ORIGINAL ARTICLE

Construction and validation of prognostic nomogram model for primary malignant cardiac tumours based on SEER database: A retrospective study

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Abstract

Objective: To build a prognostic nomogram for predicting primary malignant cardiac tumour patients' overall survival.

Method: The retrospective study was conducted in January 2023, and comprised data from January 2020 to December 2022 of primary malignant cardiac tumour patients obtained from the Surveillance, Epidemiology, and End Results database. The data was divided into training cohort A and validation cohort B. A prognostic nomogram for predicting overall survival was generated by means of independent prognostic factors. The performance nomogram was validated using the receiver operating characteristic curve, calibration curve, decision curve analysis and risk stratification. Data was analysed using SPSS 24.

Results: Of the 528 patients, 371(70.3%) were in cohort A; 275(52.1%) males and 253(47.9%) females with 404(76.5%) aged 24-76 years. There were 157(29.7%) patients in cohort B; 81(51.6%) males and 76(48.4%) females with 124(79%) aged 24-76 years ($p>0.05$). Age, American Joint Cancer Staging Committee stage, histology and chemotherapy were independent risk elements for overall survival, and were used for generating a nomogram ($p<0.001$). The area under the curve of traditional staging systems was surpassed by nomogram in both cohorts ($p<0.001$). The calibration curves suggested a strong concordance between predicted and practical survival ($p<0.001$). Decision curve analysis revealed that the nomogram had satisfactory clinical application value ($p<0.001$). The risk stratification system provided evidence of the nomogram's capacity to precisely identify high-risk patients ($p<0.001$).

Conclusion: A useful and reliable prognostic nomogram for predicting overall survival in primary malignant cardiac tumour patients was developed and validated, improving oncologists' ability to accurately assess patient outcomes.

Keywords: Primary malignant cardiac tumours, Overall survival, Nomogram, Prognosis, Surveillance, Epidemiology and End Results, SEER. (JPMA 75: S-72 [Suppl. 02]; 2025) **DOI: https://doi.org/10.47391/JPMA.SRPH-12**

Introduction

Clinically, cardiac tumours are classified as primary and secondary, and represent a rare category of malignant tumours.[1] Among these, primary cardiac tumours are even rarer, accounting for only 0.3% to 0.7% of all cardiac cancer diagnoses[2] and only 0.001% to 0.3% of cases found at autopsy.[3] Primary malignant cardiac tumours (PMCTs) are even rarer, occupying 10% of all primary cardiac tumours, and the average annual incidence has been reported to be 1.2-1.5 cases per 100,000 people.[4-7] Cardiac sarcoma includes a variety of histological subtypes and is the most common type of PMCTs.[8] The most common subtype of cardiac sarcoma is angiosarcoma,[9] followed by rhabdomyosarcoma, which is the most common subtype of PMCTs in children.[10] Other rare types of cardiac sarcoma include liposarcoma, fibrosarcoma and undifferentiated sarcoma.[11] Cardiac lymphoma is the second most common PMCT.[12] Extremely rare types include malignant cardiac mesothelioma and malignant heart chordoma.[13]

PMCTs are usually highly aggressive, and patient symptoms correlate with tumour size, location, growth rate and aggressiveness.[14] A distinguishing characteristic of these tumours is that patients may exhibit no clinical symptoms for a long period of time.[15] However, as the tumour grows, symptoms, such as valve dysfunction, pericardial effusion, arrhythmias and heart failure, may occur.[16] Once symptoms appear, many cases present as distant metastasis[17] and the prognosis is generally poor, especially without surgical intervention, with mortality up to 90% in the first year after diagnosis.[16] Currently, the treatment of these tumours remains controversial, particularly regarding the efficacy of perioperative chemotherapy and radiotherapy.[2] However, most studies and clinical experiences emphasise the critical role of early detection[18] and surgical resection in treatment.[19] Due to the biological behavioir of PMCTs, treatment outcomes are often unsatisfactory, and overall survival (OS) remains dismal, with previous research documenting median survival of only 6-18 months.[20]

Given the rarity of these tumours, the available literature on short- and long-term treatment outcomes remains very

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limited. The available information is mainly from case reports or small single-centre retrospective studies.[21] The prognostic assessment of cardiac malignant tumours is predominantly based on clinical experience and staging, and often lacks specificity and sensitivity, thus hindering the provision of personalised prognostic assessment for each patient.[22] The Surveillance, Epidemiology and End Results (SEER) database includes numerous patient data, providing an excellent opportunity to study in depth the prognostic characteristics of PMCTs.[23] The existing research on developing prognostic models for these tumours is conspicuously deficient.

The current study was planned to establish and validate a nomogram prognostic model for PMCT patients to provide clinicians with more precise and personalised tools to improve their ability to assess patient outcomes and make informed treatment decisions more effectively.

Materials and Methods

The retrospective study was conducted in January 2023, and comprised data from January 2020 to December 2022 of PMCT patients obtained from the SEER database[23] using SEER-stat version 8.3.9.2. A priori sample size calculation was done using G*Power 3.1.2 based on an earlier study.[24] Those included were patients with primary site labelled C38.0 for malignant neoplasm heart with International Classification of Disease for Oncology (ICD-O) code 3,indicating malignancy. Those excluded were patients with unknown survival months, unknown diagnostic confirmation, having other primary malignant tumours, and those with unknown American Joint Cancer Staging Committee (AJCC)[25] stage. The data was divided into training cohort A and validation cohort B.

Clinical factors potentially linked to PMCT patients' prognosis from the SEER database were identified, and ideal cut-off values were worked out.

Through univariate together with multivariate Cox regression analyses, independent predictors of PMCT patients' OS were identified, and then used to construct the nomogram. The receiver operating characteristic (ROC) curve was utilised for validating the nomogram's discriminative capacity, and the larger area under the curve (AUC) represented stronger discriminating ability. Calibration curves were employed for assessing the OS nomogram's calibration, validated by 1,000 repeated self-lifting samples. The clinical applicability of the nomogram was assessed using decision curve analysis (DCA), which quantified the net benefit under different probability thresholds. X-tile software was used to obtain the optimal risk score threshold, and PMCT patients were reclassified into high-risk and low-risk groups. The Kaplan-Meier method together with log-rank test was implemented to evaluate the differences of OS between these groups.

Data was analysed using R software version 4.1.2 and SPSS 24. X-tile software version 3.6.1 was used to determine the optimal cut-off values for continuous variables, converting all variables into categorical ones, described using frequencies and percentage. The comparison of categorical variables was done using chi-square test. Wilcoxon rank-sum test was used for evaluating the differences between factors. $P<0.05$ was regarded as statistically significant.

Results

Of the 744 PMCT patients documented in the SEER database, 528(71%) met the inclusion criteria (Figure 1). There were 371(70.3%) in cohort A; 275(52.1%) males and 253(47.9%) females with 404(76.5%) aged 24-76 years. There were 157(29.7%) patients in cohort B; 81(51.6%) males and 76(48.4%) females with 124(79%) aged 24-76 years. There was no significant difference between the cohorts ($p>0.05$) (Table 1).

A total of 11 potential predictive variables of PMCT patients' OS were identified; age, gender, race, marital status, histology, tumour size, laterality, AJCC stage, surgery, radiation and chemotherapy. Age, AJCC stage, tumour histology and chemotherapy were independent indicators of PMCT patients' OS (Table 2). The ideal cut-off values for age were 23 and 76, while for tumour size, they were 34mm and 650mm (Figure 2).

Age, AJCC stage, tumour histology and chemotherapy were integrated into the nomogram model (Figure 3).

The concordance indices (C-indices) for both training and validation cohorts in the OS nomogram were 0.682,

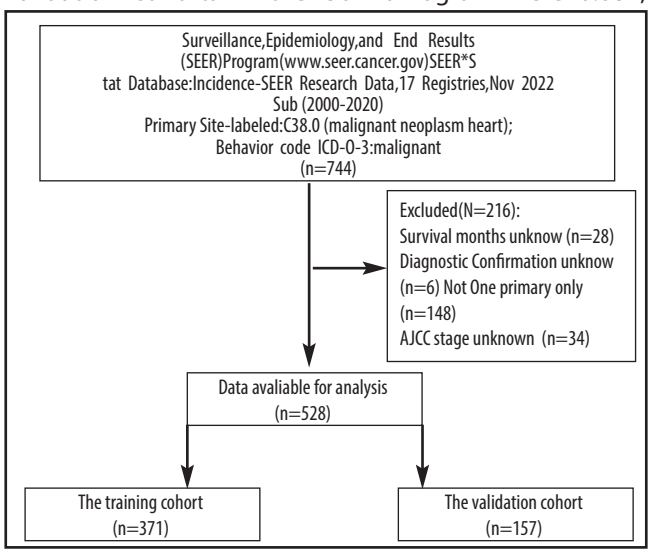

Figure-1: Screening flow chart of primary malignant cardiac tumour (PMCT) patients.

suggesting that the newly established nomogram had strong discriminatory capability. The nomogram's AUC for 1-year, 3-year and 5-year OS rate in cohort A was 0.745, 0.754 0.737, respectively, significantly higher compared with the traditional AJCC staging's corresponding AUC values of 0.602, 0.652 and 0.618. Similarly, the nomogram's AUCs in cohort B significantly exceeded those of the traditional AJCC staging; 0.702, 0.714 and 0.745 compared

Table-1: Baseline characteristics.

Variable	Overall	Validation Cohort	Training Cohort	*p*-value
	n=528 [n(%)]	n=157 [n(%)]	n=371 [n(%)]	
Age (years)				0.516
≤23	53 (10.0)	16 (10.2)	37 (10.0)	
24-76	404 (76.5)	124 (79.0)	280 (75.5)	
≥77	71 (13.4)	17 (10.8)	54 (14.6)	
Gender				0.883
Female	253 (47.9)	76 (48.4)	177 (47.7)	
Male	275 (52.1)	81 (51.6)	194 (52.3)	
Race				0.813
White	401 (75.9)	119 (75.8)	282 (76.0)	
Black	58 (11.0)	19 (12.1)	39 (10.5)	
Other	69 (13.1)	19 (12.1)	50 (13.5)	
Marital Status				0.863
Married	264 (50.0)	81 (51.6)	183 (49.3)	
Single	153 (29.0)	45 (28.7)	108 (29.1)	
Other	111 (21.0)	31 (19.7)	80 (21.6)	
Histology				0.556
Sarcoma	345 (65.3)	105 (66.9)	240 (64.7)	
Lymphoma	135 (25.6)	41 (26.1)	94 (25.3)	
Other	48 (9.1)	11 (7.0)	37 (10.0)	
Tumour Size (mm)				0.787
≤34	207 (39.2)	66 (42.0)	141 (38.0)	
35-650	81 (15.3)	21 (13.4)	60 (16.2)	
651-988	85 (16.1)	25 (15.9)	60 (16.2)	
unknown	155 (29.4)	45 (28.7)	110 (29.6)	
Laterality				0.477
Left	16 (3.0)	4 (2.5)	12 (3.2)	
Right	11 (2.1)	5 (3.2)	6 (1.6)	
Other	501 (94.9)	148 (94.3)	353 (95.1)	
AJCC Stage				0.747
Localized	176 (33.3)	56 (35.7)	120 (32.3)	
Regional	161 (30.5)	47 (29.9)	114 (30.7)	
Distant	191 (36.2)	54 (34.4)	137 (36.9)	
Surgery				0.591
Yes	273 (51.7)	84 (53.5)	189 (50.9)	
No	255 (48.3)	73 (46.5)	182 (49.1)	
Radiation				0.656
Yes	90 (17.0)	25 (15.9)	65 (17.5)	
No	438 (83.0)	132 (84.1)	306 (82.5)	
Chemotherapy				0.693
Yes	289 (54.7)	88 (56.1)	201 (54.2)	
No	239 (45.3)	69 (43.9)	170 (45.8)	
Survival Months (median [IQR])	11.00 [2.00, 25.00]	11.00 [2.00, 25.00]	10.00 [2.00, 25.00]	0.753

AJCC: American Joint Cancer Staging Committee, IQR: Interquartile range.

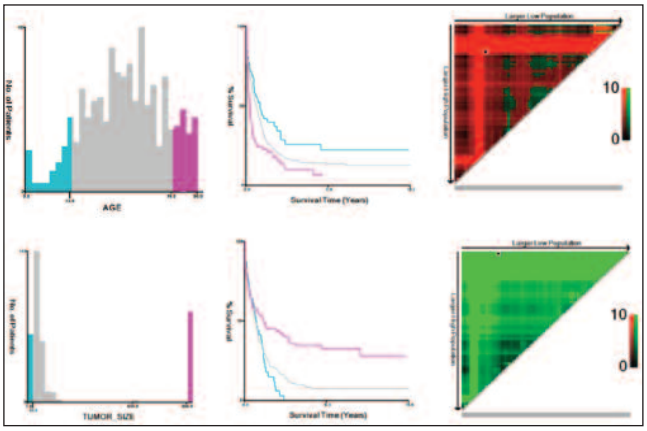

Figure-2: Optimal cut-off values for age and tumour size. (A) Age. (B) Survival time. (C) Optimal cut-off value for age. (D) Tumour size. (E) Survival time. (F) Optimal cut-off value for tumour size.

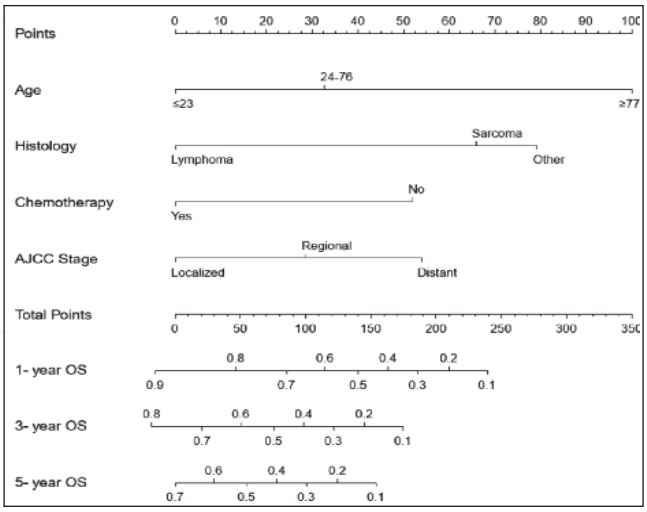

Figure-3: Nomogram predicting 1-year, 3-year and 5-year overall survival (OS) rates for primary malignant cardiac tumour (PMCT) patients.

AJCC: American Joint Cancer Staging Committee.

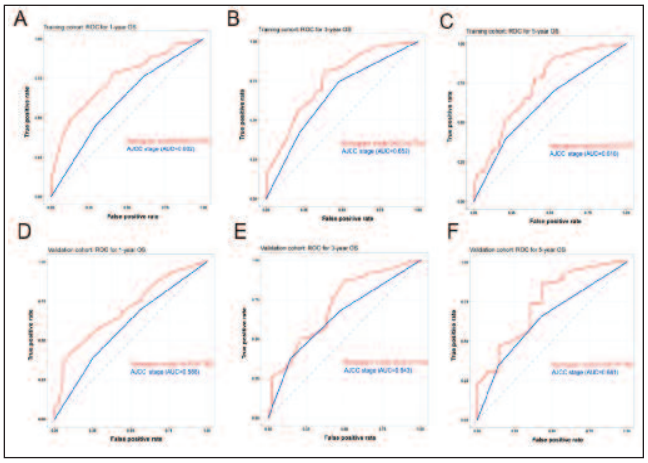

Figure-4: Receiver operating characteristic (ROC) comparison of overall survival (OS) nomogram and American Joint Cancer Staging Committee (AJCC) stage. (A-C) ROC curves for 1-year, 3-year and 5-year OS in the training cohort. (D-F) ROC curves for 1-year, 3-year and 5-year OS in the validation cohort.

to 0.588, 0.643 and 0.641, respectively (Figure 4). Across both the cohorts, the OS nomogram's calibration curves manifested a strong concordance between predicted and practical survival rates (Figure 5). Additionally, the DCA curves indicated that, relative to traditional AJCC staging, the nomogram offered a higher net benefit, demonstrating clinical applicability (Figure 6).

A risk classification system using the cumulative nomogram scores classified patients into 2 risk categories across cohort A, cohort B and the overall study cohort. Low risk was set at ≤153.9 points and high risk at >153.9 points (Figure 7).

Kaplan-Meier plots of cohort A revealed a significant decrease in OS rates with increasing risk levels, and a similar pattern was observed in cohort B and the overall study cohort (p<0.001) (Figure 8).

Table-2: Univariate and multivariate analyses of prognostic factors.

Variable	HR	Univariate Analysis 95% CI	*p*- value	HR	Multivariate Analysis 95% CI	*p*- value
Age (years)						
≤23	Reference			Reference		
24-76	1.411	0.925-2.153	0.11	1.565	1.012-2.421	0.044
>76	2.195	1.344-3.587	0.002	3.471	2.027-5.944	<0.001
Gender						
Female	Reference					
Male	0.943	0.749-1.188	0.619			
Race						
White	Reference					
Black	1.157	0.802-1.669	0.436			
Other	1.04	0.731-1.479	0.827			
Marital Status						
Married	Reference					
Single	0.932	0.710-1.222	0.609			
Other	1.08	0.806-1.449	0.605			
Histology						
Sarcoma	Reference			Reference		
Lymphoma	0.516	0.383-0.696	<0.001	0.304	0.181-0.510	<0.001
Other	1.268	0.862-1.864	0.228	1.134	0.757-1.700	0.541
Laterality						
Left	Reference					
Right	0.78	0.244-2.491	0.675			
Other	0.976	0.519-1.836	0.941			
Tumour Size (mm)						
≤34	Reference			Reference		
35-650	0.959	0.682-1.347	0.808	0.92	0.651-1.299	0.636
651-988	0.605	0.423-0.867	0.006	1.757	0.973-3.171	0.061
Unknown	0.954	0.721-1.261	0.74	1.267	0.935-1.717	0.128
AJCC Stage						
Localized	Reference			Reference		
Regional	1.369	1.016-1.844	0.039	1.409	1.036-1.917	0.029
Distant	1.772	1.336-2.350	<0.001	1.899	1.409-2.560	<0.001
Surgery						
No	Reference					
Yes	0.98	0.777-1.235	0.861			
Chemotherapy						
Yes	Reference			Reference		
No	1.964	1.558-2.476	<0.001	1.939	1.508-2.494	<0.001
Radiation						
Yes	Reference					
No	1.119	0.831-1.507	0.46			

HR: Hazard ratio, CI: Confidence interval, AJCC: American Joint Cancer Staging Committee.

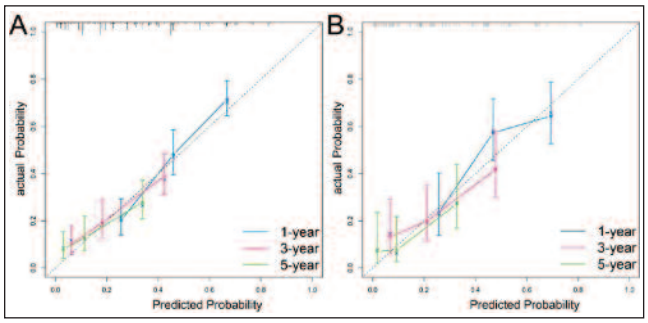

Figure-5: Calibration curves for 1-year, 3-year and 5-year overall survival (OS) in training (A) and validation (B) cohorts.

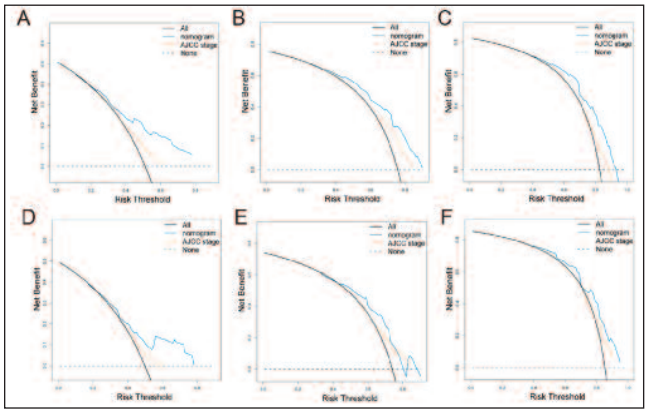

Figure-6: Decision curve analysis (DCA) for 1-year, 3-year and 5-year overall survival (OS) in the training (A-C) and validation (D-E) cohorts. AJCC: American Joint Cancer Staging Committee.

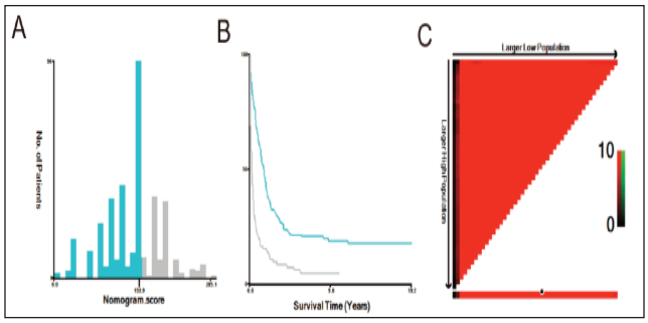

Figure-7: Calibration curves for 1-year, 3-year and 5-year overall survival (OS) in training (A) and validation (B) cohorts.

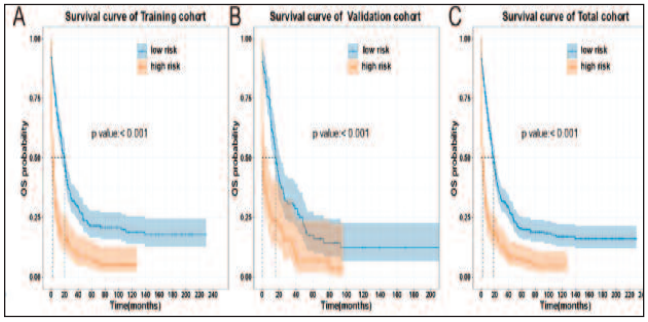

Figure-8: Risk stratification system on the basis of risk scores from overall survival (OS) nomograms for training (A), validation (B), and total cohorts (C).

Discussion

PMCTs are exceedingly rare and they are often associated with a bleak prognosis, which makes conducting large randomised controlled trials (RCTs) challenging. Absence of clinical research data hinders the ability to guide personalised and precise assessments and treatments. The conventional AJCC staging method has limitations in predicting patient outcomes, because survival and prognosis are influenced not only by the degree of tumour invasion, but also by individual differences, such as gender, marital status, age, race, histology, tumour size, radiotherapy, chemotherapy and surgical intervention. The use of AJCC staging alone to assess the prognosis of PMCT patients is not comprehensive.

The nomogram model has obvious advantages over traditional methods in evaluating the prognosis of malignant tumours, including the ability for quantitative analysis, the capability to comprehensively evaluate multiple risk factors, simplicity and intuitiveness, personalised decision support, high adaptability, and assistance in optimising resource allocation.[26,27] The nomogram model has proven to be valuable in prognostic studies of various other tumour types.[28-31] Prognostic models tailored to specific tumour types are always more accurate and useful for clinicians and researchers. Given the unique and rare nature of PMCTs, a specialised prognostic model based on extensive data is essential, and the current study was planned to accordingly.

The current study extracted PMCT patient data from the SEER database, and identified histological type, AJCC stage, chemotherapy and age as independent risk variables for OS through univariate Cox analysis followed by multivariate Cox regression. The findings associated histological type of cardiac lymphoma with a better prognosis, and age and advanced stage with a worse prognosis, which was in line with earlier studies.[2] Chemotherapy was linked to a better prognosis, which was analogous to the study of Guan T et al.[32] The role of surgery as an independent prognostic factor for PMCTs remains controversial. Several studies have shown that surgery is the best option for long-term survival.[9,19,33] A retrospective study[34] found a direct correlation between cardiac sarcoma survival rates and the degree of resection. However, in many cases, clinical manifestations often rule out radical surgical resection, limiting its impact on prognosis and resulting in extremely poor patient outcomes. Chen TWW et al.[20] analysed clinical data of 61 patients with primary cardiac sarcoma at 6 institutions across 3 continents, and found that only age was a significant prognostic factor, and surgery was not an independent significant factor. Similarly, Sultan I et al.[2] analysed a sizable cohort from the National Cancer

Database (NCDB) including more than 100,000 patients with PMCTs, and found that undergoing surgery was not an independent risk element of survival, which was in agreement with the current study. The inconsistencies in these findings may be attributed to significant surgical selection bias and a lack of data on degree of operation.

The current study also found that radiotherapy was not an independent predictor of survival in PMCT patients, which was similar to previous studies,[5,35] possibly because of the high sensitivity of cardiac tissue to radiation damage. Exposure to the ventricular wall with radiotherapy elevates the risk of heart failure and cardiomyopathy, thereby affecting prognosis.[8] Through multivariate analysis results, the current study successfully developed an OS map of PMCT patients, and found it to have good predictive accuracy, reliability and clinical applicability.

Guan T et al.[32] initially established an OS nomogram of PMCTs. However, the study utilised a more recent iteration of the SEER database, offering a broader sample base and more rigorous selection criteria, resulting in a more robust and accurate prognostic model. Additionally, unlike our study, Guan T et al. did not validate the ROC, AUC, utility and clinical decision value of their constructed prognostic nomogram model, which limits its persuasiveness. Moreover, the current study expanded its analysis to incorporate the laterality variable and pivotal factors of tumour size. The biological significance varies with side to side, which might represent differences in tumour histology and biological behaviour. For instance, cardiac sarcomas, which typically have a poor prognosis, are more common on the right side,[24] whereas laterality implies differences in surgical strategy and complexity.[36] Understanding tumour laterality can help surgeons predict surgical risks and develop the best strategy. The univariate and multivariate analyses in the current study did not identify laterality as an independent prognostic predictor of PMCTs, which may be due to the fact that most of the data was categorised as "not a paired site" (94.6%), which made specific left or right categorisation challenging and potentially inserting a bias in the results. Tumour size is often correlated with malignancy, invasiveness and risk of recurrence, directly influencing treatment decisions. Smaller tumours may be more suitable for minimally invasive surgery, while larger tumours often require more aggressive surgical approaches. Larger tumours can imply an increased likelihood of surgical complexity and complications, as well as a reduced likelihood of achieving complete (R0) resection, ultimately impacting patient prognosis. Chen X et al. confirmed that tumour size exceeding 99mm was an independent risk element for PMCT patients' adverse prognosis.[36] In the current study, tumour size was an independent risk element in univariate COX analysis, but not in the multivariate model. The inclusion of tumour size in the current model resulted in insufficient discriminative power, which was reflected in AUC <0.7 in the validation cohort. This might stem from a large percentage of indeterminate tumour sizes (29.4%), which may have skewed the results. Therefore, it was cautiously decided not to include it in the final predictive model.

The current study has limitations. First, although the SEER database covers a wide range of cases, it has its own inherent limitations, such as absent or incomplete data elements, particularly lateral and tumour size variables, as well as detailed information on surgical excision. Second, as a retrospective study, the study has inherent selection bias, information bias and other biases, and lacks multi-centre external validation data. Third, even with multiple control measures, the potential effects of confounding variables could not be completely excluded. Future research should focus on more detailed analyses, such as isolating primary cardiac sarcoma and lymphoma for specific analysis and prognostic modelling, as well as external validation using multicentre data from China.

Conclusion

Histological type, AJCC staging, chemotherapy and age were identified as independent predictors of PMCT prognosis. Utilising these results, a validated and innovative nomogram model was generated for predicting PMCT patients' OS, thereby improving oncologists' ability to accurately assess patient prognosis and provide more personalised treatment recommendations.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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