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Article

Sociodemographic Factors and Treatment Patterns Associated with Overall Survival in Splenic Marginal Zone Lymphoma: A Nationwide Retrospective Cohort Study (2000–2022)

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Simple Summary

Splenic marginal zone lymphoma is a rare blood cancer that mainly affects older adults. Because it is uncommon, doctors rely on limited data to understand which factors truly influence survival. We studied 3,548 patients in a large national cancer registry from 2000 to 2022 to identify which patient characteristics and treatments were linked to overall survival. We found that age, sex, ethnicity, and marital status were strongly associated with survival. Older age, male sex, and Hispanic ethnicity were linked to higher risk of death. Married patients had better survival than some other groups. Chemotherapy was associated with higher mortality, likely reflecting that sicker patients were more likely to receive it. Surgery and radiation were not associated with longer survival.Many deaths were due to causes other than lymphoma, such as heart and lung disease. These findings highlight the importance of comprehensive medical and supportive care alongside cancer treatment.

Abstract

Background: Splenic marginal zone lymphoma (SMZL) is a rare indolent lymphoma with extremely limited population level evidence on social and treatment correlates of survival. **Methods**: We conducted a retrospective cohort study using SEER (2000 to 2022) to evaluate OS in primary SMZL (ICD O 3 9689; spleen C42.2). We summarized baseline features and treatments and used Kaplan Meier and Cox regression. **Results:** The cohort included 3,548 patients (mean age 68.2 years; 53.6% female). Most were White (89.8%) and non Hispanic (92.1%). Ann Arbor stage was missing or blank in 39.4%. Initial therapy included chemotherapy in 26.4%, beam radiation in 0.7%, and primary site surgery in 21.4%. At last follow up, 56.8% were alive; non Hodgkin lymphoma accounted for 15.8% of the full cohort, with substantial competing causes including heart disease (6.1%). In multivariable Cox analysis, OS was independently associated with age (HR 1.073 per year, 95% CI 1.067 to 1.079), male sex (HR 1.337, 95% CI 1.203 to 1.486), Hispanic ethnicity (HR 1.426, 95% CI 1.194 to 1.703),

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chemotherapy (HR 1.246, 95% CI 1.118 to 1.390), year of diagnosis (HR 0.983 per category, 95% CI 0.973 to 0.993), marital status (married vs. divorced HR 0.720, 95% CI 0.600 to 0.863), and race (Asian or Pacific Islander vs. White HR 3.210, 95% CI 1.164 to 8.853). **Conclusions:** In our large population based analysis, OS in SMZL tracks with demographic and social variables and competing risks. Stage missingness and treatment selection limit causal inference for management effects.

Keywords: splenic marginal zone lymphoma; SEER; overall survival; Cox proportional hazards; sociodemographic factors; marital status; Hispanic ethnicity; chemotherapy; population based study; competing risks

1. Introduction

Splenic marginal zone lymphoma (SMZL) is a rare, indolent B-cell non-Hodgkin lymphoma characterized by primary involvement of the spleen, bone marrow, and peripheral blood, typically presenting in older adults with splenomegaly and cytopenias. [1-3] Accounting for less than 2% of all lymphoid malignancies, SMZL exhibits a highly heterogeneous clinical course, ranging from prolonged survival with minimal intervention to progressive disease requiring systemic therapy [4, 5]. Despite its generally favorable prognosis compared with aggressive lymphomas, long-term outcomes are influenced by a complex interplay of patient characteristics, disease biology, and treatment selection [4-7].

Management of SMZL has evolved substantially over the past two decades. Historically, splenectomy played a central role in both diagnosis and symptom control, often producing durable hematologic responses [4, 5]. More recently, the introduction of immunochemotherapy and anti-CD20–based regimens has shifted practice patterns toward non-surgical management, particularly for patients with advanced age, comorbidities, or disseminated disease [5, 8]. However, owing to the rarity of SMZL, prospective randomized trials are limited, and clinical decision-making frequently relies on retrospective studies, small series, and expert consensus rather than high-level evidence [4, 5, 8].

In addition to disease- and treatment-related factors, sociodemographic characteristics such as sex, race, ethnicity, marital status, and socioeconomic context have emerged as important determinants of survival across multiple hematologic malignancies [9]. These factors may reflect differences in baseline health, comorbidity burden, access to care, treatment tolerance, social support, and competing risks of mortality, particularly in indolent lymphomas affecting older populations [9-12]. However, the extent to which sociodemographic factors independently influence survival in SMZL remains poorly characterized, with prior studies limited by small sample sizes, short follow-up, or incomplete adjustment for competing causes of death [7,13,14].

To address these gaps by leveraging large-scale analyses of rare malignancies with extended follow-up, we performed this study using the Surveillance, Epidemiology, and End Results (SEER) dataset. This dataset captures detailed demographic, diagnostic, treatment, and survival information across diverse U.S. populations, making it a valuable resource for evaluating real-world outcomes in SMZL [15]. Importantly, in indolent lymphomas such as SMZL, where non-lymphoma mortality is substantial and cause-of-death attribution may be unreliable, overall survival represents a particularly robust and clinically meaningful endpoint for registry-based research [16].

In this study, we used SEER data spanning 2000 to 2022 to evaluate sociodemographic factors and treatment patterns associated with overall survival among patients with primary splenic marginal zone lymphoma. By leveraging a large, contemporary cohort with long-term follow-up, we aimed to clarify the relative contributions of patient characteristics and treatment exposures to survival outcomes and to provide population-level evidence to inform risk stratification and survivorship-focused care in this rare lymphoma subtype.

2. Materials and Methods

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2.1. Study Design and Data Source:

This retrospective cohort study used data from the National Cancer Institute's SEER program to evaluate sociodemographic factors and treatment patterns associated with overall survival among patients with SMZL. [15] The study period spanned January 1, 2000, through December 31, 2022. SEER is a population-based registry that captures incident cancers, selected initial treatment indicators, vital status, and cause of death for defined geographic regions in the United States. The dataset includes patient-level demographic characteristics, tumor and staging variables as available, treatment recodes, follow-up time, and vital status. Because this study relied on deidentified registry data, it qualifies as non–human participants research and hence did not require IRB review.

2.2. Study Population

Patients were eligible if they had (1) histologically confirmed splenic marginal zone lymphoma defined using ICD-O-3 histology code 9689 and (2) primary site of the spleen (ICD-O-3 site code C42.2). Patients were excluded if required variables for time-to-event analyses were missing or invalid (eg, missing survival time or event indicator).

2.3. Study Variables

Sociodemographic characteristics included sex, race, Hispanic ethnicity, marital status at diagnosis, county-level rurality, and county-level median household income. Sex was analyzed as female versus male; race was grouped as White, Black, Asian/Pacific Islander, American Indian/Alaska Native, or unknown; ethnicity was classified as Hispanic or non-Hispanic; and marital status was categorized as married, single, divorced, separated, widowed, unmarried/domestic partner, or unknown. Rurality was measured using a seven-level county classification, and median household income, adjusted to 2023 dollars, was presented as increasing income categories. Clinical factors included age and year at diagnosis, both treated as continuous variables, and Ann Arbor stage, categorized as stages I–IV, unknown, or missing. Treatment variables included receipt of chemotherapy, receipt of radiation therapy, primary site surgery, and regional lymph node surgery, with treatments analyzed according to whether they were received and, for surgical variables, by the extent or type of procedure, with infrequent categories retained and unknown or not applicable categories used as reference where appropriate.

2.4. Outcomes

The primary endpoint was overall survival (OS), defined as the time from diagnosis to death from any cause; individuals alive at last follow-up were censored. Survival time was measured in months using the SEER survival time variable.

Disease-specific survival (DSS) was not selected as the primary endpoint because SEER cause-of-death attribution is derived from death certificate coding and may be misclassified, particularly for indolent lymphomas where death may occur from treatment toxicity, infections, secondary malignancies, or comorbid disease rather than direct lymphoma progression. This concern is amplified in an older cohort with substantial competing risks. In this study, the distribution of causes of death demonstrated prominent non-lymphoma mortality (eg, cardiovascular, pulmonary, infectious, and other causes), which limits interpretability of DSS and increases susceptibility to differential misclassification across sociodemographic strata. OS was therefore chosen as the most clinically meaningful and methodologically robust endpoint for registry-based comparisons. (Supplemental Table 1)

2.5. Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics and treatment patterns. Continuous variables were reported as mean (SD) and categorical variables as frequency (percentage).

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Time-to-event analyses were conducted using Kaplan–Meier methods to estimate survival distributions by selected categorical predictors. Differences in survival curves were evaluated using log-rank tests (pooled over strata). Median survival times and corresponding standard errors and confidence intervals were reported when estimable; results for categories with very small sample sizes were interpreted cautiously given instability of estimates.

Associations between covariates and OS were evaluated using Cox proportional hazards regression. Univariate Cox models were fit for each predictor separately. For categorical variables, indicator (dummy) coding was used as appropriate. Continuous predictors (age, year of diagnosis, and median household income ordinal category) were modeled per 1-unit increase as presented in the output.

A multivariable Cox model was then fit including covariates meeting the prespecified inclusion threshold from univariate analyses ($p<0.10$) and those carried forward in the reported multivariable output with indicator parameter coding. The final adjusted model included sex, year of diagnosis, race, ethnicity, marital status, regional lymph node surgery, and chemotherapy. Adjusted hazard ratios (HRs) with 95% CIs were reported. Two-sided p values <0.05 were considered statistically significant.

Missing data were handled using complete-case analysis within each model. The rural–urban continuum indicator-coded model demonstrated non-convergence/singularity due to sparse categories, and estimates from that model were considered unstable and were not emphasized in inference. All analyses were performed using IBM SPSS Statistics (v31).

3. Results

3.1. Cohort characteristics

A total of 3,548 patients with histologically confirmed primary splenic marginal zone lymphoma were identified in SEER (2000–2022). The mean age at diagnosis was 68.2 years (SD 11.6), and 53.6% were female. Most patients were White (89.8%) and non-Hispanic (92.1%). Marital status at diagnosis was most commonly married (57.9%), followed by widowed (14.6%), single (11.0%), divorced (9.4%), and unknown (6.3%); separated (0.5%) and unmarried/domestic partner (0.3%) were uncommon. Most patients resided in metropolitan counties (≥1 million population, 61.3%). Ann Arbor stage was recorded as stage IV in 38.9% and stage I in 13.2%; however, staging was missing in 39.4% of cases. (Table 1)

With respect to initial treatment, 26.4% received chemotherapy, 0.7% received beam radiation, and 21.4% underwent primary site surgery. Regional lymph node surgery was uncommon: 49.9% had no lymph node surgery, 1.5% had 1–3 nodes removed, and 0.7% had ≥4 nodes removed; lymph node surgery was unknown/not applicable in 40.4%. (Table 1)

3.2. Cause of Deaths:

56.8% were alive at last follow-up. Among decedents, the most frequent recorded cause of death was non-Hodgkin lymphoma (15.8% of the entire cohort), followed by major competing causes including diseases of heart (6.1%) and a heterogeneous category of other causes of death (5.2%). Additional non-lymphoma causes each contributed smaller proportions, most commonly chronic respiratory disease (1.7%), cerebrovascular disease (1.3%), lung cancer (1.2%), and infection-related mortality (e.g., pneumonia/influenza 0.8%, septicemia 0.4%). Collectively, this pattern indicates that while lymphoma-related mortality constitutes a substantial share of deaths, competing cardiovascular, pulmonary, infectious, and secondary malignancy causes are prominent, consistent with the older age distribution of SMZL and underscoring the importance of survivorship-focused management alongside lymphoma-directed care. (Supplementary Table 1)

Table 1. Baseline demographic, clinical, and treatment characteristics (N = 3,548).

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Characteristic	n (%) or mean ± SD
Age at diagnosis, years	68.21 ± 11.60
Sex	
Female	1,900 (53.6)
Male	1,648 (46.4)
Race	
White	3,186 (89.8)
Black	164 (4.6)
Asian/Pacific Islander	155 (4.4)
American Indian/Alaska Native	13 (0.4)
Unknown	30 (0.8)
Ethnicity	
Non-Hispanic	3,268 (92.1)
Hispanic	280 (7.9)
Marital status at diagnosis	
Married	2,055 (57.9)
Widowed	519 (14.6)
Single (never married)	391 (11.0)
Divorced	333 (9.4)
Separated	18 (0.5)
Unmarried/domestic partner	10 (0.3)
Unknown	222 (6.3)
Rural–urban residence	
Metro ≥1,000,000	2,175 (61.3)
Metro 250,000–1,000,000	700 (19.7)
Metro <250,000	227 (6.4)
Nonmetro adjacent to metro	242 (6.8)
Nonmetro not adjacent	201 (5.7)
Unknown/missing	3 (0.1)
Median household income (inflation-adjusted to 2023)	
< $40,000	31 (0.9)
$40,000–$44,999	42 (1.2)
$45,000–$49,999	62 (1.7)
$50,000–$54,999	104 (2.9)
$55,000–$59,999	124 (3.5)
$60,000–$64,999	226 (6.4)
$65,000–$69,999	210 (5.9)
$70,000–$74,999	273 (7.7)
$75,000–$79,999	470 (13.2)
$80,000–$84,999	366 (10.3)
$85,000–$89,999	407 (11.5)
$90,000–$94,999	188 (5.3)
$95,000–$99,999	207 (5.8)
$100,000–$109,999	350 (9.9)
$110,000–$119,999	215 (6.1)
$120,000+	272 (7.7)
Unknown/missing	1 (0.0)
Ann Arbor stage	
Stage I	470 (13.2)
Stage II	127 (3.6)
Stage III	73 (2.1)

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Stage IV	1,381 (38.9)
Unknown	99 (2.8)
Missing/blank	1,398 (39.4)
Treatment	
Chemotherapy (yes)	938 (26.4)
Chemotherapy (no/unknown)	2,610 (73.6)
Beam radiation	25 (0.7)
Radiation none/unknown	3,521 (99.2)
Radiation refused	2 (0.1)
Primary site surgery (spleen)	761 (21.4)
Regional lymph node surgery	
None	1,769 (49.9)
1–3 nodes removed	54 (1.5)
≥4 nodes removed	25 (0.7)
Biopsy/aspiration	5 (0.1)
Nodes removed unknown number	32 (0.9)
Blank(s)	230 (6.5)
Unknown/not applicable	1,433 (40.4)

3.3. Survival Analyses

Kaplan-Meier analyses showed no statistically significant differences in overall survival by extent of primary site surgery (log-rank p=0.376), despite numerical variation in median survival across surgical categories. Patients who underwent site-specific resection or other major surgery exhibited median survival estimates comparable to those managed without primary site surgery, while categories with very small sample sizes showed unstable estimates with wide confidence intervals, limiting interpretability. In contrast, overall survival differed markedly by marital status (log-rank p<0.001), with widowed patients experiencing substantially shorter median survival (70 months) compared with married, divorced, single, or unknown-status patients, consistent with the strong prognostic effect observed in multivariable Cox modeling. Chemotherapy exposure was also associated with statistically significant differences in survival distributions (log-rank p=0.013), with patients receiving no or unknown chemotherapy status demonstrating longer median survival (128 months) compared with those who received chemotherapy (113 months). (Figure 1)

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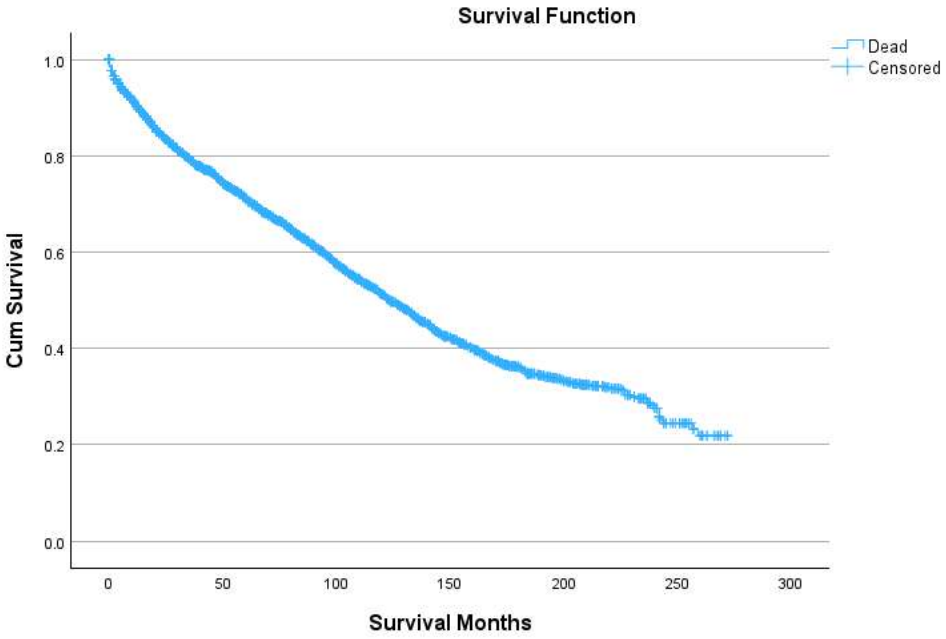

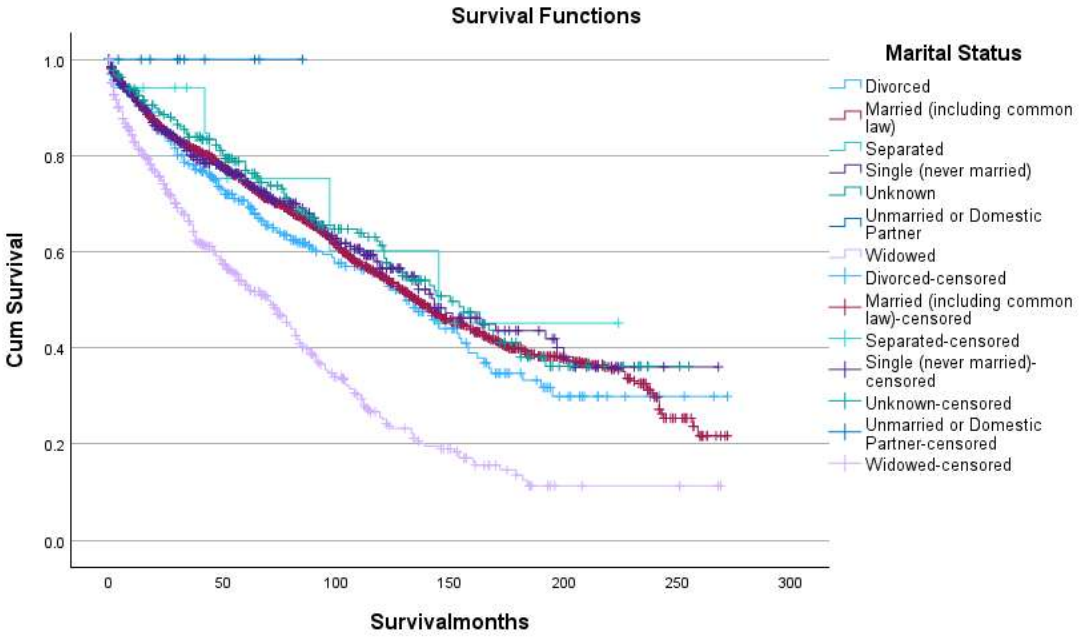

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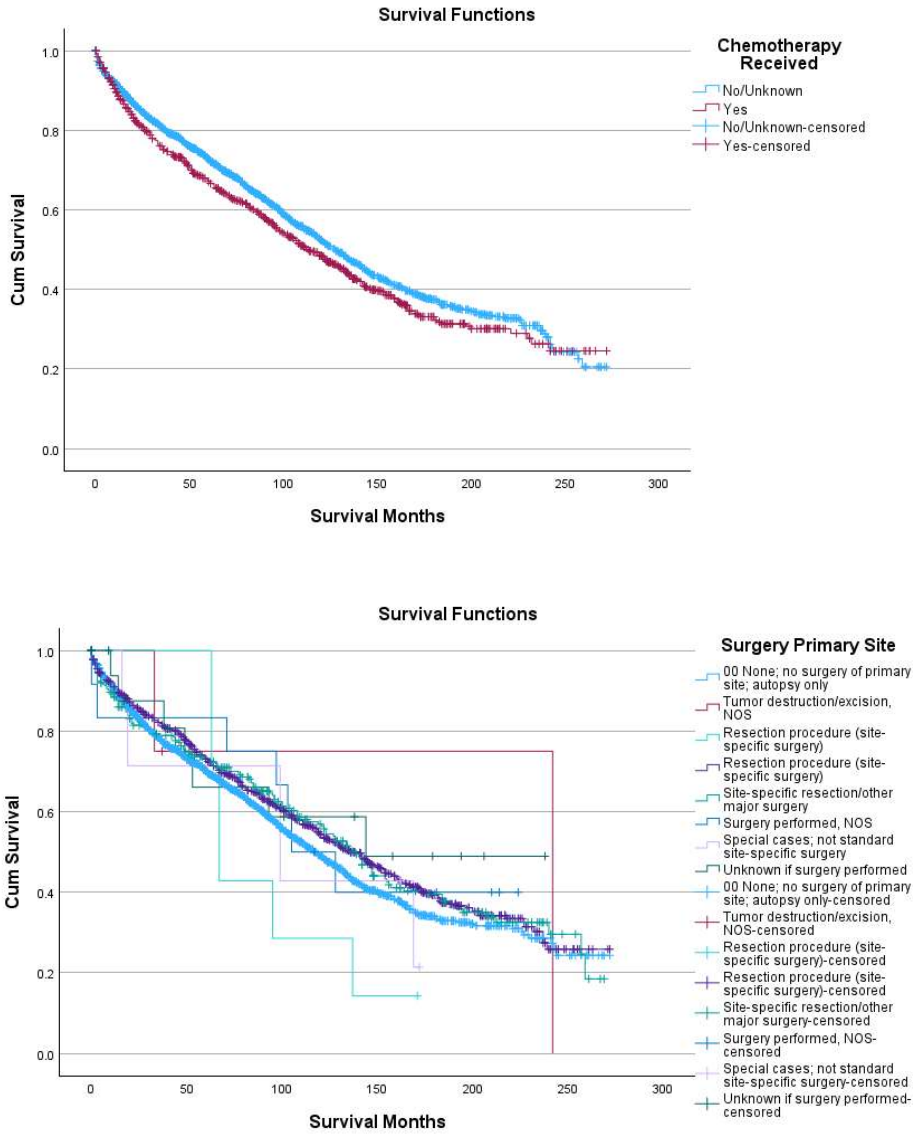

Figure 1. Kaplan Meier Survival Plots for Overall Survival in SMZL.

3.4. Univariate predictors of overall survival

In univariate Cox analysis, female sex was associated with lower mortality than male sex (HR 0.86, 95% CI 0.78 to 0.95; p = 0.003). Increasing age was strongly associated with death (HR 1.07 per year, 95% CI 1.06 to 1.08; p < 0.001). Non-Hispanic ethnicity was associated with improved survival compared with Hispanic ethnicity (HR 0.82, 95% CI 0.69 to 0.98; p = 0.030). Marital status showed a strong association with OS, with married patients demonstrating lower mortality than widowed patients (HR 0.47, 95% CI 0.41 to 0.53; p < 0.001). Chemotherapy receipt was associated with higher mortality, as patients with no or unknown chemotherapy had lower risk of death (HR 0.87, 95% CI 0.78 to 0.97; p = 0.013). (Table)

Table 2. Univariate Cox proportional hazards models for overall survival.

Variable	Comparison	Hazard Ratio (HR, 95% CI)	p-value
Sex	Female vs. Male	0.858 (0.776–0.949)	0.003
Year of diagnosis	Per 1-year increase	0.991 (0.981–1.001)	0.078
Race	American Indian/Alaska Native vs. White	0.524 (0.196–1.406)	0.196

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	Asian or Pacific Islander vs. White	0.764 (0.582–1.003)	0.052
	Black vs. White	0.898 (0.700–1.151)	0.395
	Unknown vs. White	0.151 (0.038–0.595)	0.007
Ethnicity	Non-Hispanic vs. Hispanic	0.823 (0.689–0.983)	0.030
Rural–Urban Continuum	Metro ≥1 million vs. Unknown/Not 1990–2023	143.048 (0.000–∞)	0.702
	Metro 250k–1M vs. Unknown/Not 1990–2023	157.843 (0.000–∞)	0.696
	Metro <250k vs. Unknown/Not 1990–2023	157.594 (0.000–∞)	0.696
	Nonmetro adjacent vs. Unknown/Not 1990–2023	152.519 (0.000–∞)	0.698
	Nonmetro non-adjacent vs. Unknown/Not 1990–2023	173.599 (0.000–∞)	0.691
	Unknown Alaska/Hawaii vs. Unknown/Not 1990–2023	1.001 (0.000–∞)	1.000
Median household income	Per 1-category increase (ordinal)	0.992 (0.980–1.003)	0.190
Marital status	Divorced vs. Widowed	0.525 (0.431–0.639)	<0.001
	Married vs. Widowed	0.467 (0.410–0.532)	<0.001
	Separated vs. Widowed	0.400 (0.165–0.973)	0.042
	Single (never married) vs. Widowed	0.446 (0.364–0.546)	<0.001
	Unknown vs. Widowed	0.424 (0.334–0.538)	<0.001
	Unmarried partner vs. Widowed	0.000 (0.000–∞)	0.873
Age at diagnosis	Per 1-year increase	1.070 (1.064–1.076)	<0.001
Primary site surgery	None	1.433 (0.681–3.013)	0.343
	Tumor destruction/excision, NOS	1.293 (0.334–4.998)	0.710
	Resection procedure- Limited (site-specific surgery)	2.153 (0.724–6.402)	0.168
	Resection procedure- More Extensive Segmental (site-specific surgery)	1.258 (0.597–2.651)	0.547
	Site-specific resection/other major surgery	1.279 (0.592–2.765)	0.525
	Surgery performed, NOS	1.209 (0.423–3.456)	0.723
	Special cases; not standard site-specific surgery	1.607 (0.510–5.065)	0.418
Lymph node surgery	1–3 nodes removed vs. Unknown/NA	0.667 (0.435–1.022)	0.062
	≥4 nodes removed vs. Unknown/NA	1.233 (0.749–2.030)	0.408
	Biopsy/aspiration vs. Unknown/NA	1.190 (0.383–3.699)	0.763
	Blank(s) vs. Unknown/NA	1.087 (0.911–1.297)	0.348
	None vs. Unknown/NA	0.845 (0.756–0.944)	0.003
	Number unknown vs. Unknown/NA	0.898 (0.554–1.456)	0.661
Chemotherapy	Yes vs. No/Unknown	0. 1.146 (1.029–1.276)	0.013
Radiation	Beam radiation vs. Refused	0.687 (0.092–5.118)	0.714
	None/Unknown vs. Refused	0.371 (0.052–2.626)	0.322
Ann Arbor stage	Blank(s) vs. Unknown	0.896 (0.674–1.191)	0.450
	Stage I vs. Unknown	0.962 (0.726–1.274)	0.785
	Stage II vs. Unknown	0.982 (0.698–1.381)	0.917
	Stage III vs. Unknown	1.365 (0.936–1.989)	0.105
	Stage IV vs. Unknown	0.956 (0.736–1.242)	0.734

3.5. Multivariable predictors of overall survival

After adjustment for covariates meeting prespecified inclusion criteria, increasing age strongly predicted worse OS (HR 1.07 per year, 95% CI 1.07 to 1.08; $p < 0.001$). Male sex was independently associated with higher mortality (HR 1.34, 95% CI 1.20 to 1.49; $p < 0.001$). Hispanic ethnicity remained

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associated with increased risk of death (HR 1.43, 95% CI 1.19 to 1.70; p < 0.001). Chemotherapy exposure was also associated with higher mortality (HR 1.25, 95% CI 1.12 to 1.39; p < 0.001). (Table 3)

Table 3. Multivariable Cox proportional hazards model for overall survival.

Variable	Category	B	SE	Wald	p-value	Adjusted HR (Exp(B))	95% CI
Sex	Male vs. Female (ref)	0.290	0.054	29.117	<0.001	**1.337**	1.203 – 1.486
Year of diagnosis (categorical trend)	Per category increase	-0.017	0.005	11.343	<0.001	**0.983**	0.973 – 0.993
Race (overall p=0.008)				13.903	0.008		
	American Indian/Alaska Native vs. White (ref)	0.786	0.521	2.273	0.132	2.194	0.790 – 6.091
	Asian/Pacific Islander vs. White	1.166	0.518	5.079	0.024	**3.210**	1.164 – 8.853
	Black vs. White	-0.592	0.868	0.465	0.495	0.553	0.101 – 3.031
	Unknown vs. White	0.834	0.503	2.752	0.097	2.303	0.860 – 6.168
Hispanic Ethnicity	Hispanic vs. Non-Hispanic (ref)	0.355	0.090	15.372	<0.001	**1.426**	1.194 – 1.703
Marital Status (overall p<0.001)				32.299	<0.001		
	Married vs. Divorced (ref)	-0.329	0.093	12.543	<0.001	**0.720**	0.600 – 0.863
	Separated vs. Divorced	0.141	0.456	0.096	0.757	1.152	0.471 – 2.816
	Single vs. Divorced	-0.030	0.121	0.060	0.807	0.971	0.766 – 1.230
	Unknown vs. Divorced	-0.411	0.137	9.025	0.003	**0.663**	0.507 – 0.867
	Unmarried/Domestic Partner vs. Divorced	-9.174	62.432	0.022	0.883	0.000	0.000 – 1.44E+49
	Widowed vs. Divorced	-0.042	0.106	0.156	0.693	0.959	0.779 – 1.181
Age (continuous)	Per 1-year increase	0.071	0.003	638.098	<0.001	**1.073**	1.067 – 1.079
Chemotherapy	Yes vs. No/Unknown (ref)	0.220	0.056	15.668	<0.001	**1.246**	1.118 – 1.390

* N differs slightly from 3,548 due to complete-case handling in the Cox model.
† Indicates quasi-separation/unstable estimate due to very small cell counts (interpret with caution).
Model: Cox proportional hazards model for overall survival (OS)
Reference groups: Female; White; Non-Hispanic; RUCC metro ≥1,000,000; Widowed; Chemotherapy = Yes; Radiation = Beam; Stage missing/blank.

4. Discussion

To our knowledge, this study represents the largest population based cohort of primary SMZL reported to date. In multivariable analysis, age, sex, Hispanic ethnicity, marital status, year of diagnosis, race, and chemotherapy exposure were independently associated with OS. Increasing age was the strongest continuous predictor of mortality. Male sex remained associated with higher risk of death. Hispanic ethnicity was associated with inferior survival compared with non Hispanic ethnicity. Race showed an overall association with OS, with Asian or Pacific Islander patients demonstrating higher mortality relative to White patients, while other racial comparisons were not statistically significant. These findings are consistent with prior reports in indolent B cell lymphomas that document survival differences across demographic groups [10,13,17,18].

Marital status retained a significant association with OS after adjustment. Compared with divorced patients, married patients and those with unknown marital status had lower mortality, while widowed and single patients did not differ significantly in the adjusted model. Prior oncology literature has reported survival differences by marital status [9,10–19]. Our analysis confirms that marital status remains associated with OS in SMZL within a population-based cohort.

In the context of SMZL, an indolent disease predominantly affecting older adults, the magnitude and persistence of the marital-status association suggest that social determinants and supportive care factors play a central role in shaping long-term outcomes. This interpretation is reinforced by the

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observed distribution of causes of death, which showed a substantial contribution from non-lymphoma causes, including cardiovascular, pulmonary, infectious, and secondary malignancy-related mortality [13,20].

Primary site surgery and radiation therapy were not associated with differences in OS in univariate analyses. Chemotherapy exposure was associated with higher mortality in the adjusted model. These findings should be interpreted within the context of registry based data. SEER does not capture treatment intent, specific regimens, dose intensity, performance status, or detailed measures of disease burden. As a result, the observed association between chemotherapy and OS most likely reflects underlying disease severity and treatment selection rather than a direct adverse treatment effect [5,13,22]. These results provide valuable population level insight into real world practice patterns while underscoring the need for prospective clinical data to define treatment efficacy.

Ann Arbor stage was not independently associated with OS in univariate analysis. Although stage was not recorded in 39.4 percent of cases, the available data reflect real world registry reporting patterns in SMZL and allow evaluation of survival within a large, contemporary population based cohort. The absence of a strong stage signal is consistent with prior observations that traditional anatomic staging has limited prognostic discrimination in SMZL [13,18].

This study has several notable strengths, including a large population-based cohort, extended follow up, and broad geographic representation. These features provide robust and generalizable estimates of survival in a rare lymphoma subtype that is not feasible to study in randomized trials. Although registry data do not capture detailed clinical variables or treatment intent, they offer a valuable real-world perspective on outcomes across diverse patient populations. Despite inherent limitations such as stage missingness and limited treatment granularity, the consistency and magnitude of the observed associations support the validity of the findings. Within this framework, our results demonstrate that demographic and social variables remain independently associated with OS in SMZL. These data provide clinically relevant insight and reinforce the importance of comprehensive assessment, survivorship planning, and comorbidity management in this predominantly older patient population.

5. Conclusions

In this large population-based analysis of SMZL, overall survival was independently associated with age, sex, ethnicity, marital status, and chemotherapy exposure. Male sex, Hispanic ethnicity, advancing age, and receipt of chemotherapy were associated with higher mortality, while married status was associated with improved survival. Local treatment approaches, including splenectomy and radiation, were not associated with superior survival. The substantial contribution of non-lymphoma causes of death highlights the importance of competing health risks in this older population. These findings provide population level evidence to inform risk assessment and long-term management in SMZL.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Table S1: Cause of death distribution (COD to site recode) in the SMZL cohort (SEER 2000–2022; N=3,548).

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