Clinical Features and Prognostic Factors of Elderly Individuals with Retroperitoneal Liposarcoma

Shuai Jin

Henan Provincial People's Hospital, People's Hospital of Zhengzhou University

Lianyuan Tao

Henan Provincial People's Hospital, People's Hospital of Zhengzhou University

Haibo Yu (✉ yhb2101661@163.com)

Henan Provincial People's Hospital, People's Hospital of Zhengzhou University

Research Article

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Abstract

Background: This study attempted to evaluate the clinical features and prognostic factors of elderly patients with retroperitoneal liposarcoma (RLS) and establish a nomogram to predict overall survival (OS).

Methods: Patients diagnosed with RLS from 2010 to 2015 were identified from the Surveillance Epidemiology and End Results database. Clinical features and prognostic factors were examined, and a nomogram was constructed.

Results: There were many differences between the elderly patients with RLS and the young patients with RLS; these differences included marital status, surgery, radiation, chemotherapy, and OS ($P < 0.05$). An analysis of prognostic factors showed that surgery, as the main treatment for elderly patients, can significantly improve prognosis. Histological type and AJCC stage also had a significant effect on OS. Unlike the young group, age was an independent prognostic factor for the elderly. Nomograms for the elderly population were developed based on these prognostic factors. The C-indexes of the 1-, 3- and 5-year survival nomograms were 0.737 (95% CI 0.692-0.782), 0.737 (0.692-0.782) and 0.7367 (0.692-0.782), and the AUCs at 1, 3, and 5 years were 0.749, 0.804 and 0.810, respectively. Further results demonstrate the superiority of this approach in risk stratification over the AJCC staging system.

Conclusions: Elderly patients with RLS are a particular group of individuals who are distinct from young patients in many clinical characteristics, and the constructed nomograms could accurately predict OS in elderly patients with RLS.

Background

Liposarcomas are the most common (45.8-72.4%) histological subtype of retroperitoneal sarcomas [1]. Several studies have shown that RLS is more likely to occur at an average age from 57 to 63 years old [2-16]. Moreover, age has been proven to be an unfavorable prognostic factor for RLS [8]. Hence, elderly patients with RLS may represent a special subgroup that needs more clinical attention. Many studies have reported that factors, such as AJCC stage, age, histologic subtype, and surgical resection, are critical prognostic factors for RLS [5, 6, 8, 17]. Although the prognostic factors for RLS have been widely reported, there remains a lack of an accurate prediction model for the elderly population, which is significantly different from the younger population. In this study, we analyzed the demographic characteristics, clinicopathological characteristics, and treatment methods of the elderly population and developed a novel nomogram for elderly patients with RLS.

Methods

Patient cohort

Through the Surveillance Epidemiology and End Results (SEER) *Stat Software Version 8.3.8, data from the SEER database-18 registry of the National Cancer Institute were retrieved. As a publicly available database, the application of its data did not need approval from the institutional review board. Detailed information on patients with a primary site of 'retroperitoneum' and an ICD-O-3 histology/behavior, malignant code of '8858/3: dedifferentiated liposarcoma,' '8857/3: fibroblastic liposarcoma,' '8855/3: mixed liposarcoma,' '8854/3: pleomorphic liposarcoma,' '8853/3: round cell liposarcoma,' '8852/3: myxoid liposarcoma,' '8851/3: liposarcoma, well differentiated,' or '8850/3: liposarcoma, NOS,' was derived between January 1, 2010, and December 31, 2015. Patients who lacked demographic information, such as age, sex, or race, were excluded. Since the number of patients with '8853/3: round cell liposarcoma' and '8857/3: fibroblastic liposarcoma' were so low (only 3 patients had these diagnoses among the whole search results), we also excluded those histological types from the present study.

Data collection

Information including age, race, sex, marital status, AJCC stage, T stage, N stage, M stage, distant organ metastasis (liver, lung, bone, and brain), histological subtype, surgery, lymph node dissection, chemotherapy, radiation, survival time, and vital status was collected from each patient.

According to the reclassification of soft tissue sarcomas issued by the World Health Organization (WHO), liposarcoma was divided into several subgroups: dedifferentiated, well-differentiated, myxoid, pleomorphic, and mixed [15]. Other subtypes, such as round cell or fibroblast, have been extremely seldom reported; here, we did not enroll them in this study.

Statistical analyses

Empower Stats 2.2 (<http://www.empowerstats.com/cn/>) and R-project (version 4.0.1) were applied for statistical analyses. An optimal cutoff value for age was determined through X-tile software v3.6.1 (Yale University, New Haven, CT, USA) [18]. Continuous variables are expressed as the mean $\pm$ standard deviation, and independent samples t-tests were performed for comparisons between groups. Categorical variables were analyzed using the odds ratio (OR) and chi-square (χ^2) test. Possible prognostic factors were explored through univariate and multivariate Cox regression analyses. Curve fitting was developed for the evaluation between age and vital status. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) were evaluated. A P value <0.05 was considered statistically significant. The accuracy of the nomogram was compared with that of the AJCC7 stage through the calculation of both the net reclassification improvement (NRI) and integrated discrimination improvement (IDI).

Results

Patient characteristics

A total of 992 cases of RLS (524 males and 398 females) were enrolled in our study. We first detected the prognostic factors for all the participants through univariate Cox regression analysis (Table 1). Our data indicated that age, marital status, histological type, AJCC stage, N stage, M stage, surgery, lymph node dissection, radiation, chemotherapy, and distant organ metastasis (liver, lung, bone, and brain) were prognostic factors for RLS ($P<0.05$). A multivariate analysis was then performed (Table 2). The results showed that age, histological type, AJCC stage, surgery, and chemotherapy were prognostic factors for RLS ($P<0.05$). Therefore, as an independent prognostic factor for RLS, age deserves further exploration.

The age of 70 years was also identified through X-tile software as the optimal cut-off value (Figure 1), which divided the patients with RLS into two age groups. A total of 619 patients with RLS diagnosed older than 70 years old were identified as the elderly group, and 303 patients were classified in the young group (<70 years old). Then, the characteristics of the elderly and young groups were compared, and the data showed that patients with RLS in the elderly group were significantly different from those in the young group in many aspects, such as marital status, surgery, radiation, and chemotherapy ($P<0.05$, Table 3). Of the 992 patients, mortality occurred in 268 patients (27.0%) at the follow-up deadline. By comparison, the elderly patients with RLS had a higher overall mortality rate (41.58%) compared to that in the young patients with RLS (22.94%) at the end of follow-up ($P<0.001$).

Prognostic factors of the elderly patients with RLS

Through univariate Cox regression, our results revealed that age, histological type, AJCC stage, N stage, M stage, surgery, radiation, chemotherapy, liver metastasis, and lung metastasis showed significant effects on overall survival of the patients above 70 years old ($P<0.05$, Table 4). On the other hand, unlike the elderly group, the prognostic factors for the young group were sex, histological type, AJCC stage, N stage, M stage, distant metastasis (liver, lung, and bone metastasis), surgery, lymph node dissection, and chemotherapy ($P<0.05$, Table 4). These results further revealed the difference between the two age groups.

A subsequent multivariate Cox regression analysis was performed based on the univariate Cox regression analysis, and four independent prognostic predictors (age, histological type, AJCC stage, and surgery) for the elderly group were identified. The data demonstrated that age was an unfavorable prognostic factor ($HR=1.05$, 95% $CI=1.01-1.09$). There were significant differences in prognosis between different histological types. Compared to the dedifferentiated type, the mixed type has a worse prognosis. Moreover, higher grades of AJCC stage also indicated worse overall survival. Compared to stage I, higher grades, such as stage II ($HR=2.08$, 95% $CI=1.02-4.22$), stage III (2.32, 1.31-4.10) or stage IV (3.44, 1.64-7.21), were associated with worse OS. In regard to treatment, surgery also showed a significantly positive impact on overall survival (0.31, 0.18-0.54). All the details are shown in Table 5. Such results are also different from the young patients, whose independent prognostic factors did not include age (Table 6).

The correlations of the three categorical variables among four independent predictors for the elderly group (histological type, AJCC stage, and surgery) with overall survival obtained by the log-rank test were

also demonstrated through the survival curve (Figure 2). Then, a nomogram of the elderly population was constructed based on the four independent prognostic factors.

Nomogram Construction

According to the multivariate models, nomograms that combined all five independent prognostic factors were developed to predict overall survival at 1, 3 and 5 years for the elderly group (Figure 3).

Validation and Calibration of the Nomogram

The C-indexes of the 1-, 3- and 5-year survival nomograms were 0.737 (95% CI 0.692-0.782), 0.737 (0.692-0.782) and 0.7367 (0.692-0.782) for OS in the elderly group, respectively. The discrimination ability of the nomogram for OS was evaluated by comparing the AJCC7 stage. The corresponding C-index values of the AJCC7 stage were 0.631 (95% CI 0.576-0.685), 0.6306 (0.576-0.685) and 0.6306 (0.576-0.685). Therefore, the C-index of the nomogram was significantly higher than that of the AJCC7 stage ($P<0.001$), especially at 3 and 5 years, reflecting the better overall discrimination ability of the nomogram.

Then, the discrimination ability of the nomogram at 1, 3, and 5 years was examined, and the corresponding AUCs were 0.749, 0.804 and 0.810, respectively. However, the AUCs were 0.679, 0.710 and 0.646 for the AJCC7 stage (Figure 4), which were all lower than those of the nomogram ($P<0.001$). Therefore, the newly constructed model had a better discrimination ability than that of the AJCC7 stage.

We further verified the accuracy of the nomogram using NRI and IDI in elderly individuals. The AJCC7 stage was set as the old model. The NRIs for OS at 1, 3, and 5 years were 0.371 (95% CI 0.169-0.498), 0.364 (0.235-0.519), and 0.553 (0.167-0.846), respectively. The IDIs for OS at 1, 3, and 5 years were 0.072, 0.138, and 0.211 (all $P<0.001$), respectively. Hence, the nomogram had better accuracy than the AJCC7 staging system for predicting OS at 1, 3, and 5 years.

Calibration curves demonstrated acceptable agreement between the predicted death rate and observed values of overall survival (Figure 5). Thus, we believe the nomogram model had a high accuracy for the prediction of OS at 1, 3 and 5 years for elderly patients with RLS.

Discussion

According to the fitting curves between age and OS, the patients with RLS were first divided into a young group (<70 years old) and an elderly group (≥ 70 years). Elderly patients accounted for a large portion of all patients with RLS (32.9%). Multivariate Cox regression analysis of all patients with RLS indicated that age was an independent unfavorable prognostic factor for RLS, which agrees with a previous study [8]. Moreover, further analysis also indicated that age was an independent prognostic factor for the elderly group but failed to reach a statistically significant level in the young group. These results further proved that elderly patients with RLS are a distinct group. Moreover, the proportion of patients in the elderly

group who were married (167/303, 55.12%) was significantly lower than that of young patients (394/619, 63.65%), which may be due to the high mortality rate of their spouses in their age range.

A comparison between the two age groups revealed that patients ≥ 70 years old were less likely to receive treatments such as surgery and radiation. Nonetheless, surgery was the main form of treatment, and radiation was obviously less applied. Further analysis revealed that surgery has the best therapeutic benefit, which has been proven to be the main treatment for RLS [16, 19-23]. Although radiotherapy showed a positive impact on overall survival under univariate analysis, it failed to present a correlation with OS under multivariate analysis. Such a result should be attributed to the lower sensitivity of RLS to radiotherapy [1, 21, 24, 25]. Although it failed to reach a statistically significant level, the present study indicated that chemotherapy was unfavorable to the prognosis of RLS in both age groups.

The AJCC stage has also been proven to be an independent prognostic factor for the OS of elderly patients with RLS. Moreover, our study indicated that the overall mortality rate was higher among the elderly group. One reason may be that the older the cancer patient is, the more basic diseases he or she has and the more likely he or she will die from these diseases [26]. Therefore, clinical workers should pay more attention to systemic conditions and basic diseases when treating elderly patients with RLS. Regarding the histological type, the multivariate Cox regression analysis showed that, compared with the differentiated type, the mixed type was an unfavorable prognostic factor. Despite the lack of statistical significance, our results suggested that the myxoid type was also an unfavorable prognostic factor, while the well-differentiated type or the pleomorphic type tended to indicate a favorable prognosis. Such a result has already been proven by many studies [5-9, 17, 19, 24].

There are many differences between the elderly and the young, indicating that elderly patients with RLS are a special group of individuals. To better evaluate the prognosis of this distinct population, a nomogram model for the prediction of overall survival was constructed, since the elderly population has many underlying diseases that are likely to cause death during the course of RLS. The current study developed a prediction evaluation model for 1 year, 3 years and 5 years. Therefore, a nomogram was constructed based on all the independent predictors (age, histological type, AJCC stage and surgery). To the best of our knowledge, no nomograms have been constructed specifically for elderly patients with RLS. With good discrimination and predictive accuracy, our study constructed prognostic nomograms for this special group of patients based on a population-based cohort.

Our study had several main limitations. The relatively incomplete clinical information hinders further evaluations of treatment in elderly patients. For example, many patients lacked data such as T stage, N stage, or AJCC stage. Information on the specific chemotherapy regimen used, detailed surgical scope and procedure, and radiation dose were also not available. Therefore, alternative explanations for some findings in the present study cannot be ruled out. However, our findings may be useful to assess the prognosis of elderly patients with RLS, as well as the establishment of treatment policies.

Conclusions

Elderly patients with RLS are a distinct group of individuals whose clinical features and prognosis are significantly different from those of younger patients with RLS, and our constructed nomogram could predict overall survival in elderly patients with RLS accurately and may facilitate the selection of beneficial treatment strategies.

Abbreviations

RLS: retroperitoneal liposarcoma; OS: overall survival; AJCC: American Joint Committee on Cancer; SEER: the Surveillance Epidemiology and End Results; ROC: receiver operating characteristic; AUC: the area under the curve; NRI: net reclassification improvement; IDI: integrated discrimination improvement.

Declarations

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Authors' contributions

JS and TLY designed the research study, conceived the manuscript, and analyzed data. JS, TLY and YHB analyzed and interpreted the patient data and prepared the first draft of the paper. JS and TLY were major contributors in interpreting of the results and reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data used and analyzed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication

The patients have consented to the submission of the report to the journal.

Competing interests

The authors declare that they have no competing interests.

Author details

Department of Hepatobiliary Surgery, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, No. 7 Weiwu Road, Zhengzhou, 450003, China.

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Tables

Table 1

Univariate Cox regression analysis for all patients.

Variables	HR (95%CI), P value
Sex	
Male	1.0
Female	0.73 (0.57, 0.94) 0.0130
Age	1.04 (1.03, 1.05) <0.0001
Race	
White	1.0
Other	0.99 (0.73, 1.36) 0.9697
Marital status	
Married	1.0
Other	1.32 (1.03, 1.67) 0.0258
Year of diagnosis	
2010	1.0
2011	1.23 (0.86, 1.77) 0.2512
2012	1.08 (0.72, 1.60) 0.7152
2013	1.09 (0.72, 1.67) 0.6822
2014	1.43 (0.92, 2.22) 0.1116
2015	1.10 (0.58, 2.08) 0.7776
Histological type	
Dedifferentiated	1.0
Well-differentiated	0.29 (0.21, 0.40) <0.0001
NOS	0.64 (0.46, 0.90) 0.0110
Mixed	1.60 (0.84, 3.03) 0.1535
Pleomorphic	0.70 (0.33, 1.49) 0.3539
Myxoid	0.77 (0.47, 1.27) 0.3091
Derived AJCC Stage Group, 7th	
I	1.0
II	1.79 (1.12, 2.85) 0.0144
III	2.79 (2.09, 3.73) <0.0001

IV	9.98 (6.80, 14.65) <0.0001
T stage	
T0-T1	1.0
T2	1.26 (0.69, 2.30) 0.4596
N stage	
N0	1.0
N1	2.67 (1.53, 4.68) 0.0006
M stage	
M0	1.0
M1	6.13 (4.33, 8.68) <0.0001
Tumor size(mm)	1.00 (1.00, 1.00) 0.6479
Surgery	
No	1.0
Yes	0.22 (0.17, 0.28) <0.0001
LN surg	
None	1.0
1 to 3 regional lymph nodes removed	0.50 (0.29, 0.84) 0.0087
4 or more regional lymph nodes removed	0.87 (0.57, 1.33) 0.5212
Radiation	
No	1.0
Yes	0.60 (0.43, 0.83) 0.0021
Chemotherapy	
No	1.0
Yes	2.63 (1.95, 3.55) <0.0001
Bone metastasis	
No	1.0
Yes	5.55 (1.37, 22.47) 0.0162
Brain metastasis	
No	1.0

Yes	20.87 (5.05, 86.30) <0.0001
Liver metastasis	
No	1.0
Yes	4.89 (2.41, 9.93) <0.0001
Lung metastasis	
No	1.0
Yes	10.51 (5.92, 18.67) <0.0001

Table 2

Multivariate Cox regression analysis for all patients.

Variables	HR (95%CI), P value
Sex	
Male	1.0
Female	1.01 (0.77, 1.33) 0.9343
Age	1.04 (1.03, 1.05) <0.0001
Histological explanation	
Dedifferentiated	1.0
Well-differentiated	0.51 (0.34, 0.78) 0.0018
NOS	0.56 (0.36, 0.88) 0.0113
Mixed	2.04 (1.05, 3.96) 0.0351
Pleomorphic	0.65 (0.26, 1.64) 0.3655
Myxoid liposarcoma	1.04 (0.58, 1.85) 0.8996
Derived AJCC Stage Group, 7th	
I	1.0
II	1.54 (0.92, 2.59) 0.1002
III	2.03 (1.39, 2.96) 0.0002
IV	3.90 (2.21, 6.86) <0.0001
Surgery	
No	1.0
Yes	0.28 (0.20, 0.41) <0.0001
Chemotherapy	
No	1.0
Yes	1.58 (1.10, 2.26) 0.0125
Radiation	
No	1.0
Yes	0.74 (0.52, 1.06) 0.1049
Liver metastasis	
No	1.0
Yes	0.59 (0.24, 1.45) 0.2471

Lung metastasis	
No	1.0

Table 3

Characteristics of all participants.

Variables	<70 years	≥70 years	P-value
Number	619 (67.1%)	303(32.9%)	
Tumor size(mm)	218.09 ± 131.24	203.34 ± 133.17	0.128
Sex			0.095
Male	340 (54.93%)	184 (60.73%)	
Female	279 (45.07%)	119 (39.27%)	
Race			0.092
White	499 (80.61%)	258 (85.15%)	
Other	120 (19.39%)	45 (14.85%)	
Marital status			0.013
Married	394 (63.65%)	167 (55.12%)	
Other	225 (36.35%)	136 (44.88%)	
Year of diagnosis			0.408
2010	96 (15.51%)	36 (11.88%)	
2011	109 (17.61%)	55 (18.15%)	
2012	106 (17.12%)	44 (14.52%)	
2013	100 (16.16%)	54 (17.82%)	
2014	107 (17.29%)	52 (17.16%)	
2015	101 (16.32%)	62 (20.46%)	
Histological type	0.273		
Dedifferentiated	253 (40.94%)	109 (36.45%)	
Well-differentiated	224 (36.25%)	99 (33.11%)	
NOS	92 (14.89%)	61 (20.40%)	
Mixed	9 (1.46%)	6 (2.01%)	
Pleomorphic	11 (1.78%)	7 (2.34%)	
Myxoid	29 (4.69%)	17 (5.69%)	
Derived AJCC Stage Group, 7th			0.865
I	336 (57.73%)	169 (60.14%)	
II	55 (9.45%)	23 (8.19%)	

III	158 (27.15%)	72 (25.62%)	
IV	33 (5.67%)	17 (6.05%)	
T stage			0.652
T0-T1	32 (5.62%)	13 (4.87%)	
T2	537 (94.38%)	254 (95.13%)	
N stage			0.280
N0	565 (97.75%)	275 (96.49%)	
N1	13 (2.25%)	10 (3.51%)	
M stage			0.860
M0	586 (94.67%)	286 (94.39%)	
M1	33 (5.33%)	17 (5.61%)	
Surgery			<0.001
No	58 (9.37%)	59 (19.47%)	
Yes	561 (90.63%)	244 (80.53%)	
LN surg			0.494
None	480 (78.56%)	243 (81.82%)	
1 to 3 regional lymph nodes removed	69 (11.29%)	27 (9.09%)	
4 or more regional lymph nodes removed	62 (10.15%)	27 (9.09%)	
Radiation			0.040
No	481 (77.71%)	253 (83.50%)	
Yes	138 (22.29%)	50 (16.50%)	
Chemotherapy			0.057
No	542 (87.56%)	278 (91.75%)	
Yes	77 (12.44%)	25 (8.25%)	
Overall Survival			<0.001
Live	477 (77.06%)	177 (58.42%)	
Dead	142 (22.94%)	126 (41.58%)	
Bone metastasis			0.973

No	600 (99.67%)	288 (99.65%)	
Yes	2 (0.33%)	1 (0.35%)	
Brain metastasis			0.327
No	600 (99.67%)	289 (100.00%)	
Yes	2 (0.33%)	0 (0.00%)	
Liver metastasis			0.709
No	594 (98.67%)	287 (98.97%)	
Yes	8 (1.33%)	3 (1.03%)	
Lung metastasis			0.526
No	592 (98.50%)	282 (97.92%)	
Yes	9 (1.50%)	6 (2.08%)	

Table 4

Univariate Cox regression analysis for overall survival among different age groups.

Variables	Age<70 years	Age≥70 years
Sex		
Male	1.0	1.0
Female	0.57 (0.40, 0.81) 0.0015	1.15 (0.81, 1.65) 0.4314
Age	1.02 (1.00, 1.04) 0.0823	1.08 (1.05, 1.11) <0.0001
Race		
White	1.0	1.0
Other	1.33 (0.91, 1.96) 0.1431	0.70 (0.40, 1.22) 0.2064
Marital status		
Married	1.0	1.0
Other	1.22 (0.87, 1.71) 0.2426	1.28 (0.90, 1.81) 0.1674
Year of diagnosis		
2010	1.0	1.0
2011	1.28 (0.80, 2.06) 0.3030	0.97 (0.56, 1.69) 0.9192
2012	1.11 (0.66, 1.87) 0.6822	0.91 (0.49, 1.69) 0.7706
2013	1.11 (0.63, 1.95) 0.7277	0.87 (0.46, 1.64) 0.6667
2014	1.11 (0.58, 2.14) 0.7458	1.48 (0.80, 2.75) 0.2150
2015	1.05 (0.39, 2.82) 0.9305	0.88 (0.37, 2.07) 0.7641
Histological type		
Dedifferentiated	1.0	1.0
Well-differentiated	0.23 (0.14, 0.36) <0.0001	0.35 (0.22, 0.56) <0.0001
NOS	0.42 (0.24, 0.71) 0.0013	0.83 (0.53, 1.33) 0.4437
Mixed	1.31 (0.53, 3.22) 0.5604	1.88 (0.75, 4.71) 0.1770
Pleomorphic	0.47 (0.15, 1.49) 0.1994	1.04 (0.37, 2.86) 0.9462
Myxoid liposarcoma	0.53 (0.26, 1.10) 0.0876	1.31 (0.64, 2.65) 0.4575
Derived AJCC Stage Group, 7th		
I	1.0	1.0
II	1.69 (0.82, 3.48) 0.1566	1.95 (1.06, 3.59) 0.0328
III	3.80 (2.53, 5.71) <0.0001	2.24 (1.45, 3.46) 0.0003

IV	15.25 (9.13, 25.46) <0.0001	6.56 (3.57, 12.05) <0.0001
T stage		
T0-T1	1.0	1.0
T2	1.00 (0.49, 2.05) 0.9977	1.71 (0.54, 5.39) 0.3597
N stage		
N0	1.0	1.0
N1	2.45 (1.08, 5.57) 0.0325	2.68 (1.24, 5.80) 0.0121
M stage		
M0	1.0	1.0
M1	8.29 (5.32, 12.91) <0.0001	4.26 (2.42, 7.51) <0.0001
Tumor size(mm)	1.00 (1.00, 1.00) 0.8564	1.00 (1.00, 1.00) 0.7311
Surgery		
No	1.0	1.0
Yes	0.21 (0.14, 0.31) <0.0001	0.28 (0.19, 0.41) <0.0001
Lymph node dissection,		
None	1.0	1.0
1 to 3 regional lymph nodes removed	0.48 (0.24, 0.99) 0.0465	0.55 (0.26, 1.18) 0.1259
4 or more regional lymph nodes removed	0.90 (0.50, 1.59) 0.7045	0.85 (0.46, 1.59) 0.6159
Radiation		
No	1.0	1.0
Yes	0.76 (0.51, 1.14) 0.1891	0.46 (0.26, 0.80) 0.0057
Chemotherapy		
No	1.0	1.0
Yes	3.54 (2.45, 5.12) <0.0001	2.23 (1.29, 3.86) 0.0041
Bone metastasis		
No	1.0	1.0
Yes	5.76 (0.80, 41.58) 0.0825	6.24 (0.86, 45.35) 0.0706
Brain metastasis		

No	1.0	1.0
Yes	36.27 (8.34, 157.75) <0.0001	1.0
Liver metastasis		
No	1.0	1.0
Yes	5.55 (2.26, 13.65) 0.0002	4.71 (1.48, 14.95) 0.0086
Lung metastasis		
No	1.0	1.0
Yes	14.39 (6.86, 30.19) <0.0001	7.32 (2.91, 18.39) <0.0001

Table 5

Multivariate Cox regression analysis for the elderly group.

Variables	HR (95%CI), P value
Age	1.05 (1.01, 1.09) 0.0068
Histological type	
Dedifferentiated	1.0
Well-differentiated	0.65 (0.36, 1.17) 0.1508
NOS	0.68 (0.38, 1.22) 0.1987
Mixed	2.62 (1.01, 6.81) 0.0484
Pleomorphic	0.44 (0.10, 1.94) 0.2763
Myxoid	1.89 (0.85, 4.22) 0.1191
Derived AJCC Stage Group, 7th	
I	1.0
II	2.08 (1.02, 4.22) 0.0433
III	2.32 (1.31, 4.10) 0.0037
IV	3.44 (1.64, 7.21) 0.0011
Surgery	
No	1.0
Yes	0.31 (0.18, 0.54) <0.0001
Chemotherapy	
No	1.0
Yes	1.57 (0.81, 3.06) 0.1829

Table 6

Multivariate Cox regression analysis for the young group.

Variables	HR (95%CI), P value
Sex	
Male	1.0
Female	0.77 (0.53, 1.12) 0.1741
Histological type	
Dedifferentiated	1.0
Well-differentiated	0.43 (0.24, 0.76) 0.0036
NOS	0.50 (0.26, 0.94) 0.0313
Mixed	1.28 (0.50, 3.25) 0.6069
Pleomorphic	0.71 (0.22, 2.28) 0.5635
Myxoid	0.45 (0.20, 1.02) 0.0572
Derived AJCC Stage Group, 7th	
I	1.0
II	1.17 (0.54, 2.56) 0.6859
III	2.12 (1.27, 3.53) 0.0042
IV	6.31 (3.43, 11.62) <0.0001
Surgery	
No	1.0
Yes	0.25 (0.15, 0.40) <0.0001
Chemotherapy	
No	1.0
Yes	1.27 (0.82, 1.97) 0.2757

Figures

Figure 1

Estimation of the cut-off value for the age stratification as determined by the X-tile software. The age of 70 years was estimated as the optimal cut-off value.

Figure 2

Overall survival curves of independent prognostic factors for the elderly group according to the log-rank test. Each stratification was adjusted for all the factors (histological type, AJCC stage, and surgery), except the stratification factor itself.

Figure 3

Nomogram for predicting the 1-, 3- and 5-year overall survival (OS). An individual patient's value is located on each variable axis, and the number of points received for each variable value can be determined by drawing a line upward. The sum of these numbers is located on the total points axis, and the likelihood of 1-, 3- or 5-year survival can be determined by drawing a line downward to the survival axes.

Figure 4

Receiver operating characteristic (ROC) curves for OS at 1-, 3- and 5- years according to the nomogram and the 7th edition of American Joint Committee on Cancer (AJCC7) staging system of the elderly group.

Figure 5

Calibration plot for overall survival (OS) prediction at 1-, 3- and 5- years according to the nomograms. Acceptable agreement between the predicted death rate and observed values of OS is shown in the calibration curves.