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Clinical features and prognostic analysis of early-onset gastric cancer treated with radiotherapy

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► ***Original article***

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ABSTRACT

Background: This study examines the clinicopathological characteristics, recurrence patterns, and survival outcomes of early-onset gastric cancer (EOGC) patients treated with radiotherapy, comparing them with non-early-onset gastric cancer (NEOGC) patients to evaluate prognostic differences and the effectiveness of radiotherapy-based treatments. ***Materials and Methods:*** A retrospective cohort study was conducted using the Surveillance, Epidemiology, and End Results (SEER) database (2010-2015), analyzing 814 EOGC and 4,997 NEOGC patients who underwent radiotherapy. Descriptive statistics characterized clinical and pathological features. Kaplan-Meier survival analysis and log-rank tests compared overall survival (OS). Cox proportional hazards regression models identified independent prognostic factors. ***Results:*** EOGC patients showed a higher proportion of females (42.3%) and advanced-stage disease (44.3%) compared to NEOGC. Signet-ring cell carcinoma was more prevalent in EOGC (26.8% vs. 14.7%, P < 0.001). Tumors in EOGC were predominantly located in the gastric body, fundus, and greater curvature (P < 0.001). Adjuvant radiotherapy was more common in EOGC (78.9% vs. 68.3%, P < 0.001). Survival analysis indicated that radiotherapy alone provided superior OS compared to combined chemoradiotherapy or surgery-radiotherapy approaches. Cox regression identified tumor stage, histological subtype, and radiotherapy modality as key prognostic factors. ***Conclusion:*** EOGC treated with radiotherapy exhibits distinct clinicopathological features, including more aggressive histological subtypes. Radiotherapy as monotherapy offers better long-term survival than multimodal treatments. These findings underscore the need for personalized radiotherapy strategies to optimize prognosis in EOGC.

INTRODUCTION

Gastric cancer remains a significant global health challenge, ranking among the most common malignancies worldwide, despite a gradual decline in its overall incidence in many regions [1, 2]. In contrast, early-onset gastric cancer (EOGC), typically defined as gastric cancer diagnosed in patients younger than 45 years, has shown a concerning rise in prevalence in both Western and Asian populations [3, 4]. This subtype is increasingly recognized for its distinct clinicopathological characteristics, including a higher prevalence of aggressive histological subtypes such as signet-ring cell carcinoma, a tendency to present at advanced stages, and a greater likelihood of lymph node metastasis compared with non-early-onset gastric cancer (NEOGC), which predominantly affects older individuals [5, 6].

Recent comprehensive reviews emphasize that EOGC may follow different molecular pathways and biological behaviors compared with conventional gastric cancer, supporting its recognition as a unique clinical entity [7]. Large cohort analyses have also demonstrated differences in metastasis patterns and overall survival between younger and older gastric cancer patients, with younger cases often showing more diffuse histology and worse outcomes [8]. A comparative SEER-based investigation further indicated that multimodal therapies, such as chemoradiotherapy or surgery combined with radiotherapy, may not always confer survival advantages in EOGC, raising questions about the applicability of standard treatment algorithms in this subgroup [9].

The role of radiotherapy in gastric cancer management remains controversial. While adjuvant or definitive radiotherapy has demonstrated benefit in certain contexts, particularly in unresectable disease or high-risk postoperative settings, other studies argue that its routine use is limited and should be carefully tailored [10, 11]. Moreover, although hereditary cancer syndromes explain a minority of EOGC cases, the majority are nonhereditary, representing an unmet clinical need where optimal treatment remains undefined [12]. At a broader level, recent international data highlight heterogeneous use

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of radiotherapy across gastrointestinal malignancies, underscoring variability in practice and the need for context-specific evidence [13].

Despite extensive research on gastric cancer overall, a clear consensus on the diagnostic criteria, risk stratification, and optimal treatment of EOGC is lacking. The absence of a unified definition complicates comparative analysis across populations, while debates persist regarding its unique pathology, recurrence patterns, and therapeutic responses.

This study aims to address these gaps by leveraging the Surveillance, Epidemiology, and End Results (SEER) database (2010–2015) to systematically analyze the clinicopathological characteristics, recurrence patterns, and survival outcomes of EOGC patients treated with radiotherapy. By directly comparing these patients with their NEOGC counterparts, we evaluate prognostic differences and the relative effectiveness of radiotherapy-based treatment strategies, including radiotherapy as a monotherapy versus multimodal approaches. The novelty of this study lies in providing large-scale, population-based evidence on radiotherapy outcomes in EOGC, highlighting treatment-response differences between younger and older patients, and offering insights that may guide age-specific therapeutic strategies.

MATERIALS AND METHODS

Data source

This study utilized data from the Surveillance, Epidemiology, and End Results (SEER) database, covering the years 2010–2015. A total of 11,230 patients with a confirmed diagnosis of gastric cancer who received radiotherapy as part of their treatment were initially identified. Patients were stratified into two groups according to age at diagnosis: early-onset gastric cancer (EOGC, ≤50 years) and non-early-onset gastric cancer (NEOGC, >50 years). After applying inclusion and exclusion criteria, 814 EOGC patients and 4,997 NEOGC patients were included in the final analysis. Data extraction was conducted using SEER*Stat software (version 8.4.4, National Cancer Institute, Bethesda, MD, USA), with the database set to "Incidence-SEER Research Data, 8 Registries, Nov 2023 Sub [1975–2021]."

Data collection

The following variables were collected for each patient: demographic characteristics (age, sex, race, and year of diagnosis), clinicopathological features (tumor location, histological type, grade, TNM stage, and tumor size), and treatment modalities. Treatment modalities were categorized as radiotherapy alone, radiotherapy combined with surgery, or radiotherapy combined with chemotherapy. Prognostic information was obtained in the form of overall survival (OS), defined as the time from initial diagnosis to death from any cause or to the last follow-up date.

Because the SEER database provides only de-identified patient-level data, this study was exempt from institutional review board approval and informed consent requirements.

Inclusion and exclusion criteria

Patients were eligible if they were diagnosed with gastric cancer between 2010 and 2015, received radiotherapy as part of treatment, and had complete survival data available. Patients were excluded if they were younger than 18 years at diagnosis, had other primary tumors, had missing or zero survival data, or did not receive radiotherapy. After exclusions, 5,811 patients were included for analysis.

Treatment details

The SEER database does not capture the specific type of radiotherapy (e.g., external beam radiotherapy, three-dimensional conformal radiotherapy, or intensity-modulated radiotherapy), nor the total dose or dose per fraction administered. Similarly, information on chemotherapy regimens, drug dosages, trade names, and countries of origin is not available in the database. Therefore, these details could not be reported in this study and represent a limitation that should be considered when interpreting the results.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range (IQR) for non-normally distributed data. Group comparisons were performed using the independent t-test or the Wilcoxon rank-sum test, as appropriate. Categorical variables were expressed as frequencies and percentages and were compared using the chi-square test or Fisher's exact test, depending on expected cell counts.

Survival outcomes were assessed using the Kaplan–Meier method, and survival distributions between groups were compared using the log-rank test. To identify independent prognostic factors for OS, Cox proportional hazards regression models were constructed. Model I included gastric cancer type (EOGC vs. NEOGC) and radiotherapy-based treatment modality (radiotherapy alone, radiotherapy plus surgery, or radiotherapy plus chemotherapy). Model II further adjusted for age, sex, race, marital status, tumor location, histological subtype, tumor grade, and TNM stage. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated.

All analyses were conducted using R statistical software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria). A two-sided P value <0.05 was considered statistically significant.

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RESULTS

Clinical and pathological characteristics

After applying inclusion and exclusion criteria, a total of 5,811 patients with gastric cancer who received radiotherapy were included in the analysis. Of these, 814 patients (14%) were classified as having early-onset gastric cancer (EOGC), while 4,997 patients (86%) had non-early-onset gastric cancer (NEOGC). Compared with NEOGC, EOGC patients had a significantly higher proportion of females (42.3% vs. 36.4%, *P*=0.001) and were more frequently diagnosed with advanced-stage disease, with 44.3% of cases presenting at stage IV compared to 31.3% in the NEOGC group (*P*<0.001). In addition, EOGC patients more often exhibited T4 tumors (23.6% vs. 19.2%, *P* < 0.001) and distant metastasis at diagnosis (M1: 44.0% vs. 31.2%, *P*<0.001).

Histological distribution also differed markedly between groups. Signet-ring cell carcinoma was nearly twice as common in EOGC compared with NEOGC (26.8% vs. 14.7%, *P* < 0.001). Tumor location varied as well: EOGC tumors were more frequently observed in the gastric body (10.3%), fundus (6.0%), and greater curvature (5.4%), while NEOGC tumors predominated in the cardia (37.2%) and gastric antrum (15.7%) (*P*<0.001).

The use of adjuvant radiotherapy was significantly more common among EOGC patients (78.9%) than among NEOGC patients (68.3%, *P*<0.001). No statistically significant differences were found between the two groups in terms of race, nodal stage, or tumor size (all *P*>0.05). The detailed clinical and pathological features are summarized in table 1.

Survival outcomes

The Kaplan–Meier survival analysis revealed similar short-term outcomes between the two groups. The 2-year survival rates were 47.7% for EOGC and 48.2% for NEOGC, while the 5-year survival rates were 31.5% and 30.9%, respectively. Despite these similarities, the log-rank test demonstrated a statistically significant difference in overall survival (OS) between EOGC and NEOGC patients (*P*=0.008) (figure 1).

When radiotherapy-based treatment strategies were compared, significant differences in median survival times emerged. Patients who received radiotherapy alone achieved the longest survival, with a median OS of 99 months (95% CI: 84–109). In contrast, those treated with radiotherapy plus chemotherapy or radiotherapy plus surgery had markedly shorter median survival times of 40 months (95% CI: 36–45) and 30 months (95% CI: 27–34), respectively (*P*<0.001) (figure 2).

Table 1. Clinical and pathological characteristics of patients with early-onset gastric cancer (EOGC) and non-early-onset gastric cancer (NEOGC) treated with radiotherapy (N = 5,811). Data are presented as n (%). Abbreviations: EOGC, early-onset gastric cancer; NEOGC, non-early-onset gastric cancer; NOS, not otherwise specified.

Characteristic	Overall (n = 5,811)	EOGC (n = 814)	LOGC (n = 4,997)	P value
Sex				**0.001**
Male	3,647 (62.8)	470 (57.7)	3,177 (63.6)	
Female	2,164 (37.2)	344 (42.3)	1,820 (36.4)	
Race				**0.345**
White	3,861 (66.4)	523 (64.3)	3,338 (66.8)	
Black	678 (11.7)	99 (12.2)	579 (11.6)	
Others	1,272 (21.9)	192 (23.6)	1,080 (21.6)	
Tumor location				**<0.001**
Cardia	2,074 (35.7)	215 (26.4)	1,859 (37.2)	
Others	1,200 (20.7)	224 (27.5)	976 (19.5)	
Gastric antrum	916 (15.8)	130 (16.0)	786 (15.7)	
Body	534 (9.19)	84 (10.3)	450 (9.01)	
Lesser curvature	448 (7.71)	60 (7.37)	388 (7.76)	
Fundus	305 (5.25)	49 (6.02)	256 (5.12)	
Greater curvature	232 (3.99)	44 (5.41)	188 (3.76)	
Pylorus	102 (1.76)	8 (0.98)	94 (1.88)	
Histology				**<0.001**
Adenocarcinoma, NOS	2,723 (46.9)	299 (36.7)	2,424 (48.5)	
Signet ring cell carcinoma	954 (16.4)	218 (26.8)	736 (14.7)	
Adenocarcinoma, intestinal type	493 (8.48)	32 (3.93)	461 (9.23)	
Mucinous adeno-carcinoma	76 (1.31)	8 (0.98)	68 (1.36)	
Others	1,565 (26.9)	257 (31.6)	1,308 (26.2)	
Grade				**<0.001**
I	1,233 (21.2)	138 (17.0)	1,095 (21.9)	
II	953 (16.4)	103 (12.7)	850 (17.0)	
III	1,331 (22.9)	169 (20.8)	1,162 (23.3)	
IV	1,923 (33.1)	361 (44.3)	1,562 (31.3)	
Unknown	371 (6.38)	43 (5.28)	328 (6.56)	
T stage				**<0.001**
T1	1,308 (22.5)	155 (19.0)	1,153 (23.1)	
T2	706 (12.1)	83 (10.2)	623 (12.5)	
T3	1,647 (28.3)	221 (27.1)	1,426 (28.5)	
T4	1,149 (19.8)	192 (23.6)	957 (19.2)	
Others	1,001 (17.2)	163 (20.0)	838 (16.8)	
N stage				**0.281**
N0	2,684 (46.2)	351 (43.1)	2,333 (46.7)	
N1	1,565 (26.9)	223 (27.4)	1,342 (26.9)	
N2	559 (9.62)	81 (9.95)	478 (9.57)	
N3	575 (9.90)	93 (11.4)	482 (9.65)	
Others	428 (7.37)	66 (8.11)	362 (7.24)	
M stage				**<0.001**
M0	3,884 (66.8)	454 (55.8)	3,430 (68.6)	
M1	1,916 (33.0)	358 (44.0)	1,558 (31.2)	
Unknown	11 (0.19)	2 (0.25)	9 (0.18)	
Tumor size				**0.007**
<5 cm	144 (2.48)	29 (3.56)	115 (2.30)	
≥5 cm	3,904 (67.2)	513 (63.0)	3,391 (67.9)	
Unknown	1,763 (30.3)	272 (33.4)	1,491 (29.8)	

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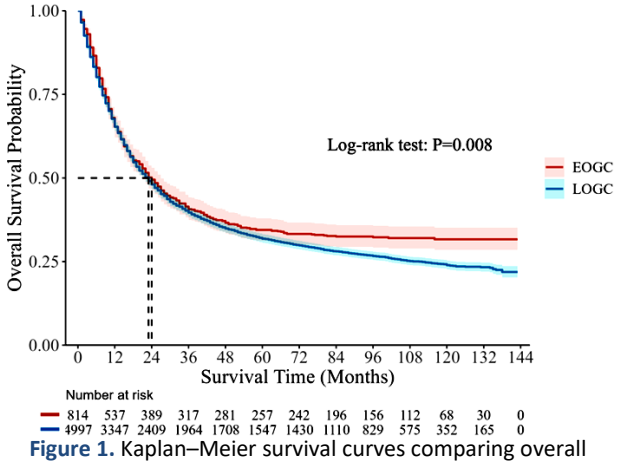

Figure 1. Kaplan–Meier survival curves comparing overall survival (OS) between early-onset gastric cancer (EOGC) and non-early-onset gastric cancer (NEOGC) patients treated with radiotherapy.

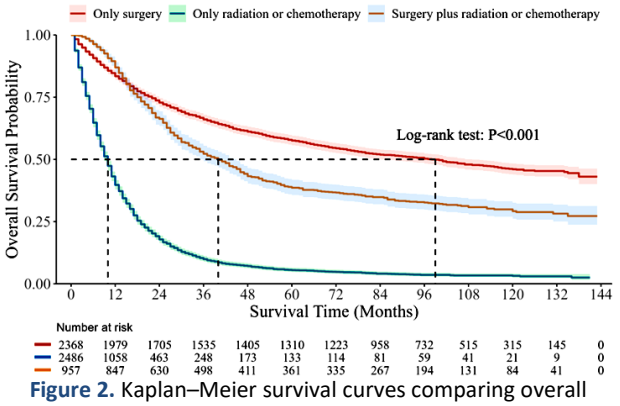

Figure 2. Kaplan–Meier survival curves comparing overall survival (OS) by radiotherapy-based treatment strategies: radiotherapy alone, radiotherapy plus chemotherapy, and radiotherapy plus surgery. Abbreviation: CI, confidence interval.

A stratified analysis among EOGC patients highlighted the prognostic importance of surgery. Patients treated with surgery alone demonstrated superior long-term survival compared to those who underwent multimodal therapy. Specifically, the 2-year survival rates for surgery-only and surgery plus radiotherapy/chemotherapy were 85.9% and 88.6%, respectively; however, the 5-year survival rates diverged substantially, at 61.4% for surgery alone and only 32.6% for combined therapy (figure 3).

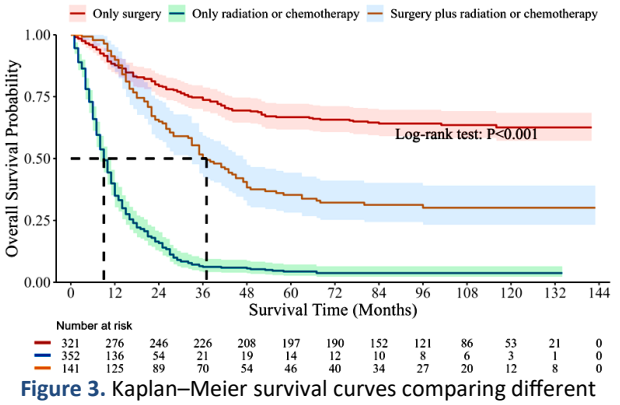

Figure 3. Kaplan–Meier survival curves comparing different treatment strategies among early-onset gastric cancer (EOGC) patients: surgery alone versus surgery combined with radiotherapy and/or chemotherapy.

In the NEOGC group, different trends were observed. Surgery combined with radiotherapy or chemotherapy provided the best survival advantage, followed by surgery alone, whereas radiotherapy/chemotherapy alone was associated with the poorest prognosis (figure 4). These findings underscore the differential impact of treatment strategies across age-defined gastric cancer subgroups.

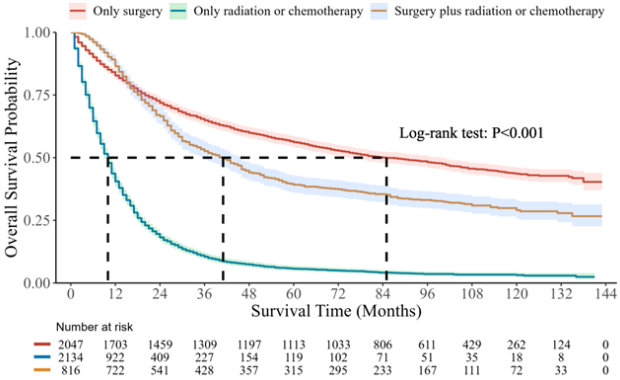

Figure 4. Kaplan–Meier survival curves comparing different treatment strategies among non-early-onset gastric cancer (NEOGC) patients: surgery alone, surgery plus radiotherapy/chemotherapy, and radiotherapy/chemotherapy alone.

Cox regression analysis

Univariate and multivariate Cox proportional hazards regression models were constructed to identify independent prognostic factors for OS (table 2). In univariate analysis, patients receiving radiotherapy/chemotherapy alone had an 8.74-fold higher risk of mortality compared to those undergoing surgery alone (P<0.001). Similarly, patients receiving surgery combined with radiotherapy/chemotherapy had a 2.35-fold increased mortality risk (P<0.001).

After adjustment for relevant covariates, including sex, tumor location, histology, grade, T stage, N stage, and tumor size, these associations remained significant. The adjusted hazard ratio (aHR) for radiotherapy/chemotherapy alone was 4.59 (P<0.001), and for surgery plus radiotherapy/chemotherapy it was 1.46 (P=0.008), compared with surgery alone. Additional prognostic indicators included histological subtype and tumor invasion depth. Patients with signet-ring cell carcinoma had a 20% increased risk of mortality (HR=1.20, P<0.001), while those with Grade II and Grade III tumors had progressively higher risks (HR = 1.53 and 1.95, respectively, both P<0.001). Advanced T4 stage was also independently associated with poorer outcomes (HR=1.26, P<0.001).

Model-based survival predictions supported these findings. Among EOGC patients, surgery alone consistently yielded the most favorable long-term survival, while combined therapies offered no additional advantage and were associated with increased risk. In contrast, NEOGC patients derived greater benefit from multimodal strategies (figure 5).

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Table 2. Univariate and multivariate Cox proportional hazards regression analysis of overall survival (OS) in patients with gastric cancer. Abbreviations: HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; EOGC, early-onset gastric cancer; NEOGC, non-early-onset gastric cancer; NOS, not otherwise specified.

Characteristic	Model I		Model II	
	HR (95% CI)	P value	aHR (95% CI)	P value
Treatment strategy				
Only surgery	*Reference*		*Reference*	
Only radiation or chemotherapy	8.74 (7.04 - 10.85)	<0.001	4.59 (3.66 - 5.75)	<0.001
Surgery plus radiation or chemotherapy	2.35 (1.79 - 3.09)	<0.001	1.46(1.10 - 1.92)	0.008
Type				
EOGC	*Reference*		*Reference*	
LOGC	1.63 (1.35 - 1.99)	<0.001	0.96 (0.78 - 1.20)	0.737
Treatment strategy * type				
Only radiation or chemotherapy: LOGC	0.56 (0.45 - 0.71)	<0.001	0.61 (0.49 - 0.77)	<0.001
Surgery plus radiation or chemotherapy: LOGC	0.60 (0.45 - 0.80)	<0.001	0.65 (0.48 - 0.87)	0.004
Sex				
Male			*Reference*	
Female			0.93 (0.87 - 1.00)	0.044
Race	-	-		
White	-	-	*Reference*	
Black	-	-	1.02 (0.92 - 1.13)	0.664
Others	-	-	1.00 (0.92 - 1.08)	0.914
Marital status	-	-		
Unmarried, single	-	-	*Reference*	
Married	-	-	0.80 (0.73 - 0.87)	<0.001
Others	-	-	0.90 (0.82 - 1.00)	0.052
Tumor location	-	-		
Cardia	-	-	*Reference*	
Others	-	-	1.03 (0.94 - 1.13)	0.529
Gastric antrum	-	-	1.00 (0.90 - 1.11)	0.995
Body	-	-	0.88 (0.77 - 1.00)	0.045
Lesser curvature	-	-	0.90 (0.78 - 1.02)	0.103
Fundus	-	-	0.87 (0.74 - 1.02)	0.095
Greater curvature	-	-	0.84 (0.70 - 1.02)	0.072
Pylorus	-	-	0.99 (0.78 - 1.25)	0.926
Histology	-	-		
Adenocarcinoma, NOS	-	-	*Reference*	
Signet ring cell carcinoma	-	-	1.20 (1.10 - 1.31)	<0.001
Adenocarcinoma, intestinal type	-	-	0.97 (0.87 - 1.09)	0.665
Mucinous adenocarcinoma	-	-	0.85 (0.65 - 1.11)	0.242
Others	-	-	0.70 (0.64 - 0.76)	<0.001
Grade	-	-		
I	-	-	*Reference*	
II	-	-	1.53 (1.32 - 1.77)	<0.001
III	-	-	1.95 (1.65 - 2.30)	<0.001
IV	-	-	1.50 (0.61 - 3.66)	0.377
Unknown	-	-	1.23 (1.01 - 1.48)	0.035
T stage	-	-		
T1	-	-	*Reference*	
T2	-	-	0.93 (0.82 - 1.06)	0.279
T3	-	-	0.96 (0.85 - 1.07)	0.460
T4	-	-	1.26 (1.12 - 1.43)	<0.001
Others	-	-	1.07 (0.95 - 1.21)	0.256
N stage	-	-		
N0	-	-	*Reference*	
N1	-	-	1.18 (1.08 - 1.29)	<0.001
N2	-	-	1.34 (1.18 - 1.52)	<0.001
N3	-	-	1.96 (1.73 - 2.22)	<0.001
Others	-	-	1.43 (1.26 - 1.62)	<0.001
M stage	-	-		
M0	-	-	*Reference*	
M1	-	-	1.91 (0.79 - 4.64)	0.153
Unknown	-	-	1.39 (0.65 - 2.98)	0.391
Tumor size	-	-		
<5 cm	-	-	*Reference*	
≥5 cm	-	-	1.63 (1.20 - 2.23)	0.002
Unknown	-	-	1.79 (1.31 - 2.46)	<0.001

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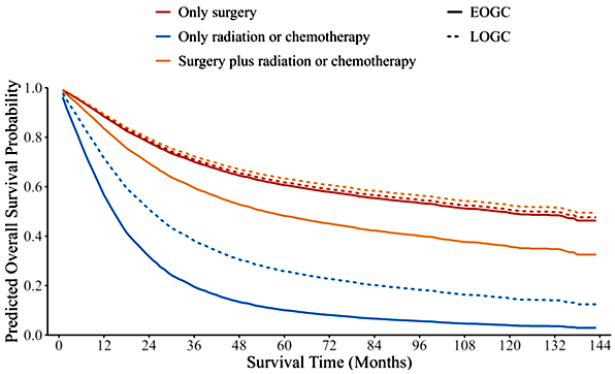

Figure 5. Predicted overall survival (OS) probabilities for patients with **(A)** early-onset gastric cancer (EOGC) and **(B)** non-early-onset gastric cancer (NEOGC), stratified by treatment strategy (surgery alone, surgery plus radiotherapy/ chemotherapy, or radiotherapy/chemotherapy alone).

Summary of findings

Taken together, these results demonstrate that EOGC patients are more likely to present with advanced disease and aggressive histological subtypes compared with NEOGC patients. Radiotherapy alone provided superior survival outcomes in EOGC, while multimodal treatments did not improve prognosis in this subgroup. Conversely, multimodal therapy showed benefit among NEOGC patients. These results highlight the importance of tailoring treatment strategies according to patient age and tumor biology.

DISCUSSION

This population-based study provides new evidence on the clinicopathological characteristics and survival outcomes of early-onset gastric cancer (EOGC) patients treated with radiotherapy, compared with non-early-onset gastric cancer (NEOGC). Consistent with earlier reports, EOGC patients demonstrated a higher prevalence of female sex, advanced-stage disease, and aggressive histological subtypes such as signet-ring cell carcinoma, features that contribute to their unfavorable prognosis [14-16]. These patterns highlight the distinct biology of EOGC and the importance of considering patient age in therapeutic decision-making.

A key observation in our analysis is that radiotherapy alone was associated with superior long-term overall survival in EOGC, whereas multimodal therapies that combined radiotherapy with chemotherapy or surgery failed to improve outcomes. This finding contrasts with the INT-0116 trial, which established the role of adjuvant chemoradiotherapy in resectable gastric cancer [17], but is consistent with more recent analyses suggesting that younger patients may not benefit equally from such combined approaches [9]. The superior performance of radiotherapy alone in EOGC may reflect the relatively lower comorbidity burden and higher treatment tolerance in younger patients, allowing them to derive maximum benefit from targeted irradiation without the added toxicities of multimodality regimens. Similar conclusions were reached in a recent review highlighting that nonhereditary EOGC remains an unmet clinical need where traditional multimodal regimens may not always be advantageous [12].

In contrast, NEOGC patients in our cohort appeared to gain benefit from combined approaches, particularly surgery with adjuvant radiotherapy or chemoradiotherapy, echoing the results of the ARTIST trial and similar studies that demonstrated improved outcomes in older patients with node-positive disease [18]. This divergence underscores potential biological differences: diffuse-type histology, more common in EOGC, is known to be less chemosensitive but may exhibit greater radiosensitivity [19]. Tumor location may also influence these differences, as EOGC tumors were more often located in the gastric body and fundus, which may be more amenable to precise radiation planning than the cardia, where NEOGC predominates. Moreover, a recent global radiotherapy utilization analysis showed striking heterogeneity in gastric cancer management, reinforcing the importance of context-specific strategies [13].

Multivariate Cox regression confirmed that tumor stage, histological subtype, and radiotherapy modality were independent prognostic factors, with signet-ring cell carcinoma and advanced T4 disease portending poor outcomes. These results are in line with findings from the China National Cancer Center, which reported particularly poor prognosis among younger patients with advanced-stage disease [20]. Together, these observations emphasize the importance of careful patient selection when considering radiotherapy-based strategies in EOGC. Comparative work has also shown that younger gastric cancer patients exhibit unique metastatic patterns, particularly peritoneal spread, which complicates prognosis and may explain differential treatment responses [8].

The interpretation of our findings must acknowledge certain limitations. As a retrospective study using the SEER database, detailed information on radiotherapy techniques, total dose and fractionation, chemotherapy regimens, and recurrence patterns was unavailable. These constraints may have limited the ability to fully evaluate treatment-related variables. Nevertheless, the large cohort size, robust survival analysis, and stratification by age provide meaningful insights into prognostic differences between EOGC and NEOGC. Future prospective studies with detailed treatment parameters and molecular profiling are warranted to validate these results and to identify biomarkers predictive of radiosensitivity. Emerging therapeutic approaches, including immune checkpoint inhibitors and novel targeted therapies, may further refine

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treatment strategies for aggressive EOGC subtypes [7, 21].

CONCLUSION

In summary, EOGC is characterized by distinct clinicopathological features, including advanced presentation and aggressive histological patterns. Unlike NEOGC, where multimodal therapy appears beneficial, radiotherapy as a monotherapy was associated with superior survival in younger patients. These findings highlight the need for personalized treatment strategies tailored to age and tumor biology. Further research should aim to optimize radiotherapy protocols and integrate novel systemic therapies to improve outcomes for this challenging patient population.

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Conflict of interest: The authors declare that they have no conflicts of interest regarding the publication of this work.

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Ethical considerations: This study was based on publicly available, de-identified data from the SEER database. As such, approval from an institutional review board and informed patient consent were not required. The conduct of the study adhered to the ethical principles outlined in the Declaration of Helsinki.

Authors' contributions:

X.K., contributed to study design, data analysis, and drafting of the manuscript. Y.N., was responsible for data curation, statistical analysis, and interpretation of results. G.G., carried out the literature review, contributed to methodology, and assisted with preparation of figures and tables. Y.N., as the corresponding author, supervised the study, critically revised the manuscript, and approved the final version for submission. All authors read and approved the final manuscript.

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