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Development and validation of a nomogram for predicting survival in patients with gastrointestinal stromal tumours

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ABSTRACT

Background: This study aimed to develop and validate nomograms for predicting long-term overall survival (OS) and cancer-specific survival (CSS) in gastrointestinal stromal tumours (GISTs).

Methods: Patients diagnosed with GISTs between 2004 and 2015 were selected for the study from the Surveillance, Epidemiology, and End Results (SEER) database. Patients were randomly separated into the training set and the validation set. Multivariate analysis was used on the training set to obtain independent prognostic factors to build nomograms for predicting 3- and 5-year OS and CSS. The discrimination and calibration plots were used to evaluate the predictive accuracy of the nomograms.

Results: Data for a total of 5622 patients with GISTs were collected from the SEER database. Nomograms were established based on variables that were significantly associated with OS and CSS identified by the Cox regression model. The nomograms for predicting OS and CSS displayed better discrimination power than did the SEER stage and Tumour-Node-Metastasis (TNM) staging systems (7th edition) in the training set and validation set. Calibration plots of the nomograms indicated that OS and CSS closely corresponded to actual observation.

Conclusions: The nomograms were able to more accurately predict 3- and 5-year OS and CSS of patients with GISTs than were existing models.

Introduction

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal (GI) tract, representing approximately 0.1%–3% of all GI malignancies [1]. They can occur anywhere along the alimentary tract, most commonly in the stomach and small bowel; other locations such as the oesophagus, colon, rectum, and extra-gastrointestinal tract locations are much rare [2]. GISTs are thought to arise from the interstitial cells of Cajal (ICC) or the pacemaker cells of the GI tract [3], and, in most cases, are the result of activating mutations in the KIT proto-oncogene [4,5]. According to the NCCN (National Comprehensive Cancer Network) and the ESMO (European Society for Medical Oncology) guidelines, radical resection with negative microscopic margins (R0) is the most effective therapy for a primary localized GIST [6,7]. Nevertheless, the postoperative recurrence rate for patients with localized GISTs can be 50% [8,9]. Therefore, a more refined staging system considering both the tumour characteristics and host status is needed.

At present, the American Joint Committee on Cancer (AJCC) TNM staging system that has been widely used for prognostic evaluation of GISTs only takes tumour size and histological metastasis into account. The TNM staging system has played an important role in predicting prognosis of malignancies for a long time. Nevertheless, increasing numbers of researchers have come to realize that other factors such as age, sex, tumour site, tumour size, mitotic index, tumour grade and surgery performed also significantly affect the survival of individual patients. Therefore, there is an urgent need to develop a staging system that is technically feasible and easily accessible to stratify the prognosis of patients with GISTs.

The nomogram, a simple statistical predictive tool, has been widely used in clinical practice to predict prognosis [10–12]. Construction of a nomogram not only considers the prognostic weight

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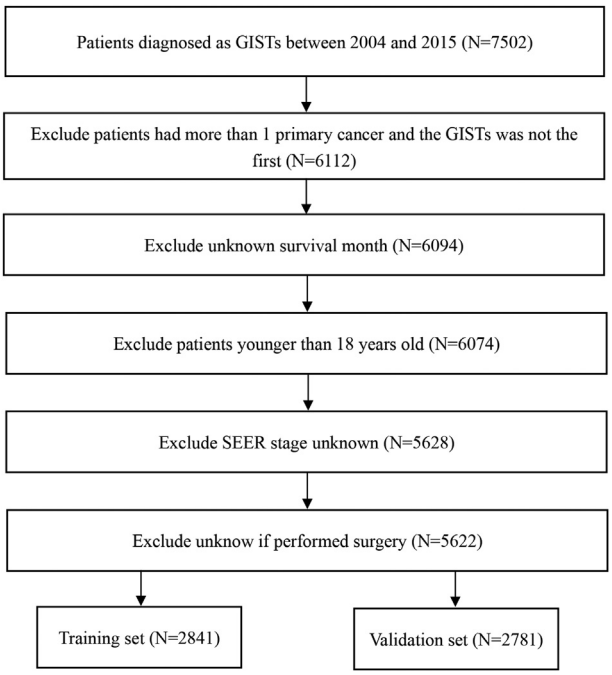

Fig. 1. Flow diagram of the data selection process.

of each factor when calculating the probability of an outcome but also combines several independent factors to draw the best conclusion. Compared to the AJCC TNM staging system, nomograms can more accurately estimate survival for individual patients by integrating important prognostic variables [13,14]. Nevertheless, to the best of our knowledge, nomograms for patients with GISTs on the basis of population-based data have not been reported. Therefore, the purpose of this study was to develop and validate nomograms to predict the OS and CSS of GISTs based on multi-institution and multi-population data from the SEER database.

Materials and methods

Patients

The SEER program of the US National Cancer Institute provides data on cancer incidence and survival in the United States and covers approximately 30% of the US population across several geographic regions [15]. The study population was composed of patients diagnosed with GISTs between 2004 and 2015 from the SEER program of the National Cancer Institute. Patients with GISTs were identified by the cancer staging scheme, version 0204, and the histologic code (International Classification of Diseases for Oncology, Third Edition [ICD-O-3], code 8936). The exclusion criteria were as follows: (1) patients with more than 1 primary cancer, and the GIST was not the first cancer to be diagnosed; (2) patients were diagnosed only from a death certificate or autopsy; (3) patients were less than 18 years old; and (4) patients had missing or incomplete clinicopathological information (survival month, follow-up months, stage and cause of death). To establish and validate the nomograms, all patients were randomly allocated to a training set and a validation set. Institutional review board approval was not required in the current study because the SEER research data is publicly available, and we received permission from SEER to access the research data (accession number: 10165-Nov 2017).

Variables

Demographic and clinical variables were extracted from the SEER database, including age, sex, race, marital status, primary site, tumour size, mitotic index, histological differentiation, SEER stage, TNM stage, surgery performed, follow-up information and cause of death. Age and tumour size as continuous variables were transformed into categorical variables on the basis of recognized cut-off values. The primary endpoints were OS and CSS. OS was defined as the interval from diagnosis of GIST to death or last follow-up, with no restriction as to the cause of death. CSS was defined as the interval from diagnosis to death from GIST or censoring (if a patient was alive at the last follow-up or dead from other causes).

Statistical analyses

Construction of the nomogram

Categorical data were shown as frequencies and proportions and compared with a chi-square test and Fisher's exact test. The

Table 1
Patient demographics and pathological characteristics.

Variables	All patients (n = 5622)		Training set (n = 2841)		Validation set (n = 2781)	
	No.	%	No.	%	No.	%
Age						
≤60	2496	44.4	1255	44.2	1241	44.6
>60	3126	55.6	1586	55.8	1540	55.4
Sex						
Male	2951	52.5	1486	52.3	1465	52.7
Female	2671	45.5	1355	47.7	1316	47.3
Race						
White	3785	67.3	1921	67.6	1864	67.0
Black	1023	18.2	512	18.0	511	18.4
Other[a]	814	14.5	408	14.4	406	14.6
Marital status						
Married	3252	57.8	1635	57.6	1617	58.1
Unmarried	2096	37.3	1067	37.6	1029	37.0
Unknown	274	4.9	139	4.9	135	4.9
Primary site						
Stomach	3564	63.4	1806	63.6	1758	63.2
Small intestine	1626	28.9	819	28.8	807	29.0
Rectum	155	2.8	75	2.6	80	2.9
Colon	103	1.8	53	1.9	50	1.8
Others	174	3.1	88	3.1	86	3.1
Tumour size						
≤2 cm	493	8.8	238	8.4	255	9.2
>2 to ≤5 cm	1564	27.8	821	28.9	743	26.7
>5 to ≤10 cm	1774	31.6	880	31.0	894	32.1
>10 cm	1403	25.0	709	25.0	694	25.0
Unknown	388	6.9	193	6.8	195	7.0
Mitotic index, mitoses/50 HPF						
<5	1781	31.7	887	31.2	894	32.1
5-10	371	6.6	181	6.4	190	6.8
>10	324	5.8	158	5.6	166	6.0
Unknown	3146	56.0	1615	56.8	1531	55.1
Grade						
I	769	13.7	390	13.7	379	13.6
II	559	9.9	292	10.3	267	9.6
III	243	4.3	113	4.0	130	4.7
IV	328	5.8	163	5.7	165	5.9
Unknown	3723	66.2	1883	66.3	1840	66.2
Stage						
Localized	3737	66.5	1866	65.7	1870	67.2
Regional	729	13.0	373	13.1	356	12.8
Distant	1157	20.6	602	21.2	555	20.0
Surgery						
Performed	4675	83.2	2356	82.9	2319	83.4
None	947	16.8	485	17.1	462	16.6

[a] Other includes American Indian/Alaska native, Asian/Pacific Islander, and unknown.

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