A nomogram for predicting cancer-specific survival in different age groups for operable gastric cancer: a population-based study

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Background: The age thresholds for differentiating young and elderly patients are still under debate. This study aimed to evaluate the cut-off age for differentiating patients along with the prognostic value of age for operable gastric cancer (GC).

Methods: Patients diagnosed with resected gastric adenocarcinoma were identified from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database (training cohort and internal validation cohort) and Liaoning Cancer Hospital (external validation cohort). Kaplan-Meier plots were used to compare cancer-specific survival (CSS) across different age groups. Univariate and multivariate analysis was conducted using a Cox regression model. Predictive ability of the nomogram was determined by the Harrell's concordance index (C-index), calibration curves, and Akaike's Information Criterion (AIC).

Results: A total of 17,339 patients with GC were included. According to the univariate analysis results, CSS was similar among patients aged 20–69 years old, started to worsen for patients over the age of 70, and was the worst for patients older than 79 years in the training cohort. Thus, we further divided the age groups into 20–69, 70–79, and >79, and multivariate analysis showed that patients above 70 years of age had worse CSS. The nomogram was established based on the results of the multivariate analysis. The C-indexes for the training, internal, and external validation cohorts were 0.7531, 0.7344, and 0.7431, respectively.

Conclusions: This study showed that age had a relative predictive ability for CSS, 70 years should be the cut-off age, and age ≥70 years is an independent prognostic risk factor for GC patients who undergo surgery. These data highlight the importance of individualized treatment to improve the prognosis of patients with GC.

Keywords: Age; gastric cancer (GC); prognosis; nomogram

Introduction

Gastric cancer (GC) is the fifth most common cancer in the world and the third leading cause of cancer-related mortality (1). Although great progress has been made in the treatment of GC, the prognosis is still not optimistic.

Apart from typical pathological prognostic factors, the demographic characteristics of patients, especially age, have been proven to affect survival outcomes of multiple cancers, including colorectal (2) and prostate cancer (3). The GC incidence rate increases gradually with age (4). The age of patients at GC onset is generally between

50–70 years old, and 60% of patients with GC are aged over 65 years (5,6), although the incidence of GC among younger people is increasing (7). Old age has been a problem for choosing effective treatment strategies, and clarifying the association between age and long-term survival of GC to improve therapeutic efficacy is critical. Previous findings on the prognosis of young and elderly patients have not formed a consensus. Some studies reported that younger patients had a better prognosis (5,8), whereas others have indicated unfavorable characteristics and poorer prognosis in young patients (9,10). Still other studies found no significant differences in stage-specific survival between the 2 age groups (6,11,12). However, the study population sizes were relatively small or the age thresholds for differentiating young from elderly patients were not fixed in these studies. In contrast, the U.S. National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database comprises larger samples of data on GC than those of other studies, enabling us to evaluate the impact of age at diagnosis on gastric cancer-specific survival (GCSS). Therefore, this study aimed to determine whether differences in cancer-specific survival (CSS) exist between different age groups, to evaluate a cut-off age, and to establish a predictive model for GC patients based on age.

Methods

Patient selection

Data were obtained from the SEER 18 Regs Custom Data (with additional treatment fields), Nov 2017 Sub (1973–2015 varying). From the SEER database, patients diagnosed between 2010 and 2015 were set as the training cohort, and patients diagnosed between 2004 and 2009 were set as the internal validation cohort. Patients from Liaoning Cancer Hospital between 2011 and 2016 formed the external validation cohort. The inclusion criteria were as follows: patients older than 20, pathological confirmation of gastric adenocarcinoma (codes: M-8140/3, M8143-3 to M-8145/3, M-8210/3, M-8211/3, M-8255/3, M-8260/3 to M-8263/3, M-8310/3, M-8323/3, M-8480/3, M-8481/3), patients received surgery, and American Joint Committee on Cancer (AJCC) eighth edition stages I–III. The exclusion criteria were as follows: patients with an unknown number of lymph node (LN) retrieved, an unknown number of positive LNs, an unknown AJCC stage, survival of less than 1 month, unknown survival time or death because of any other cause.

The CONSORT diagram is listed in *Figures S1,S2*.

Statistical analysis

Patient data including age at diagnosis, gender, race, histological grade, T stage, N stage, TNM stage, radiotherapy, positive number of LNs, total number of retrieved LNs, tumor size, cause-specific death classification, survival time (months), and status were retrieved from both the SEER database and the Liaoning Cancer Hospital dataset. To better establish the impact of age on CSS, age at diagnosis was classified into the following groups: 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and older than 79 years. Categorical variables were compared by χ^2 test. Survival rates were estimated using the Kaplan-Meier method. The nomogram, Harrell's concordance index (C-index), Akaike's Information Criterion (AIC), and calibration curves were generated to compare the predictive accuracy for different age groups. Statistical Package for Social Science (SPSS; IBM, Armonk, NY, USA) version 23.0 and R software (version 3.4.4) were used to conduct all statistical analyses. P<0.05 was considered a statistically significant value.

Results

Clinicopathological characteristics

A total of 17,339 patients were eligible for this study, and the clinicopathological characteristics of these patients are summarized in *Table 1*. Statistical significance (P<0.05) was found for all the variables when the training set and the external validation set were compared. Meanwhile, except for race, the variables of the internal validation set were significantly different from those of the training set. It was apparent that the patients in the external validation set were younger than those in the training set (23.2% *vs.* 38.3% of the group ≥70 years). Patients in the internal and external validation sets had a greater number of unfavorable features, including larger tumor size, advanced T stage, LN metastasis, and poorer histological grade. However, more patients in the external validation set had ≥15 LNs retrieved and less in the internal validation set than those of training set.

Overall survival (OS) of GC among different age groups

The Kaplan-Meier plot for the training set is shown in *Figure 1A*. The patients who were older than 79 years

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Table 1 Clinicopathological characteristics of study populations

Characteristics	Training set (A) (N=7,493), N (%)	Internal validation set (B) (N=8,129), N (%)	P value (A vs. B)	External validation set (C) (N=1,717), N (%)	P value (A vs. C)
Age (years)			<0.001		<0.001
20–29	47 (0.6)	29 (0.4)		6 (0.3)	
30–39	208 (2.8)	224 (2.8)		34 (2.0)	
40–49	638 (8.5)	788 (9.7)		129 (7.5)	
50–59	1,547 (20.6)	1,549 (19.1)		440 (25.6)	
60–69	2,188 (29.2)	2,150 (26.4)		709 (41.3)	
70–79	1,975 (26.4)	2,179 (26.8)		318 (18.5)	
>79	890 (11.9)	1,210 (14.9)		81 (4.7)	
Gender			0.025		<0.001
Male	4,800 (64.1)	5,067 (62.3)		1,252 (72.9)	
Female	2,693 (35.9)	3,062 (37.7)		465 (27.1)	
Race			0.708		–
White	4,952 (66.1)	5,380 (66.2)		–	
Black	928 (12.4)	1,034 (12.7)		–	
Other[a]	1,613 (21.5)	1,715 (21.1)		–	
T stage			<0.001		<0.001
T1	1,863 (24.9)	1,868 (23.0)		218 (12.7)	
T2	924 (12.3)	1,000 (12.3)		307 (17.9)	
T3	2,546 (34.0)	2,845 (35.0)		34 (2.0)	
T4a	1,721 (23.0)	1,818 (22.4)		970 (56.5)	
T4b	439 (5.9)	598 (7.4)		188 (10.9)	
N stage			<0.001		<0.001
N0	3,532 (47.1)	3,363 (41.4)		590 (34.4)	
N1	1,337 (17.8)	1,456 (17.9)		335 (19.5)	
N2	1,198 (16.0)	1,455 (17.9)		373 (21.7)	
N3a	999 (13.3)	1,321 (16.3)		297 (17.3)	
N3b	427 (5.7)	534 (6.6)		122 (7.1)	
TNM stage			<0.001		<0.001
I	2,268 (30.3)	2,290 (28.2)		370 (21.5)	
II	2,331 (31.1)	2,240 (27.6)		368 (21.4)	
III	2,894 (38.6)	3,599 (44.2)		979 (57.0)	
LN examined			<0.001		<0.001
<15	3,069 (41.0)	4,241 (52.2)		345 (20.1)	

Table 1 (*Continued*)

Table 1 (*Continued*)

Characteristics	Training set (A) (N=7,493), N (%)	Internal validation set (B) (N=8,129), N (%)	P value (A *vs.* B)	External validation set (C) (N=1,717), N (%)	P value (A *vs.* C)
≥15	4,424 (59.0)	3,888 (47.8)		1,372 (79.9)	
Grade			0.001		<0.001
1	416 (5.8)	360 (4.6)		51 (3.0)	
2	1,988 (27.9)	2,092 (27.0)		437 (25.5)	
3 and UD	4,728 (66.3)	5,310 (68.4)		1,229 (71.6)	
Site			0.005		<0.001
Upper stomach	2,436 (41.5)	2,464 (39.8)		696 (41.9)	
Middle stomach	720 (12.3)	697 (11.3)		253 (15.2)	
Lower stomach	2,174 (37.0)	2,483 (40.1)		711 (42.8)	
Overlapping type	543 (9.2)	543 (8.8)		–	
Tumor size (cm)			<0.001		<0.001
<5	4,055 (60.9)	3,963 (56.5)		652 (49.1)	
≥5	2,603 (39.1)	3,056 (43.5)		677 (50.9)	

[a], Other includes American Indian/AK Native, Asian/Pacific Islander. LN, lymph node; UD, undifferentiated type.

of age at the time of diagnosis presented with the worst survival rate with a 5-year CSS rate of 57.2%, 51.1%, 57.0%, 52.7%, 54.6%, 52.2%, and 43.9% for patients ages 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and >79 years, respectively. We then evaluated the long-term survival of the validation sets (*Figure 1B,C*). The results were consistent with those of the training set. Mean survival times were 44.2, 41.5, 41.3, 41.2, 39.9, 36.9, and 32.0 months for each age group, respectively, in the internal validation set, and 48.0, 44.2, 46.9, 46.4, 45.3, 40.9, and 34.8 months for each age group, respectively, in the external validation set. There were significant differences found in all analyses (log-rank: P<0.001).

Comparisons of survival using Cox regression model in the training cohort

Univariate analysis results of the training set using Cox regression model are listed in *Table S1*. In the univariate analysis, using ages 60–69 years as reference, the patients who were younger than 69 years had almost the same prognosis and showed no significant difference (P=0.596, 0.708, 0.307, and 0.895 for the age groups 20–29, 30–39, 40–49, and 50–59 years, respectively). The CSS decreased with age only over 70 years [hazard radio (HR), 1.14; 95%

confidence interval (CI), 1.02–1.26; P=0.021] and was the worst in the >79-year age group (HR, 1.63; 95% CI, 1.44–1.85; P<0.001) (*Table S1*). The age groups were then divided into 20–69, 70–79, and >79 years for multivariate analysis to be performed. Moreover, race, histological grade, T stage, N stage, number of retrieved LNs, site, tumor size, and radiation were also associated with CSS. Each of these variables was included in the multivariate analysis. The multivariate analysis showed that older age (70–79 and >79 years), race (white), histological grade [poorly differentiated and undifferentiated type (UD)], T stage (T2/3/4), N stage (N1/2/3), number of retrieved LNs (<15), site (upper stomach), tumor size (≥5 cm), and the absence of radiation therapy were independent risk factors for prognosis (*Table 2*).

Development and validation of a prediction model

Independent risk factors of the training set were used to generate the nomogram (*Figure 2*). The calibration curve is shown in *Figure 3A*, and the C-index was 0.7531. We then validated the results. Relatively good calibrations were also observed between the predictive and actual 5-year CSS for the validation sets (*Figure 3B,C*). The C-index of the internal and external validation sets was 0.7344 and 0.7431,
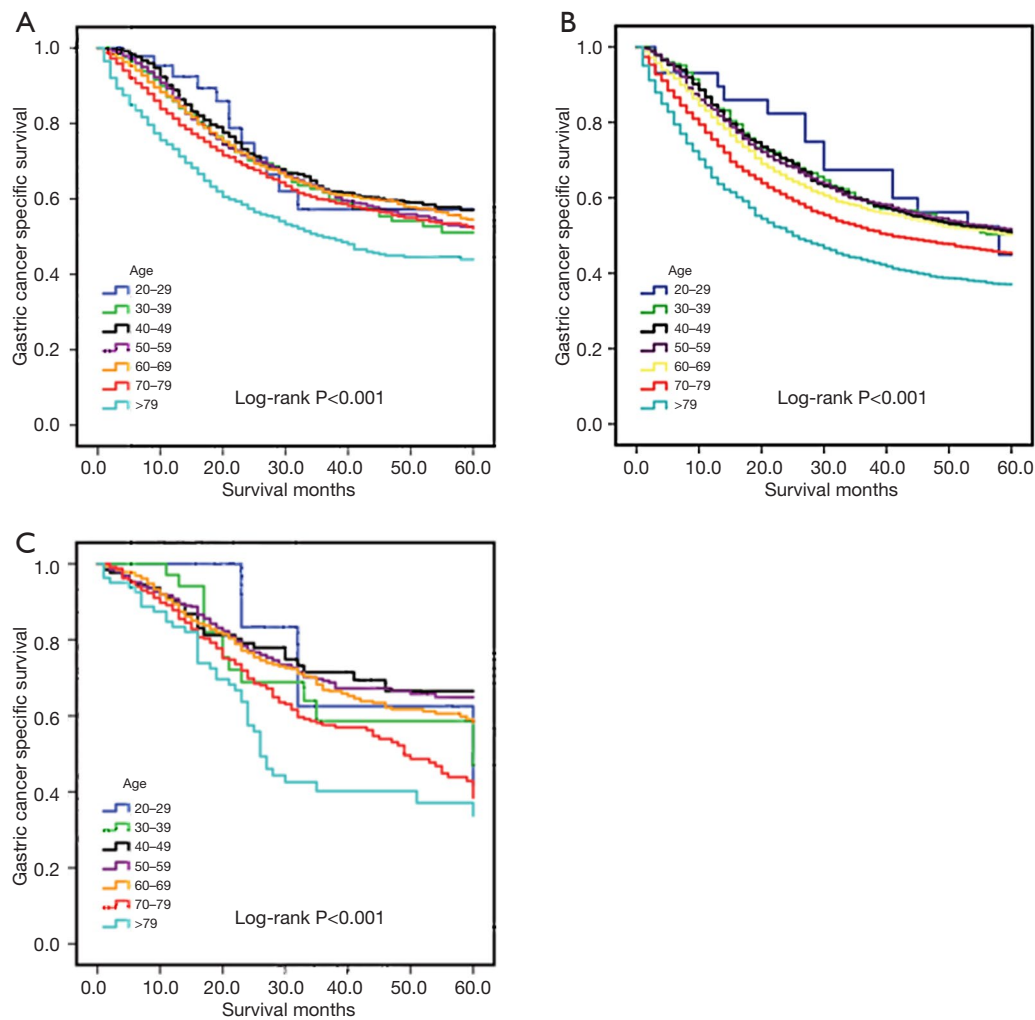
Figure 1 Kaplan-Meier estimates of OS in the training set (A), internal validation set (B), and external validation set (C). OS, overall survival.

respectively. Univariate and multivariate analysis of the validation sets indicated that patients aged 70–79 and over 79 years experienced worse prognosis, which also supported the age-based prediction model (*Tables 3,S2*).

We further compared the predictive efficacy of age serving as a continuous variable and categorical variable (3 groups and 6 groups). As listed in *Table 4*, when assessed as a continuous type, age had a better predictive accuracy and goodness of fit with the C-index (0.7539 *vs.* 0.7359) and AIC (7,773.2 *vs.* 8,695.0) of the training and internal validation sets, respectively. Age in the 3 age groups and the 6 age groups had a similar prognostic performance (C-index: 0.7531 *vs.* 0.7532; AIC: 7,769.7 *vs.* 7,777.9 for the training set, and C-index: 0.7344 *vs.* 0.7350; AIC: 8,714.3 *vs.* 8,712.9

for the internal validation set). Notably, age divided into 3 groups (C-index: 0.7431; AIC: 1,772.1) had a superior performance compared to 6 groups (C-index: 0.7391; AIC: 1,802.8) and was comparable with continuous type (C-index: 0.7426; AIC: 1,794.1).

Discussion

GC is widely recognized as an age-related disease, and despite growing evidence that neoadjuvant therapy or adjuvant therapy is beneficial for locally advanced GC, the prognosis has remained poor. Understanding the related factors of GC progression can lead to better individualized therapy and prognosis prediction for GC. Considering that

Table 2 Multivariate analysis of CSS in the training set

Variables	HR (95% CI)	P value
Age (years)		
20–69	Reference	–
70–79	1.33 (1.21–1.46)	<0.001
>79	1.71 (1.52–1.93)	<0.001
Race		
White	Reference	–
Black	1.04 (0.92–1.17)	0.107
Other[a]	0.82 (0.73–0.91)	<0.001
T stage		
T1	Reference	–
T2/T3/T4	3.04 (2.58–3.58)	<0.001
N stage		
N0	Reference	–
N1/2/3	3.02 (2.72–3.35)	<0.001
LN examined		
<15	Reference	–
≥15	0.72 (0.67–0.78)	<0.001
Grade		
1/2	Reference	–
3 and UD	1.47 (1.33–1.62)	<0.001
Site		
Upper stomach	Reference	–
Middle stomach	0.76 (0.65–0.89)	0.001
Lower stomach	0.79 (0.70–0.88)	<0.001
Overlapping type	0.94 (0.81–1.10)	0.453
Tumor size (cm)		
<5	Reference	–
≥5	1.31 (1.26–1.50)	<0.001
Radiation		
No	Reference	–
Yes	0.76 (0.69–0.83)	<0.001

[a], Other includes American Indian/AK Native, Asian/Pacific Islander. CSS, cancer-specific survival; HR, hazard radio; CI, confidence interval; LN, lymph node; UD, undifferentiated type.

the relationship between age and OS rates might be complicated, especially in elderly patients, we selected GCSS as the primary study outcome to evaluate the prognostic value of age.

As a key factor, the correlation between age and survival has been widely analyzed in several cancers (3,13,14). In terms of GC, it has been reported that young patients exhibited worse survival due to the high malignancy of tumor characteristics (10). Jiang *et al.* (15) reported that younger GC patients usually have metastasis to LNs. Seo *et al.* also indicated that younger patients had more advanced GC, while the overexpression of p53, HER-2, and MSI were found to be significantly decreased in younger age groups (12). Chen *et al.* (16) indicated that in patients who received surgery, those aged between 56 and 65 years had better CSS and presented with favorable clinicopathological features. By contrast, Song *et al.* (17) suggested that elderly patients experienced a lower OS rate compared with young patients in operable GC.

However, the cut-off values of age assessed by the above studies were inconsistent. In our study, age groups were divided into 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and older than 79 years. After adjusting the available data by known GC prognostic factors, CSS changed with age, being lower among patients older than 70 years. The impact of age on CSS was consistent in both the training and validation sets. Thus, our findings indicate that 70 years should be cut-off age and that elderly GC patients have poorer GCSS than younger patients.

We included Western and Eastern populations to establish the age-based prediction model. Although clinicopathological characteristics between the training and validation sets were significantly different, the C-index was above 0.70 each time. Further evaluation found that, compared with the initial age grouping, age split into 3 groups had a similar and even better predictive accuracy and goodness of fit, which confirmed the model has good extrapolation and prediction efficiency.

Old age is one of the risk factors that preclude surgical treatment for patients. Contrary to non-elderly patients, elderly patients are more likely to
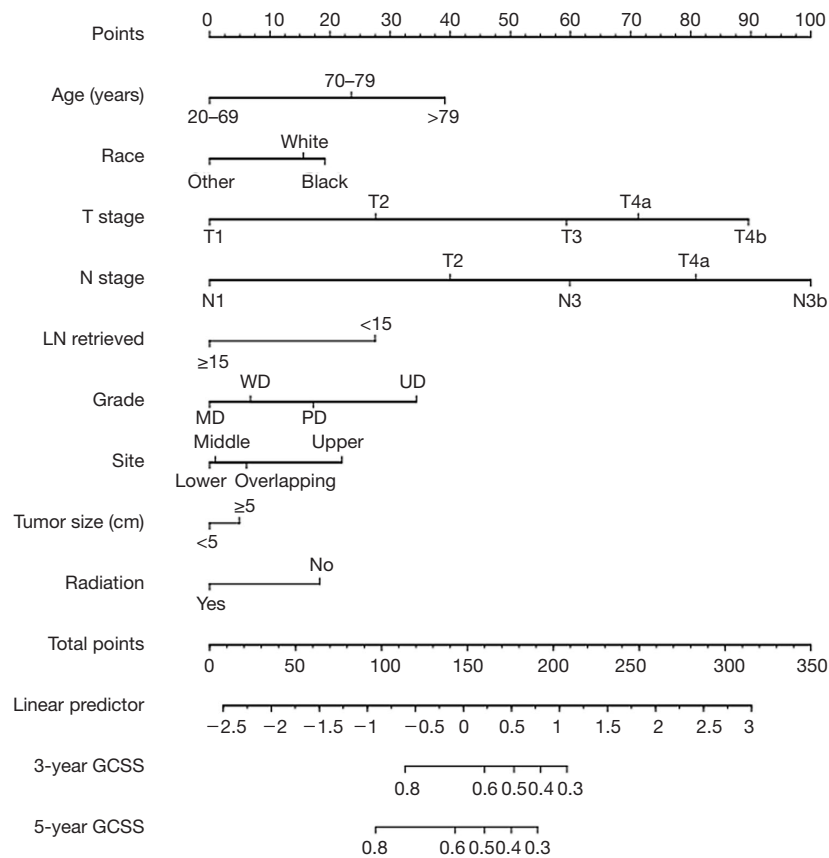
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Figure 2 Nomogram of OS in the training set. OS, overall survival; LN, lymph node; GCSS, gastric cancer-specific survival.

have postoperative complications, and poor compensatory capacity leads to poor tolerance of surgical trauma (18,19). Moreover, the feasibility of inadequate perioperative therapy also increases with age. Previous studies have revealed that chemotherapy and radiotherapy were less likely to be performed on older patients, because they might experience a high incidence and risk of comorbidities, and decreased life expectancy (20,21). This might explain why our results had a poor prognosis for elderly patients.

Other research has demonstrated that elderly patients may be able to gain better prognosis from invasive treatment. Choo *et al.* showed that although patients aged over 80 years suffered from coronary heart disease, cerebral infarction, renal insufficiency, hypertension, and other diseases, surgical intervention was superior to supportive treatment (22). Pan *et al.* performed a meta-analysis on laparoscopic gastrectomy (LG) for elderly patients and concluded that short outcomes were acceptable from LG for elderly patients and that old age alone should not be regarded as a contraindication of LG (23).

For adjuvant chemotherapy, the Adjuvant Chemotherapy Trial of TS-1 for Gastric Cancer (ACTS-GC) (24) found that compared with surgery alone, patients aged from 60 to 80 years experienced a better OS and relapse-free survival (RFS) with the postoperative treatment of TS-1. The CLASSIC trial (25) also indicated that patients over 65 years with positive LNs could benefit from surgery in addition to adjuvant chemotherapy.

Numerous studies have also investigated the efficacy and safety of targeted therapies for elderly patients with advanced GC. The Trastuzumab for Gastric Cancer (ToGA) trial (26) revealed that trastuzumab had a beneficial effect on the elderly group (≥60), with no significant increase in the incidence of severe toxicities. The RAINBOW (27) and REGARD (28) trials reported that ramucirumab or ramucirumab plus paclitaxel could serve as an alternative therapy for elderly GC patients with distant metastasis.

However, prospective studies have imposed age limits for eligible populations, so specific evidence of phase III trials regarding treatment for elderly patients is currently
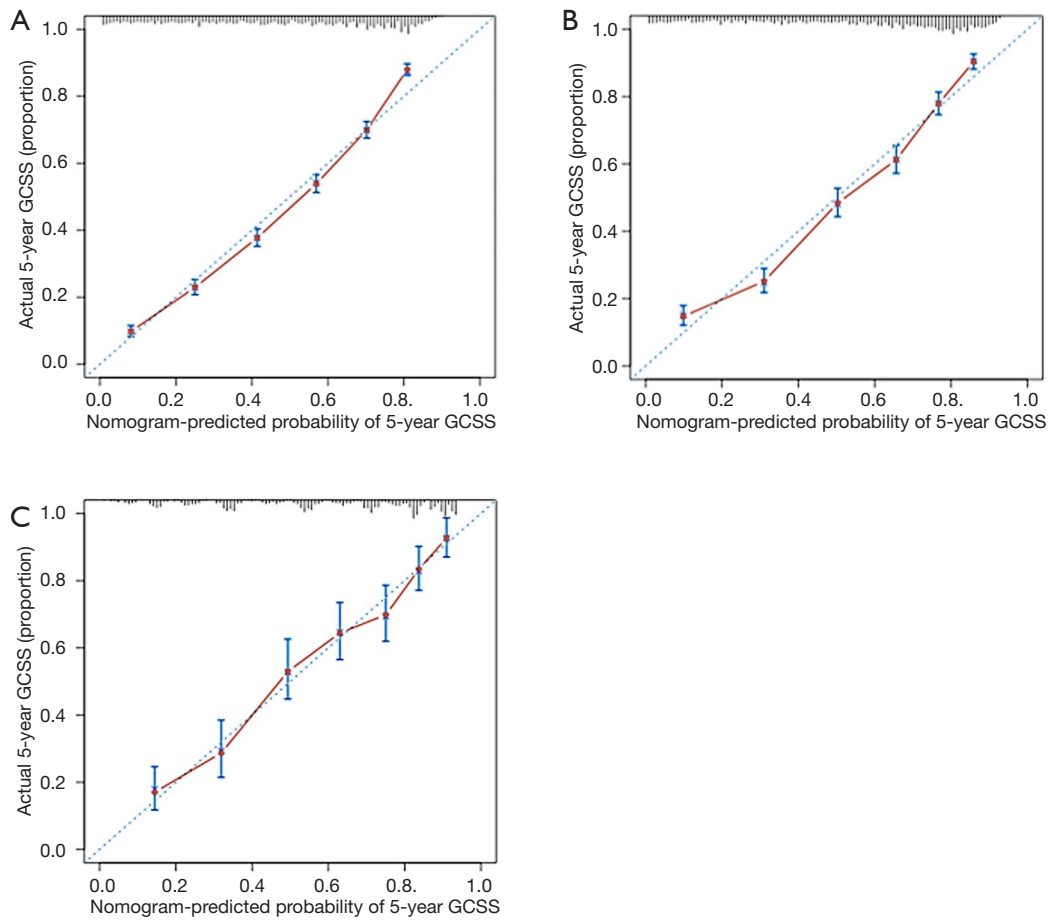
Figure 3 The calibration curves for predicting OS of patients at 3 and 5 years, in the training set (A), internal validation set (B), and external validation set (C). OS, overall survival; GCSS, gastric cancer-specific survival.

Table 3 Multivariate analysis of CSS in the internal and external validation sets

Variables	Internal validation set		External validation set	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)				
20–69	Reference	–	Reference	–
70–79	1.42 (1.32–1.52)	<0.001	1.34 (1.10–1.63)	0.004
>79	1.81 (1.66–1.98)	<0.001	1.76 (1.28–2.42)	0.001
Gender				
Male	–	–	–	–
Female	–	–	–	–
Race				
White	Reference	–	–	–
Black	1.03 (0.94–1.14)	0.485	–	–
Other[a]	0.77 (0.71–0.84)	<0.001	–	–

Table 3 (*Continued*)

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Table 3 (*Continued*)

Variables	Internal validation set		External validation set	
	HR (95% CI)	P value	HR (95% CI)	P value
T stage				
T1	Reference	–	Reference	–
T2/T3/T4	2.94 (2.62–3.31)	<0.001	2.59 (1.59–4.22)	<0.001
N stage				
N0	Reference	–	Reference	–
N1/2/3	2.78 (2.56–3.00)	<0.001	3.68 (2.83–4.80)	<0.001
LN examined				
<15	–	–	Reference	–
≥15	–	–	0.76 (0.63-0.93)	0.007
Grade				
1/2	Reference	–	Reference	–
3 and UD	1.43 (1.33–1.54)	<0.001	1.25 (1.02–1.53)	0.028
Site				
Upper stomach	Reference	–	Reference	–
Middle stomach	0.73 (0.64–0.82)	<0.001	0.70 (0.52–0.94)	0.018
Lower stomach	0.76 (0.70–0.83)	<0.001	0.82 (0.68–0.98)	0.032
Overlapping type	0.98 (0.89–1.08)	0.422	–	–
Tumor size (cm)				
<5	Reference	–	Reference	–
≥5	1.16 (1.09–1.24)	<0.001	1.32 (1.09–1.61)	0.006
Radiation				
No	Reference	–	–	–
Yes	0.72 (0.67–0.76)	<0.001	–	–

[a], Other includes American Indian/AK Native, Asian/Pacific Islander. CSS, cancer-specific survival; HR, hazard radio; CI, confidence interval; LN, lymph node; UD, undifferentiated type.

Table 4 Predictive accuracy of age in continuous type and categorical type (6 groups and 3 groups)

Age	Training set		Internal validation set		External validation set	
	C-index	AIC	C-index	AIC	C-index	AIC
Continuous	0.7539	7,773.2	0.7359	8,695.0	0.7426	1,794.1
Categorical (6 groups)	0.7532	7,777.9	0.7350	8,712.9	0.7391	1,802.8
Categorical (3 groups)	0.7531	7,769.7	0.7344	8,714.3	0.7431	1,772.1

C-index, Harrell's concordance index; AIC, Akaike's Information Criterion.

unavailable (29,30). Relevant findings were usually derived from subgroup analysis. Further prospective trials are needed to determine guidelines for GC therapy, particularly in elderly patients.

Some limitations existed in our study. First, it was a retrospective study, thus bias might potentially exist. Second, the SEER database did not contain treatment details such as chemotherapy and target therapy. Third, relatively few patients aged 20–29 were involved, which might have affected the results.

Conclusions

In conclusion, this study showed that age had relative predictive ability of GCSS. Furthermore, it found that 70 years should be the cut-off age and that age ≥70 years is an independent prognostic risk factor for GC patients who undergo surgery. These data highlight the importance of individualized treatment for improving the prognosis of patients with GC.

Acknowledgments

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2020.02.37). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by an independent ethical committee review board at Liaoning Cancer Hospital & Institute Ethical Committee (No. 20181226). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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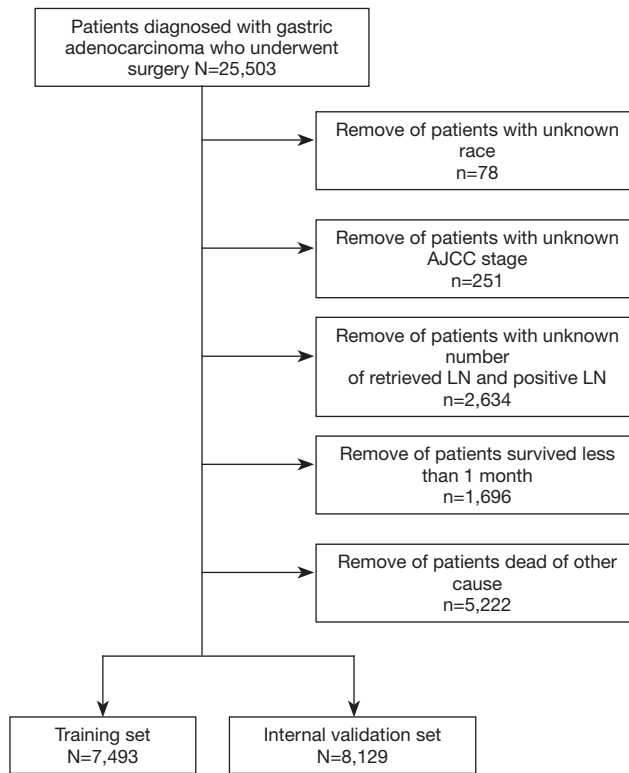
Figure S1 CONSORT diagram of the training and internal validation cohorts. AJCC, eighth edition. AJCC, American Joint Committee on Cancer; LN, lymph node.
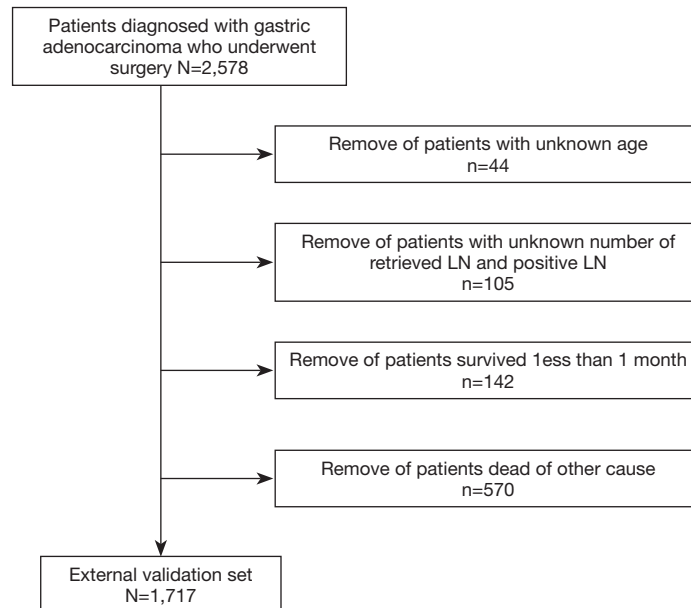

Figure S2 CONSORT diagram of the external validation cohort. AJCC, eighth edition. AJCC, American Joint Committee on Cancer; LN, lymph node.

Table S1 Univariate analysis of CSS in the training set

Variables	Training set	
	HR (95% CI)	P value
Age (years)		
20–29	0.86 (0.48–1.52)	0.596
30–39	1.05 (0.82–1.34)	0.708
40–49	0.92 (0.78–1.08)	0.307
50–59	1.01 (0.90–1.13)	0.895
60–69	Reference	–
70–79	1.14 (1.02–1.26)	0.021
>79	1.63 (1.44–1.85)	<0.001
Gender		
Male	Reference	–
Female	0.97 (0.90–1.06)	0.517
Race		
White	Reference	–
Black	1.03 (0.91–1.16)	0.669
Other[a]	0.74 (0.67–0.82)	<0.001
T stage		
T1	Reference	–
T2/T3/T4	5.39 (4.63–6.28)	<0.001
N stage		
N0	Reference	–
N1/2/3	4.03 (3.66–4.43)	<0.001
LN examined		
<15	Reference	–
≥15	0.92 (0.85–1.00)	0.050
Grade		
1/2	Reference	–
3 and UD	1.95 (1.77–2.15)	<0.001
Site		
Upper stomach	Reference	–
Middle stomach	0.87 (0.74–1.01)	0.066
Lower stomach	0.90 (0.82–1.00)	0.051
Overlapping type	1.40 (1.21–1.63)	<0.001
Tumor size (cm)		
<5	Reference	–
≥5	2.08 (1.91–2.26)	<0.001
Radiation		
No	Reference	–
Yes	1.15 (1.06–1.24)	0.001

[a], Other includes American Indian/AK Native, Asian/Pacific Islander. CSS, cancer-specific survival; HR, hazard radio; CI, confidence interval; LN, lymph node; UD, undifferentiated type.

Table S2 Univariate analysis of CSS in the internal and external validation sets

Variables	Internal validation set		External validation set	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)				
20–29	0.98 (0.59–1.63)	0.930	1.18 (0.38–3.69)	0.778
30–39	0.95 (0.78–1.16)	0.612	1.20 (0.68–2.10)	0.531
40–49	0.95 (0.85–1.07)	0.389	0.87 (0.60–1.27)	0.468
50–59	0.95 (0.86–1.04)	0.240	0.90 (0.71–1.12)	0.338
60–69	Reference	–	Reference	–
70–79	1.18 (1.09–1.28)	<0.001	1.45 (1.17–1.80)	0.001
>79	1.54 (1.40–1.69)	<0.001	2.04 (1.47–2.84)	<0.001
Gender				
Male	Reference	–	Reference	–
Female	0.99 (0.93–1.05)	0.640	0.93 (0.77–1.12)	0.424
Race				
White	Reference	–	–	–
Black	0.96 (0.87–1.05)	0.324	–	–
Other[a]	0.71 (0.66–0.77)	<0.001	–	–
T stage				
T1	Reference	–	Reference	–
T2/T3/T4	4.59 (4.11–5.11)	<0.001	5.13 (3.24–8.28)	<0.001
N stage				
N0	Reference	–	Reference	–
N1/2/3	3.59 (3.34–3.86)	<0.001	4.69 (3.63–6.05)	<0.001
LN examined				
<15	Reference	–	Reference	–
≥15	1.00 (0.94–1.06)	0.003	0.80 (0.65–0.98)	0.028
Grade				
1/2	Reference	–	Reference	–
3 and UD	1.80 (1.67–1.93)	<0.001	1.37 (1.13–1.67)	0.001
Site				
Upper stomach	Reference	–	Reference	–
Middle stomach	0.74 (0.66–0.84)	<0.001	0.58 (0.43–0.77)	<0.001
Lower stomach	0.81 (0.75–0.88)	<0.001	0.75 (0.62–0.90)	0.002
Overlapping type	1.31 (1.17–1.47)	<0.001	–	–
Tumor size (cm)				
<5	Reference	–	Reference	–
≥5	1.76 (1.65–1.88)	<0.001	1.73 (1.42–2.10)	<0.001
Radiation				
No	Reference	–	–	–
Yes	1.10 (1.04–1.17)	0.002	–	–

[a], Other includes American Indian/AK Native, Asian/Pacific Islander. CSS, cancer-specific survival; HR, hazard radio; CI, confidence interval; LN, lymph node; UD, undifferentiated type.