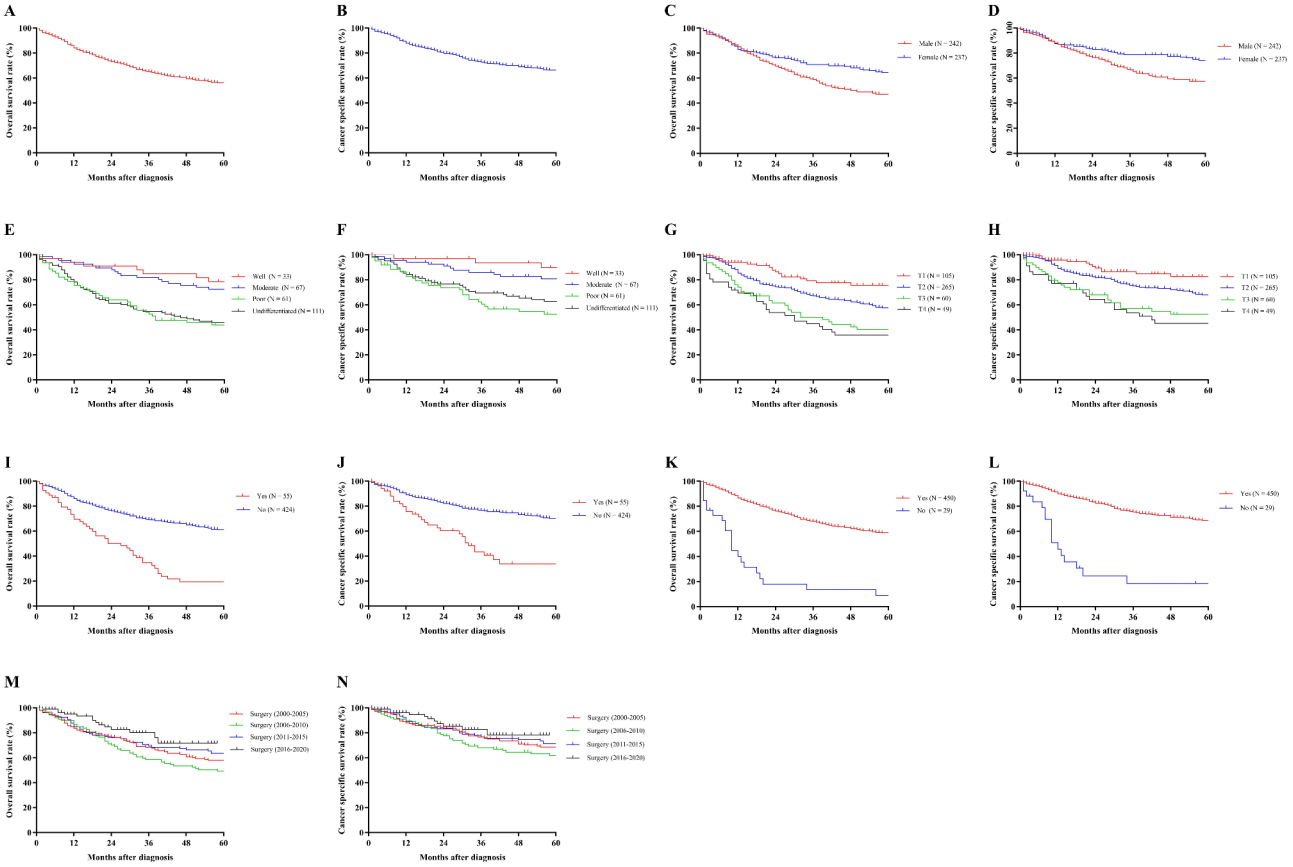

Fig. 3. Kaplan–Meier curve analysis for certain variables of patients with GILMS. (**A**) OS curve for patients with GILMS. (**B**) CSS curve for patients with GILMS. (**C**) OS analysis for males and females. (**D**) CSS analysis for males and females; (**E**) OS outcomes of different differentiation subtypes. (**F**) CSS outcomes of different differentiation subtypes. (**G**) OS analysis based on different T stages. (**H**) CSS analysis based on different T stages. (**I**) OS outcomes for patients with or without lymph node metastasis. (**J**) CSS outcomes for patients with or without lymph node metastasis. (**K**) Influence of surgery on OS for patients with GILMS. (**L**) Influence of surgery on CSS for patients with GILMS. (**M**) Influence of surgery on OS for patients with GILMS during different diagnosis years. (**N**) Influence of surgery on CSS for patients with GILMS during different diagnosis years. GILMS, gastrointestinal leiomyosarcoma; OS, overall survival; CSS, cancer-specific survival.

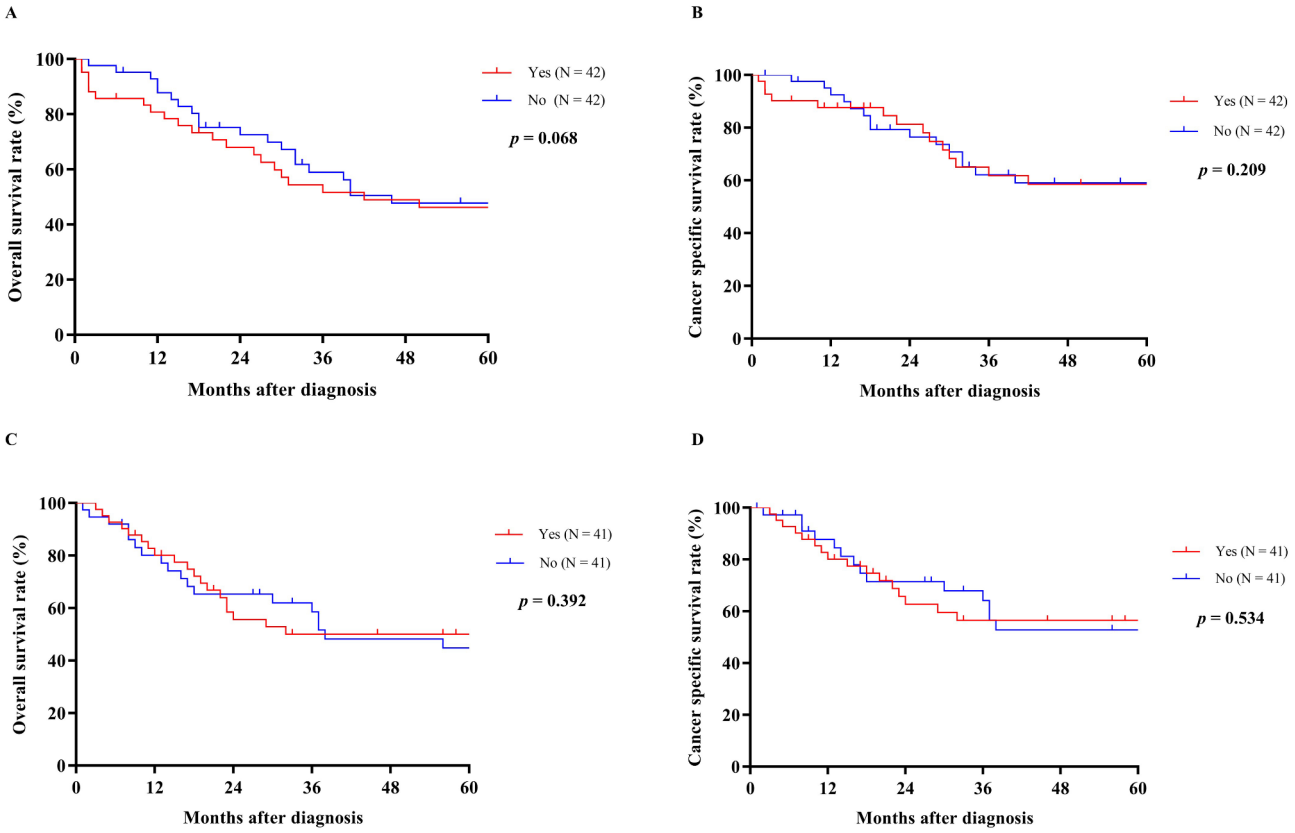

Fig. 4. Kaplan–Meier curve analysis of chemotherapy and radiotherapy after PSM. (**A**) OS curve for patients with GILMS with or without chemotherapy. (**B**) CSS curve for patients with GILMS with or without chemotherapy. (**C**) OS analysis for patients with GILMS with or without radiotherapy. (**D**) CSS analysis for patients with GILMS with or without radiotherapy. PSM, propensity score matching; GILMS, gastrointestinal leiomyosarcoma; OS, overall survival; CSS, cancer-specific survival

Variables	OS rate			CSS rate		
	1-year	3-year	5-year	1-year	3-year	5-year
Gender						
Male	0.834 (0.787–0.881)	0.576 (0.509–0.643)	0.463 (0.394–0.532)	0.869 (0.826–0.912)	0.657 (0.59–0.724)	0.568 (0.495–0.641)
Female	0.815 (0.764–0.866)	0.697 (0.636–0.758)	0.634 (0.569–0.699)	0.86 (0.815–0.905)	0.773 (0.716–0.83)	0.731 (0.668–0.794)
Age at diagnosis (years)						
< 50	0.959 (0.914–1.004)	0.799 (0.705–0.893)	0.681 (0.567–0.795)	0.959 (0.914–1.004)	0.812 (0.72–0.904)	0.739 (0.631–0.847)
50–64	0.872 (0.819–0.925)	0.678 (0.602–0.754)	0.570 (0.488–0.652)	0.902 (0.855–0.949)	0.765 (0.694–0.836)	0.676 (0.594–0.758)
65–79	0.803 (0.742–0.864)	0.587 (0.509–0.665)	0.482 (0.400–0.564)	0.855 (0.800–0.910)	0.695 (0.619–0.771)	0.613 (0.529–0.697)
≥ 80	0.607 (0.489–0.725)	0.477 (0.354–0.600)	0.403 (0.28–0.526)	0.680 (0.564–0.796)	0.532 (0.403–0.661)	0.488 (0.357–0.619)
Years of diagnosis						
2000–2005	0.780 (0.715–0.845)	0.635 (0.561–0.709)	0.528 (0.450–0.606)	0.825 (0.764–0.886)	0.715 (0.642–0.788)	0.634 (0.556–0.712)
2006–2010	0.788 (0.698–0.878)	0.556 (0.446–0.666)	0.439 (0.329–0.549)	0.822 (0.738–0.906)	0.663 (0.555–0.771)	0.597 (0.481–0.713)
2011–2015	0.864 (0.799–0.929)	0.617 (0.527–0.707)	0.553 (0.459–0.647)	0.907 (0.852–0.962)	0.704 (0.614–0.794)	0.641 (0.547–0.735)
2016–2020	0.873 (0.810–0.936)	0.723 (0.629–0.817)	0.603 (0.466–0.740)	0.906 (0.851–0.961)	0.761 (0.667–0.855)	0.652 (0.511–0.793)
Ethnicity						
Asian	0.773 (0.634–0.912)	0.619 (0.454–0.784)	0.583 (0.405–0.761)	0.798 (0.665–0.931)	0.731 (0.580–0.882)	0.675 (0.501–0.849)
African-American	0.828 (0.732–0.924)	0.634 (0.507–0.761)	0.505 (0.366–0.644)	0.894 (0.814–0.974)	0.744 (0.622–0.866)	0.662 (0.523–0.801)
Caucasian	0.829 (0.790–0.868)	0.640 (0.589–0.691)	0.554 (0.501–0.607)	0.863 (0.828–0.898)	0.704 (0.655–0.753)	0.644 (0.591–0.697)
Primary sites						
Stomach	0.797 (0.724–0.87)	0.606 (0.516–0.696)	0.536 (0.442–0.630)	0.811 (0.740–0.882)	0.669 (0.581–0.757)	0.612 (0.518–0.706)
Small intestine	0.821 (0.76–0.882)	0.598 (0.520–0.676)	0.476 (0.394–0.558)	0.888 (0.837–0.939)	0.711 (0.633–0.789)	0.615 (0.527–0.703)
Colorectum	0.853 (0.8–0.906)	0.708 (0.637–0.779)	0.608 (0.530–0.686)	0.893 (0.846–0.940)	0.770 (0.701–0.839)	0.700 (0.624–0.776)
Esophagus	0.778 (0.586–0.97)	0.538 (0.303–0.773)	0.404 (0.165–0.643)	0.778 (0.586–0.970)	0.538 (0.303–0.773)	0.462 (0.217–0.707)
Pathological differentiation						
Well	0.909 (0.811–1.007)	0.846 (0.723–0.969)	0.784 (0.643–0.925)	0.969 (0.908–1.03)	0.934 (0.846–1.022)	0.898 (0.788–1.008)
Moderate	0.924 (0.859–0.989)	0.817 (0.723–0.911)	0.707 (0.595–0.819)	0.939 (0.882–0.996)	0.859 (0.773–0.945)	0.808 (0.710–0.906)
Poor	0.754 (0.646–0.862)	0.525 (0.4–0.65)	0.399 (0.274–0.524)	0.828 (0.73–0.926)	0.605 (0.476–0.734)	0.476 (0.339–0.613)
Undifferentiated	0.755 (0.675–0.835)	0.526 (0.432–0.62)	0.421 (0.327–0.515)	0.820 (0.747–0.893)	0.675 (0.581–0.769)	0.596 (0.494–0.698)
Unknown	0.832 (0.779–0.885)	0.638 (0.564–0.712)	0.538 (0.458–0.618)	0.857 (0.806–0.908)	0.685 (0.612–0.758)	0.602 (0.522–0.682)
Tumor size (cm)						
0–5 cm	0.866 (0.815–0.917)	0.745 (0.676–0.814)	0.668 (0.592–0.744)	0.893 (0.846–0.940)	0.801 (0.738–0.864)	0.742 (0.669–0.815)
5–10 cm	0.836 (0.783–0.889)	0.598 (0.525–0.671)	0.490 (0.416–0.564)	0.870 (0.821–0.919)	0.675 (0.604–0.746)	0.595 (0.519–0.671)
> 10 cm	0.722 (0.634–0.81)	0.533 (0.433–0.633)	0.410 (0.310–0.510)	0.792 (0.710–0.874)	0.635 (0.535–0.735)	0.546 (0.436–0.656)
Tumor extension						
T1	0.926 (0.397–1.455)	0.774 (0.680–0.868)	0.733 (0.627–0.839)	0.945 (0.898–0.992)	0.846 (0.764–0.928)	0.825 (0.735–0.915)
T2	0.830 (0.785–0.875)	0.653 (0.594–0.712)	0.546 (0.483–0.609)	0.873 (0.832–0.914)	0.736 (0.679–0.793)	0.650 (0.587–0.713)
T3	0.742 (0.628–0.856)	0.482 (0.351–0.613)	0.364 (0.235–0.493)	0.776 (0.668–0.884)	0.571 (0.436–0.706)	0.497 (0.356–0.638)
T4	0.667 (0.534–0.800)	0.409 (0.268–0.550)	0.321 (0.188–0.454)	0.740 (0.613–0.867)	0.487 (0.334–0.640)	0.404 (0.251–0.557)
Lymphatic metastasis						
Yes	0.728 (0.585–0.871)	0.492 (0.325–0.659)	0.400 (0.235–0.565)	0.772 (0.633–0.911)	0.598 (0.426–0.77)	0.556 (0.376–0.736)
No	0.833 (0.798–0.868)	0.650 (0.603–0.697)	0.548 (0.497–0.599)	0.872 (0.841–0.903)	0.723 (0.678–0.768)	0.646 (0.595–0.697)
Distant metastasis						
Yes	0.683 (0.558–0.808)	0.318 (0.191–0.445)	0.148 (0.048–0.248)	0.742 (0.620–0.864)	0.398 (0.253–0.543)	0.258 (0.113–0.403)
No	0.843 (0.808–0.878)	0.679 (0.632–0.726)	0.584 (0.533–0.635)	0.880 (0.849–0.911)	0.754 (0.709–0.799)	0.678 (0.627–0.729)
Surgery						
Yes	0.854 (0.821–0.887)	0.67 (0.625–0.715)	0.565 (0.516–0.614)	0.889 (0.860–0.918)	0.747 (0.704–0.790)	0.665 (0.616–0.714)
No	0.359 (0.179–0.539)	0.120 (0–0.245)	0.120 (0–0.245)	0.427 (0.227–0.627)	0.171 (0.004–0.338)	0
Radiotherapy						
Yes	0.801 (0.678–0.924)	0.501 (0.340–0.662)	0.465 (0.302–0.628)	0.801 (0.678–0.924)	0.564 (0.399–0.729)	0.524 (0.353–0.695)
No	0.827 (0.792–0.862)	0.650 (0.603–0.697)	0.543 (0.492–0.594)	0.871 (0.838–0.904)	0.731 (0.686–0.776)	0.650 (0.599–0.701)
Chemotherapy						
Yes	0.816 (0.722–0.910)	0.461 (0.338–0.584)	0.342 (0.222–0.462)	0.844 (0.756–0.932)	0.503 (0.376–0.630)	0.439 (0.308–0.570)
No	0.826 (0.789–0.863)	0.668 (0.621–0.715)	0.570 (0.519–0.621)	0.868 (0.835–0.901)	0.754 (0.709–0.799)	0.671 (0.620–0.722)

Table 4. Overall cumulative and cancer-specific survival data of 479 patients with GILMS.

	OS				CSS			
	Univariate		Multivariate		Univariate		Multivariate	
Variables	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Gender								
Male	Reference		Reference		Reference		Reference	
Female	0.622 (0.489–0.791)	**< 0.001**	0.711 (0.549–0.921)	**0.010**	0.587 (0.442–0.779)	**< 0.001**	0.657 (0.485–0.890)	**0.007**
Age at diagnosis (years)		**< 0.001**		**< 0.001**		**< 0.001**		**< 0.001**
< 50	Reference		Reference		Reference		Reference	
50–64	1.539 (1.018–2.327)	**0.041**	1.432 (0.930–2.205)	0.103	1.411 (0.877–2.269)	0.156	1.277 (0.779–2.093)	0.333
65–79	2.317 (1.551–3.460)	**< 0.001**	2.356 (1.544–3.597)	**< 0.001**	2.086 (1.316–3.308)	**0.002**	2.107 (1.292–3.435)	**0.003**
≥ 80	3.572 (2.277–5.602)	**< 0.001**	3.879 (2.414–6.234)	**< 0.001**	3.382 (2.022–5.656)	**< 0.001**	3.787 (2.198–6.526)	**< 0.001**
Years of diagnosis		0.119				0.462		
2000–2005	Reference				Reference			
2006–2010	1.184 (0.865–1.621)	0.292			1.161 (0.799–1.688)	1.161		
2011–2015	0.94 (0.691–1.279)	0.695			0.944 (0.657–1.355)	0.944		
2016–2020	0.686 (0.453–1.039)	0.075			0.771 (0.481–1.235)	0.771		
Ethnicity		0.944				0.660		
Asian	Reference				Reference			
African-American	0.952 (0.552–1.64)	0.952			0.787 (0.403–1.538)	0.484		
Caucasian	0.929 (0.593–1.453)	0.929			0.973 (0.573–1.651)	0.918		
Primary sites		**0.037**		0.587		0.135		
Stomach	Reference		Reference		Reference			
Small intestine	1.159 (0.862–1.559)	0.328	1.058 (0.775–1.444)	0.723	1.005 (0.708–1.426)	0.979		
Colorectum	0.772 (0.564–1.056)	0.106	0.855 (0.609–1.2)	0.365	0.744 (0.518–1.069)	0.110		
Esophagus	1.28 (0.71–2.306)	0.411	1.01 (0.544–1.874)	0.975	1.405 (0.737–2.679)	0.301		
Pathological differentiation		**< 0.001**		**0.001**		**< 0.001**		**0.010**
Well	Reference		Reference		Reference		Reference	
Moderate	1.023 (0.563–1.858)	0.941	0.98 (0.531–1.806)	0.948	1.084 (0.513–2.29)	0.832	1.008 (0.471–2.158)	0.984
Poor	2.306 (1.294–4.109)	**0.005**	2.044 (1.128–3.703)	**0.018**	2.868 (1.411–5.831)	**0.004**	2.507 (1.215–5.175)	**0.013**
Undifferentiated	2.567 (1.502–4.386)	**0.001**	1.936 (1.113–3.37)	**0.019**	2.638 (1.343–5.184)	**0.005**	1.825 (0.911–3.659)	0.090
Unknown	1.703 (1.002–2.892)	**0.049**	1.325 (0.767–2.29)	0.313	2.155 (1.114–4.168)	**0.023**	1.6 (0.811–3.157)	0.175
Tumor size (cm)		**< 0.001**		**0.006**		**0.002**		0.140
0–5 cm	Reference		Reference		Reference		Reference	
5–10 cm	1.697 (1.279–2.252)	**< 0.001**	1.318 (0.971–1.789)	0.076	1.638 (1.18–2.272)	**0.003**	1.295 (0.918–1.827)	0.141
> 10 cm	2.096 (1.516–2.898)	**< 0.001**	1.771 (1.247–2.515)	**0.001**	1.855 (1.263–2.726)	**0.002**	1.492 (0.991–2.246)	0.056
Tumor extension		**< 0.001**		**0.014**		**< 0.001**		**0.005**
T1	Reference		Reference		Reference		Reference	
T2	1.99 (1.332–2.971)	**0.001**	1.563 (1.03–2.372)	**0.036**	2.062 (1.269–3.351)	**0.003**	1.659 (1.005–2.740)	**0.048**
T3	2.928 (1.819–4.713)	**< 0.001**	2.228 (1.334–3.723)	**0.002**	3.321 (1.888–5.842)	**< 0.001**	2.706 (1.474–4.967)	**0.001**
T4	3.172 (1.946–5.171)	**< 0.001**	1.98 (1.177–3.333)	**0.010**	3.701 (2.083–6.579)	**< 0.001**	2.465 (1.34–4.534)	**0.004**
Lymphatic metastasis								
Yes	Reference		Reference		Reference		Reference	
No	1.56 (1.049–2.322)	**0.028**	1.166 (0.756–1.799)	0.487	1.611 (1.014–2.558)	**0.043**	1.047 (0.635–1.724)	0.858
Distant metastasis								
Yes	Reference		Reference		Reference		Reference	
No	2.57 (1.862–3.545)	**< 0.001**	1.886 (1.305–2.726)	**0.001**	2.625 (1.803–3.82)	**< 0.001**	1.875 (1.226–2.867)	**0.004**
Surgery								
Yes	Reference		Reference		Reference		Reference	
No	4.594 (3.045–6.931)	**< 0.001**	3.333 (2.083–5.334)	**< 0.001**	4.907 (3.064–7.86)	**< 0.001**	3.436 (2.048–5.765)	**< 0.001**
Radiotherapy								
Yes	Reference				Reference			
No	0.754 (0.507–1.123)	0.165			0.661 (0.424–1.031)	0.068		
Chemotherapy								
Yes	Reference		Reference		Reference		Reference	
No	0.559 (0.412–0.759)	**< 0.001**	0.904 (0.623–1.311)	0.595	0.49 (0.347–0.693)	**< 0.001**	0.77 (0.505–1.174)	0.225

Table 5. Univariate and multivariate analysis for patients with GILM (N = 479). Significant values are in bold.

Data availability

The data that support this study can be found in the SEER database and supplementary file.

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Author contributions

Y.B., X.Y., and Q.Z made equal contributions to this article. Y.B., X.Y., and Q.Z: Writing—Original Draft, Conceptualization, Methodology. Formal analysis, Investigation, Resources, Visualization, Validation, Data curation. W.L.: Writing—Review & Editing, Supervision. Visualization, Resources, Validation, Data curation.

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Declarations

Competing interests
The authors declare no competing interests.

Informed consent
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