surgeries

MDPI

Article

Pandemic-Era Stage Migration, Registry-Recorded Primary-Site Surgery, and Survival in Early-Onset Testicular Germ Cell Tumors: A SEER Population-Based Study

Sıtkı Ün [1], Yasemin Adalı [2,3,*] and Ömer Emin Çınar [4,5]

[1] Department of Urology, Faculty of Medicine, Pamukkale University, Denizli 20160, Türkiye; sitki@doctor.com
[2] Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast BT12 6BA, UK
[3] Division of Epidemiology, Department of Public Health, Faculty of Medicine, Pamukkale University, Denizli 20160, Türkiye
[4] School of Electronics, Electrical Engineering and Computer Science, Queen's University Belfast, Belfast BT9 5BN, UK
[5] Department of Computer Engineering, Faculty of Engineering and Architecture, Recep Tayyip Erdogan University, Rize 53100, Türkiye
* Correspondence: y.adali@qub.ac.uk or yadali@pau.edu.tr

Abstract

Background: This study evaluated temporal changes in stage distribution, registry-recorded primary-site surgery, survival outcomes, and exploratory short-term mortality prediction among patients with early-onset testicular germ cell tumors, defined in this study as tumors diagnosed in patients aged 15–49 years, across the study periods. Materials and Methods: This retrospective cohort study used Incidence-SEER Research Data, 17 Registries, November 2025 Submission. Male patients aged 15–49 years diagnosed with malignant testicular germ cell tumors between 2018 and 2023 were included. Diagnosis periods were categorized as the pre-COVID-19 period (2018–2019), COVID-19 period (2020–2021), and 2022–2023 period. Logistic Regression was used to assess factors associated with regional or distant-stage disease. Overall survival was evaluated using Cox regression, while testicular cancer-specific death was additionally evaluated using Aalen–Johansen cumulative incidence estimates and Fine–Gray competing-risk regression. Follow-up was also restricted to 12 months in sensitivity analyses. Machine learning models were developed as an exploratory secondary analysis of 12-month all-cause mortality. Results: A total of 13,303 patients were included. Among patients with known stage, regional or distant-stage disease increased from 31.2% before the pandemic to 33.5% during the COVID-19 period and 34.4% during the 2022–2023 period. In adjusted analysis, COVID-19 (OR = 1.11, 95% CI: 1.02–1.22) and diagnoses during the 2022–2023 period (OR = 1.16, 95% CI: 1.06–1.28) were associated with higher odds of regional or distant-stage disease. In full follow-up analyses, diagnosis during the 2022–2023 period was associated with higher all-cause mortality (HR = 1.29, 95% CI: 1.01–1.65) and testicular cancer-specific death in both cause-specific Cox (HR = 1.49, 95% CI: 1.12–2.00) and Fine–Gray models (sHR = 1.45, 95% CI: 1.09–1.93). In 12-month analyses, the overall survival association was attenuated, whereas the association with testicular cancer-specific death remained significant in the Fine–Gray model (sHR = 1.46, 95% CI: 1.03–2.07). Conclusions: Early-onset testicular germ cell tumors diagnosed during the COVID-19 period and in 2022–2023 showed a modest shift toward regional or distant-stage presentation, while diagnosis in 2022–2023 was associated with higher testicular cancer-specific mortality in competing-risk analyses.

Check for updates

Academic Editor: Ferdinando Agresta

Received: 11 June 2026
Revised: 17 August 2026
Accepted: 18 August 2026
Published: 21 August 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

Keywords: testicular cancer; testicular germ cell tumors; stage migration; COVID-19; SEER; survival analysis; machine learning; ROC analysis

1. Introduction

Testicular cancer is a relatively uncommon malignancy in the general male population, but it represents the most frequent solid tumor among adolescent and young adult men. More than 90% of testicular cancers are germ cell tumors, and the burden of disease is concentrated in younger age groups, making this malignancy clinically and epidemiologically important despite its low overall incidence [1,2]. Because testicular germ cell tumors often occur during reproductive, educational, and economically productive years, even small changes in diagnostic timing, registry-recorded treatment characteristics, or survivorship outcomes may have substantial individual and public health implications [2,3].

The prognosis of testicular germ cell tumors is generally favorable, particularly for patients diagnosed with localized disease. Modern treatment strategies, including orchiectomy, platinum-based chemotherapy, radiotherapy in selected seminoma cases, retroperitoneal lymph node dissection when indicated, and risk-adapted surveillance, have resulted in excellent long-term survival [1,4]. Nevertheless, survival is not uniform across all patient groups. Disease extent at diagnosis, metastatic status, histological subtype, serum tumor markers, age, race, socioeconomic factors, and treatment access have all been associated with clinical outcomes [4–7]. Population-based SEER analyses have shown that patients with regional or distant disease experience worse outcomes than those with localized disease, and that demographic and social determinants may contribute to disparities in metastatic presentation and cancer-specific mortality [4,5].

Histological classification is central to the management and prognosis of testicular germ cell tumors. Seminoma and non-seminoma differ in clinical behavior, treatment sensitivity, patterns of spread, and survival. Within non-seminomatous germ cell tumors, mixed histologies and specific components such as teratoma or embryonal carcinoma may further influence prognosis and treatment decisions [6,8]. Previous SEER-based studies have demonstrated that age, stage, and morphology-adjusted survival differ across subgroups, underscoring the importance of evaluating epidemiological and survival outcomes within clinically meaningful patient populations [5]. In this context, early-onset testicular germ cell tumors require focused investigation because their age distribution, histological composition, and survivorship concerns may differ from those of older patients [2,3].

The COVID-19 pandemic caused widespread disruption to cancer diagnostic and treatment pathways worldwide. Reductions in primary care access, diagnostic imaging, specialist referrals, surgical capacity, and oncology services raised concerns that delayed presentation could lead to stage migration and poorer cancer outcomes [9,10]. Although testicular cancer is highly curable, timely evaluation of testicular symptoms remains essential because delayed diagnosis may increase the likelihood of nodal or distant spread, intensify treatment requirements, and increase the burden of long-term adverse effects. Emerging studies of testicular germ cell tumors during the pandemic have suggested possible changes in diagnostic patterns and stage distribution, but available evidence remains limited and inconsistent [11–13]. Therefore, population-based analyses using contemporary registry data are needed to determine whether pandemic-related healthcare disruption was associated with measurable changes in stage distribution, registry-recorded treatment characteristics, and survival among patients with early-onset testicular germ cell tumors.

In addition to conventional epidemiological and survival analyses, machine learning methods may provide complementary insights into short-term mortality prediction by

integrating multiple demographic, tumor-related, socioeconomic, and treatment-related variables. Previous SEER-based prognostic modeling studies in testicular cancer have shown that prediction tools incorporating patient and tumor characteristics may outperform staging systems alone for individualized survival estimation [7]. However, the performance of machine learning models for predicting 12-month mortality among patients with early-onset testicular germ cell tumors across the pre-COVID-19 period, COVID-19 period, and 2022–2023 period has not been well characterized. Such analyses may be useful for evaluating whether routinely available registry variables can provide exploratory information on short-term mortality prediction during periods of healthcare system disruption.

Therefore, this population-based SEER study aimed to evaluate epidemiological patterns, stage distribution, registry-recorded primary-site surgery, overall survival, and testicular cancer-specific mortality among male patients aged 15–49 years diagnosed with malignant testicular germ cell tumors between 2018 and 2023. Diagnosis periods were categorized as the pre-COVID-19 period, COVID-19 period, and 2022–2023 period. Primary-site surgery and time from diagnosis to treatment were examined strictly as registry-recorded indicators and not as measures of detailed surgical pathways, treatment intent, referral delay, or operative quality. In addition, machine learning models were developed as an exploratory secondary analysis of 12-month all-cause mortality. This study was designed to determine whether the COVID-19 and 2022–2023 periods were associated with a modest shift toward regional or distant-stage disease, whether registry-recorded primary-site surgery differed across periods, and whether diagnosis period was associated with mortality within the available follow-up period.

2. Materials and Methods

2.1. The Data Source and Study Population

This population-based retrospective cohort study used data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. Data were obtained from the Incidence—SEER Research Data, 17 Registries, November 2025 Submission, using SEER*Stat software version 9.0.42 (National Cancer Institute, Bethesda, MD, USA), which includes cancer cases diagnosed from 2000 to 2023. For the present analysis, patients diagnosed between 2018 and 2023 were selected. Testicular cancer cases were identified using ICD-O-3 primary site codes C62.0, C62.1, and C62.9, corresponding to undescended testis, descended testis, and testis not otherwise specified, respectively. The cohort was restricted to male patients with malignant tumors. Cases identified using autopsy only or death certificate only were excluded to improve the reliability of survival analyses.

To obtain a clinically more homogeneous cohort, the analysis was restricted to early-onset testicular germ cell tumors, defined in this study as tumors diagnosed among patients aged 15–49 years. Germ cell tumor histologies were identified using ICD-O-3 morphology codes 9060–9064, 9070–9072, 9080–9085, and 9100–9101. The 9060–9064 range included spermatocytic tumor (code 9063); however, only 15 patients (0.11% of the total cohort) had this morphology, and all met the predefined age criterion of 15–49 years. These cases were therefore retained in the population-based cohort. The selected morphology codes included seminoma and non-seminoma germ cell tumors, while non-germ cell tumors such as rhabdomyosarcoma, juvenile granulosa cell tumors, and malignant neoplasm not otherwise specified were excluded. Patients were categorized into three diagnosis periods according to year of diagnosis: 2018–2019 as the pre-COVID-19 period, 2020–2021 as the COVID-19 period, and 2022–2023 as the 2022–2023 period (Figure 1).

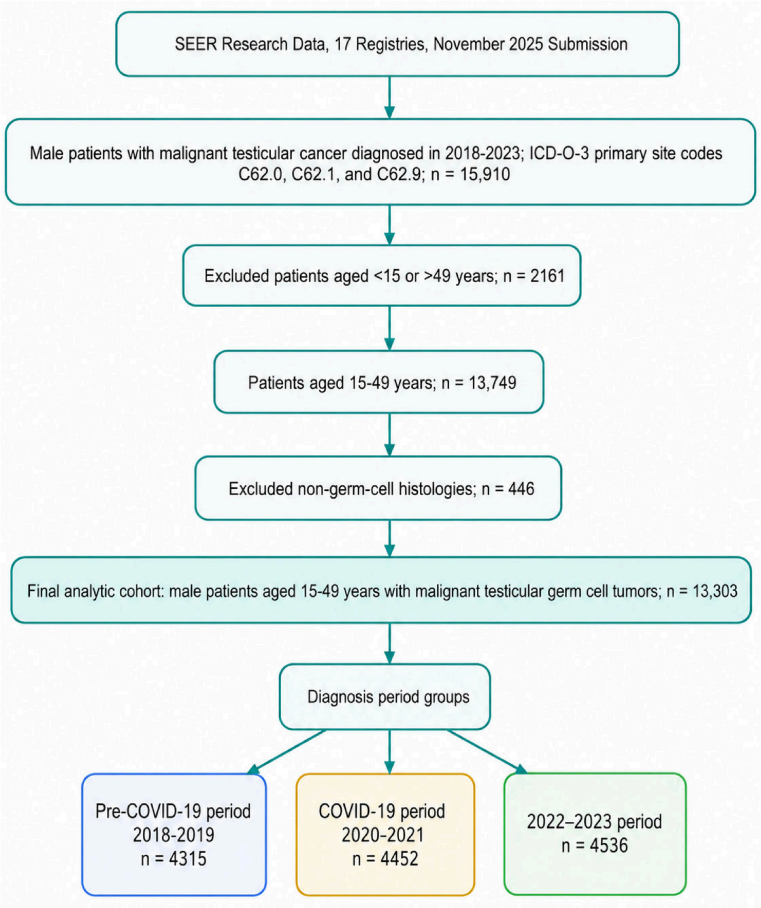


Figure 1. Patient selection flow diagram for the SEER-based cohort of early-onset testicular germ cell tumors.

2.2. Variables and Outcomes

Demographic variables included age at diagnosis, race, marital status at diagnosis, median household income adjusted to 2024 inflation, and rural–urban continuum code. Age at diagnosis was categorized as 15–24, 25–34, and 35–49 years. Median household income was grouped as <$70,000, $70,000–$89,999, $90,000–$109,999, and ≥$110,000. Rural–urban status was grouped as large metropolitan, small/medium metropolitan, and nonmetropolitan. Tumor-related variables included primary site, laterality, ICD-O-3 histology, histological subtype, combined summary stage, EOD 2018 stage group, and EOD T, N, and M categories. Histology was grouped as seminoma and non-seminoma. Summary stage was categorized as localized, regional, distant, or unknown/unstaged. A binary known-stage disease extent variable grouped regional and distant disease and excluded unknown/unstaged cases. Treatment-related variables included registry-recorded surgery of the primary site, surgery/radiation sequence, radiation recode, chemotherapy recode, reason for no cancer-directed surgery, and time from diagnosis to treatment. These variables do not identify radical inguinal orchiectomy, testis-sparing surgery, retroperitoneal lymph node dissection, post-chemotherapy residual mass surgery, operative intent, or referral-related delay. The primary outcome was stage distribution at diagnosis, with particular attention to regional or distant-stage disease among patients with known stage. Secondary outcomes were overall survival and testicular cancer-specific death. Overall survival was defined as time from diagnosis to death from any cause or last follow-up. For competing-risk analyses, testicular cancer-specific death was the event of interest and death from other causes was treated as a competing event.

2.3. Statistical Analysis

Descriptive statistics were used to summarize demographic, tumor, registry-recorded treatment, and survival-related characteristics. Categorical variables were presented as frequencies and percentages and compared using Pearson's chi-square test. Multivariable Logistic Regression evaluated factors associated with regional or distant-stage disease among patients with known stage and was adjusted for diagnosis period, age group, race, histological subtype, marital status, median household income group, and rural–urban residence. Overall survival and cause-specific testicular cancer mortality were evaluated using Cox proportional hazards regression. In addition, Aalen–Johansen cumulative incidence estimates were generated for testicular cancer-specific death, treating death from other causes as a competing event, and Fine–Gray regression was used to estimate adjusted subdistribution hazard ratios. Survival models were adjusted for diagnosis period, age group, race, histological subtype, summary stage, registry-recorded primary-site surgery, chemotherapy, radiotherapy, marital status, median household income group, and rural–urban residence; unknown/unstaged cases were excluded. Patients with a recorded survival time of 0 months were assigned 0.5 months of follow-up so that deaths occurring within the month of diagnosis were retained. Because follow-up differed substantially across periods, all survival analyses were repeated with follow-up administratively restricted to 12 months. The proportional hazards assumption was assessed using Schoenfeld residuals. Although the global test indicated non-proportionality for several adjustment covariates, no evidence of violation was observed for diagnosis period; period-specific estimates were therefore interpreted cautiously, with competing-risk analysis considered the principal approach for testicular cancer-specific death. All tests were two-sided, and $p < 0.05$ was considered statistically significant. Analyses were performed using Stata/IC version 16.1 (StataCorp LLC, College Station, TX, USA). Treatment covariates were included for descriptive adjustment and were not interpreted as causal effects because SEER lacks detailed information on treatment intent, regimen, adherence, recurrence, and complete treatment timing.

2.4. Machine Learning Analysis

To evaluate 12-month all-cause mortality among patients with early-onset testicular germ cell tumors, an exploratory machine learning framework was established across four temporal cohorts: the pre-COVID-19 period (2018–2019), the COVID-19 period (2020–2021), the 2022–2023 period, and the overall cohort including the entire study period (2018–2023). The binary outcome was defined as death from any cause within 12 months of diagnosis.

Candidate predictors included demographic characteristics, diagnosis period, tumor-related variables, stage-related variables, histological subtype, socioeconomic indicators, rural–urban residence, tumor marker recodes, and registry-recorded treatment variables. Clinical intervention variables were included to account descriptively for registry-recorded treatment characteristics across diagnosis periods rather than to estimate causal treatment effects. To minimize data leakage, survival time, vital status, SEER cause-specific death classification, cancer-specific survival event status, and any variables directly defining the outcome were excluded from the predictor set.

For each temporal cohort, the dataset was randomly divided into training and testing subsets using an 80:20 split with stratification according to the 12-month mortality outcome. Model training was performed only in the training set, and final model performance was evaluated in the independent test set. Four supervised machine learning algorithms were implemented: Logistic Regression, Random Forest, Gradient Boosting, and Support Vector Machine. Categorical variables were transformed using one-hot encoding, and numeric matrices were generated for model training and evaluation. Where applicable, hyperparameters were optimized within the training set using cross-validation.

Model performance was assessed using accuracy, sensitivity, specificity, precision, recall, F1-score, receiver operating characteristic area under the curve (ROC AUC), and Matthews correlation coefficient (MCC). Because 12-month mortality was uncommon in this cohort, model interpretation focused primarily on ROC AUC and MCC rather than accuracy alone. Given the exploratory nature of the machine learning component and the low frequency of 12-month mortality events, the analysis focused on model discrimination and classification performance rather than feature-attribution interpretation. The machine learning analyses were performed using Python version 3.12 in the Google Colab environment. The Python source codes and execution scripts are provided as Supplementary Material.

3. Results

3.1. Study Population and Cohort Characteristics

A total of 13,303 male patients aged 15–49 years with early-onset testicular germ cell tumors diagnosed between 2018 and 2023 were included in the final cohort. Of these, 4315 patients were diagnosed in the pre-COVID-19 period, 4452 in the COVID-19 period, and 4536 in the 2022–2023 period (Table 1). The largest age group was 25–34 years, accounting for 44.8% of the total cohort, followed by patients aged 35–49 years (36.3%) and 15–24 years (18.9%). The proportion of patients aged 15–24 years decreased from 20.5% in the pre-COVID-19 period to 17.8% in 2022–2023, corresponding to an absolute difference of 2.7 percentage points. Race distribution was generally similar across periods, and most patients were White (85.7%). Marital-status distributions showed only modest absolute differences; for example, the proportion of single/never-married patients increased from 52.2% to 55.0% between the pre-COVID-19 and 2022–2023 periods. More pronounced changes were observed in household-income categories: the proportion of patients in the $70,000-$89,999 group decreased from 38.5% to 21.3%, whereas the proportion in the $90,000-$109,999 group increased from 23.2% to 42.3%. Rural–urban residence was broadly similar across periods. Histological distribution remained stable, with seminoma comprising 53.5% and non-seminoma 46.5% of cases overall; the proportion of seminoma varied by only 0.6 percentage points between the pre-COVID-19 and 2022–2023 periods (Table 1).

Table 1. Baseline demographic and epidemiological characteristics of patients with early-onset testicular germ cell tumors according to diagnosis period.

Variable	Total *n* = 13,303	Pre-COVID-19 *n* = 4315	COVID-19 *n* = 4452	2022–2023 *n* = 4536
Age group, years				
15–24	2520 (18.9)	885 (20.5)	826 (18.6)	809 (17.8)
25–34	5958 (44.8)	1889 (43.8)	2024 (45.5)	2045 (45.1)
35–49	4825 (36.3)	1541 (35.7)	1602 (36.0)	1682 (37.1)
Race				
White	11,403 (85.7)	3732 (86.5)	3840 (86.3)	3831 (84.5)
Black	398 (3.0)	129 (3.0)	123 (2.8)	146 (3.2)
Asian or Pacific Islander	738 (5.5)	223 (5.2)	241 (5.4)	274 (6.0)
American Indian/Alaska Native	156 (1.2)	53 (1.2)	49 (1.1)	54 (1.2)
Unknown	608 (4.6)	178 (4.1)	199 (4.5)	231 (5.1)

Table 1. *Cont.*

Variable	Total *n* = 13,303	Pre-COVID-19 *n* = 4315	COVID-19 *n* = 4452	2022–2023 *n* = 4536
Marital status				
Married/common law	4535 (34.1)	1535 (35.6)	1482 (33.3)	1518 (33.5)
Single, never married	7211 (54.2)	2252 (52.2)	2466 (55.4)	2493 (55.0)
Divorced	305 (2.3)	118 (2.7)	100 (2.2)	87 (1.9)
Separated	80 (0.6)	28 (0.6)	32 (0.7)	20 (0.4)
Widowed	14 (0.1)	6 (0.1)	2 (0.0)	6 (0.1)
Unmarried/domestic partner	190 (1.4)	45 (1.0)	59 (1.3)	86 (1.9)
Unknown	968 (7.3)	331 (7.7)	311 (7.0)	326 (7.2)
Median household income				
<$70,000	1969 (14.8)	651 (15.1)	647 (14.5)	671 (14.8)
$70,000–$89,999	3873 (29.1)	1660 (38.5)	1249 (28.1)	964 (21.3)
$90,000–$109,999	4481 (33.7)	1003 (23.2)	1561 (35.1)	1917 (42.3)
≥$110,000	2979 (22.4)	1001 (23.2)	995 (22.3)	983 (21.7)
Unknown/missing	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
Rural–urban residence				
Large metropolitan	8542 (64.2)	2804 (65.0)	2896 (65.1)	2842 (62.7)
Small/medium metropolitan	3668 (27.6)	1185 (27.5)	1198 (26.9)	1285 (28.3)
Nonmetropolitan	1064 (8.0)	318 (7.4)	349 (7.8)	397 (8.8)
Unknown/missing	29 (0.2)	8 (0.2)	9 (0.2)	12 (0.3)
Histology				
Seminoma	7117 (53.5)	2294 (53.2)	2383 (53.5)	2440 (53.8)
Non-seminoma	6186 (46.5)	2021 (46.8)	2069 (46.5)	2096 (46.2)

Values are presented as *n* (%). Percentages are column percentages. Pearson's chi-square test was used for comparisons across diagnosis periods.

3.2. Stage and Registry-Recorded Treatment Characteristics Across Diagnosis Periods

Tumor stage and treatment characteristics according to diagnosis period are presented in Table 2. Summary stage distribution differed significantly across diagnosis periods ($p < 0.001$). The proportion of localized disease decreased from 67.2% in the pre-COVID-19 period to 65.2% during the COVID-19 period and 63.6% during the 2022–2023 period. In contrast, regional-stage disease increased from 18.7% to 20.7% and 21.2%, respectively. Distant-stage disease remained relatively stable across periods, ranging from 11.7% to 12.2%.

Among patients with known stage, disease extent also differed significantly across periods ($p = 0.005$). The proportion of regional or distant-stage disease increased from 31.2% in the pre-COVID-19 period to 33.5% during the COVID-19 period and 34.4% during the 2022–2023 period. In contrast, EOD 2018 stage group distribution did not differ significantly across diagnosis periods ($p = 0.358$). Stage I disease accounted for 67.2% of the total cohort, while Stage II and Stage III disease accounted for 10.7% and 14.1%, respectively.

Table 2. Tumor stage and treatment characteristics of patients with early-onset testicular germ cell tumors according to diagnosis period.

Variable	Total	Pre-COVID-19 2018–2019	COVID-19 2020–2021	2022–2023	*p* Value
Summary stage					$p < 0.001$ *
Localized	8685 (65.3)	2898 (67.2)	2904 (65.2)	2883 (63.6)	
Regional	2688 (20.2)	808 (18.7)	920 (20.7)	960 (21.2)	
Distant	1595 (12.0)	504 (11.7)	541 (12.2)	550 (12.1)	
Unknown/unstaged	335 (2.5)	105 (2.4)	87 (2.0)	143 (3.2)	
Stage disease extent					$p = 0.005$ *
Localized	8685 (67.0)	2898 (68.8)	2904 (66.5)	2883 (65.6)	
Regional/distant	4283 (33.0)	1312 (31.2)	1461 (33.5)	1510 (34.4)	
EOD 2018 stage group					$p = 0.358$
Stage I	8938 (67.2)	2952 (68.4)	2941 (66.1)	3045 (67.1)	
Stage II	1418 (10.7)	435 (10.1)	500 (11.2)	483 (10.6)	
Stage III	1882 (14.1)	599 (13.9)	636 (14.3)	647 (14.3)	
Unknown/not applicable	1065 (8.0)	329 (7.6)	375 (8.4)	361 (8.0)	
Surgery					$p = 0.037$ *
Surgery performed	12,704 (95.5)	4127 (95.6)	4273 (96.0)	4304 (94.9)	
No surgery/not performed/unknown	599 (4.5)	188 (4.4)	179 (4.0)	232 (5.1)	
Chemotherapy					$p = 0.022$ *
Yes	5094 (38.3)	1671 (38.7)	1757 (39.5)	1666 (36.7)	
No/Unknown	8209 (61.7)	2644 (61.3)	2695 (60.5)	2870 (63.3)	
Radiotherapy					$p = 0.197$
Radiotherapy	385 (2.9)	141 (3.3)	123 (2.8)	121 (2.7)	
None/Unknown	12,918 (97.1)	4174 (96.7)	4329 (97.2)	4415 (97.3)	
Time from diagnosis to treatment					$p = 0.154$
0 days	8797 (68.4)	2803 (67.3)	3002 (69.1)	2992 (68.6)	
1–30 days	3590 (27.9)	1212 (29.1)	1187 (27.3)	1191 (27.3)	
>30 days	481 (3.7)	149 (3.6)	153 (3.5)	179 (4.1)	

Values are presented as n (%). Percentages are column percentages. Pearson chi-square test was used for comparisons across diagnosis periods. Known-stage disease extent was assessed after excluding unknown/unstaged summary-stage cases and grouping regional and distant disease together. In testicular germ cell tumors, EOD 2018 stage group is reported as Stage I-III; metastatic disease is represented within Stage III rather than Stage IV. * $p < 0.05$.

Treatment characteristics showed statistically significant differences across periods for surgery and chemotherapy. Surgery was performed in 95.5% of the cohort, with a slightly lower proportion in the 2022–2023 period (94.9%) compared with the pre-COVID-19 period (95.6%) and COVID-19 period (96.0%) ($p = 0.037$). Chemotherapy use also differed significantly across periods ($p = 0.022$), with the highest proportion during the COVID-19 period (39.5%) and the lowest during the 2022–2023 period (36.7%). Radiotherapy use did not differ significantly across periods ($p = 0.197$). Among patients with non-missing treatment timing data, time from diagnosis to treatment was similar across periods ($p = 0.154$) (Table 2).

3.3. Factors Associated with Regional or Distant-Stage Disease

In Multivariable Logistic Regression analysis, diagnosis during the COVID-19 period was associated with higher odds of regional or distant-stage disease compared with the pre-COVID-19 period (OR = 1.11, 95% CI: 1.02–1.22, $p = 0.023$). The association was similar in magnitude for the 2022–2023 period (OR = 1.16, 95% CI: 1.06–1.28, $p = 0.002$) (Table 3). Non-seminoma histology was strongly associated with regional or distant-stage disease compared with seminoma (OR = 1.91, 95% CI: 1.77–2.07, $p < 0.001$) (Table 3). Age group was not significantly associated with regional or distant-stage disease after adjustment.

Table 3. Multivariable Logistic Regression analysis of factors associated with regional or distant-stage disease among patients with early-onset testicular germ cell tumors.

Variable	OR	95% CI	*p* Value
Diagnosis period			
Pre-COVID-19	1.00	Reference	-
COVID-19	1.11	1.02–1.22	0.023 *
2022–2023	1.16	1.06–1.28	0.002 *
Age group, years			
15–24	1.00	Reference	-
25–34	0.91	0.82–1.01	0.083
35–49	1.10	0.98–1.24	0.109
Race			
White	1.00	Reference	-
American Indian/Alaska Native	1.74	1.22–2.50	0.002 *
Asian or Pacific Islander	0.92	0.78–1.09	0.331
Black	1.11	0.90–1.38	0.334
Unknown	0.64	0.51–0.80	<0.001 *
Histology			
Seminoma	1.00	Reference	-
Non-seminoma	1.91	1.77–2.07	<0.001 *
Marital status			
Single, never married	1.00	Reference	-
Divorced	1.06	0.82–1.35	0.663
Married/common law	0.79	0.72–0.86	<0.001 *
Separated	0.79	0.48–1.28	0.335
Unmarried/domestic partner	0.93	0.68–1.27	0.644
Widowed	1.25	0.46–3.40	0.662
Unknown	0.47	0.39–0.57	<0.001 *
Median household income			
<$70,000	1.00	Reference	-
$70,000–$89,999	1.02	0.90–1.17	0.718

Table 3. *Cont.*

Variable	OR	95% CI	*p* Value
$90,000–$109,999	0.99	0.86–1.14	0.907
≥$110,000	0.96	0.82–1.11	0.564
Rural–urban residence			
Large metropolitan	1.00	Reference	-
Small/medium metropolitan	0.99	0.90–1.09	0.812
Nonmetropolitan	1.09	0.92–1.28	0.317

The outcome was regional or distant-stage disease compared with localized disease. The model was adjusted for diagnosis period, age group, race, histological subtype, marital status, median household income group, and rural–urban residence. Unknown/unstaged cases were excluded. The analysis included 12,967 patients; one patient in the single-member unknown-income category was not used because that category perfectly predicted the outcome. * $p < 0.05$.

Compared with White patients, American Indian/Alaska Native patients had higher odds of regional or distant-stage disease (OR = 1.74, 95% CI: 1.22–2.50, $p = 0.002$) (Table 3). Asian or Pacific Islander race and Black race were not significantly associated with regional or distant-stage disease. Patients with unknown race had lower odds of regional or distant-stage disease compared with White patients (OR = 0.64, 95% CI: 0.51–0.80, $p < 0.001$) (Table 3).

Compared with single/never-married patients, married/common-law patients had lower odds of regional or distant-stage disease (OR = 0.79, 95% CI: 0.72–0.86, $p < 0.001$) (Table 3). Divorced, separated, unmarried/domestic partner, and widowed status were not significantly associated with regional or distant-stage disease. Patients with unknown marital status had lower odds of regional or distant-stage disease compared with single/never-married patients (OR = 0.47, 95% CI: 0.39–0.57, $p < 0.001$) (Table 3). Median household income and rural–urban residence were not significantly associated with regional or distant-stage disease in the adjusted model.

3.4. Survival Outcomes

During the study period, 542 deaths from any cause and 378 testicular cancer-specific deaths were observed. Crude death proportions were lower in the 2022–2023 group because that group had substantially shorter follow-up. In the adjusted full-follow-up model, COVID-19 diagnosis was not associated with overall mortality (HR = 1.11, 95% CI: 0.91–1.37, $p = 0.304$), whereas diagnosis during the 2022–2023 period was associated with higher overall mortality (HR = 1.29, 95% CI: 1.01–1.65, $p = 0.041$). For testicular cancer-specific death, diagnosis during the 2022–2023 period was associated with higher mortality in both the cause-specific Cox model (HR = 1.49, 95% CI: 1.12–2.00, $p = 0.007$) and the Fine–Gray model (sHR = 1.45, 95% CI: 1.09–1.93, $p = 0.012$); the corresponding COVID-19 estimates were not statistically significant (Table 4).

When follow-up was restricted to 12 months, diagnosis period was not significantly associated with overall mortality: the adjusted HRs were 1.08 (95% CI: 0.81–1.44, $p = 0.589$) for COVID-19 and 1.24 (95% CI: 0.93–1.67, $p = 0.144$) for the 2022–2023 period. In contrast, the association for the 2022–2023 period with testicular cancer-specific death remained statistically significant in both the cause-specific Cox model (HR = 1.45, 95% CI: 1.02–2.05, $p = 0.037$) and the Fine–Gray model (sHR = 1.46, 95% CI: 1.03–2.07, $p = 0.034$). COVID-19 period estimates remained non-significant (Table 5). Aalen–Johansen cumulative incidence curves for testicular cancer-specific death according to diagnosis period are presented in Figure 2, with death from other causes treated as a competing event. The curves should be interpreted in view of the shorter observable follow-up in the 2022–2023 cohort.

Table 4. Adjusted full-follow-up analyses of overall mortality and testicular cancer-specific death among patients with early-onset testicular germ cell tumors.

Diagnosis Period	Adjusted OS HR (95% CI)	*p* Value	Cause-Specific HR (95% CI)	*p* Value	Fine–Gray sHR (95% CI)	*p* Value
Pre-COVID-19	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-
COVID-19	1.11 (0.91–1.37)	0.304	1.22 (0.95–1.56)	0.123	1.22 (0.95–1.57)	0.111
2022–2023	1.29 (1.01–1.65)	0.041 *	1.49 (1.12–2.00)	0.007 *	1.45 (1.09–1.93)	0.012 *

Overall survival models included 12,967 patients and 528 deaths. Cause-specific Cox and Fine–Gray models included 12,960 patients, 369 testicular cancer-specific deaths, and 152 competing deaths. Models were adjusted for age group, race, histological subtype, summary stage, registry-recorded primary-site surgery, chemotherapy, radiotherapy, marital status, median household income group, and rural–urban residence. The pre-COVID-19 period was the reference category. * $p < 0.05$.

Table 5. Twelve-month restricted analyses of overall mortality and testicular cancer-specific death among patients with early-onset testicular germ cell tumors.

Diagnosis Period	Adjusted OS HR (95% CI)	*p* Value	Cause-Specific HR (95% CI)	*p* Value	Fine–Gray sHR (95% CI)	*p* Value
Pre-COVID-19	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-
COVID-19	1.08 (0.81–1.44)	0.589	1.19 (0.85–1.67)	0.318	1.21 (0.86–1.70)	0.276
2022–2023	1.24 (0.93–1.67)	0.144	1.45 (1.02–2.05)	0.037 *	1.46 (1.03–2.07)	0.034 *

The 12-month overall survival model included 12,967 patients and 303 deaths. The 12-month cause-specific Cox and Fine–Gray models included 12,960 patients, 220 testicular cancer-specific deaths, and 80 competing deaths. Models used the same covariate adjustment as the full-follow-up analyses. The pre-COVID-19 period was the reference category. * $p < 0.05$.

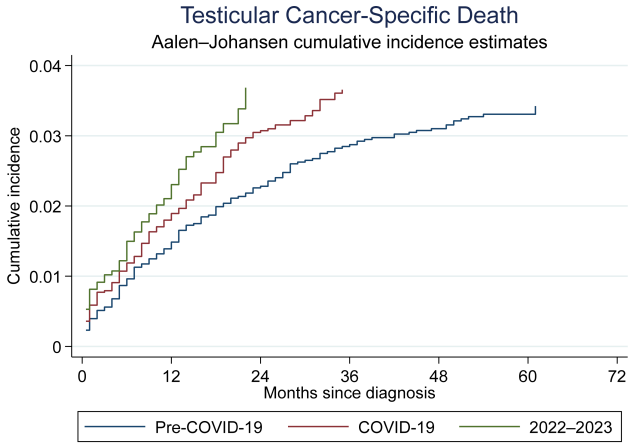


Figure 2. Aalen–Johansen cumulative incidence estimates for testicular cancer-specific death according to diagnosis period, with death from other causes treated as a competing event. Follow-up duration differed across diagnosis periods, resulting in shorter observable follow-up for the 2022–2023 cohort.

3.5. Machine Learning-Based 12-Month Mortality Prediction

Machine learning models demonstrated moderate discrimination for 12-month all-cause mortality prediction across diagnosis periods (Table 6). In the pre-COVID-19 cohort, Support Vector Machine achieved the highest ROC AUC of 0.5739 (95% CI: 0.4469–0.6904). During the COVID-19 period, Logistic Regression showed the highest ROC AUC of 0.7638 (95% CI: 0.6235–0.8885), and also performed best in the 2022–2023 period with a ROC AUC of 0.7639 (95% CI: 0.6192–0.8874). In the overall 2018–2023 cohort, Logistic Regression achieved the highest ROC AUC of 0.7394 (95% CI: 0.6649–0.8104).

Table 6. Summary of machine learning model performance for 12-month all-cause mortality prediction across diagnosis periods.

Diagnosis Period	Best-Performing Model by ROC AUC	Train Events (Death)	Train Non-Events (Survival	Test Events (Death)	Test Non-Events (Survival)	Confusion Matrix [TN, FP, FN, TP]	ROC AUC (95% CI)	PR AUC (95% CI)	Accuracy	Balanced Accuracy	Sensitivity (Death)	Specificity (Survival)	PPV/Precision (Death)	F1-Score (Death)	MCC
Pre-COVID-19	Support Vector Machine	77	3272	19	819	[503, 316, 10, 9]	0.5739 (0.4469–0.6904)	0.0264 (0.0153–0.0453)	0.611	0.5439	0.4737	0.6142	0.0277	0.0523	0.0268
COVID-19	Logistic Regression	89	3273	22	819	[493, 326, 4, 18]	0.7638 (0.6235–0.8885)	0.1665 (0.0707–0.3263)	0.6076	0.7101	0.8182	0.602	0.0523	0.0984	0.1364
2022–2023	Logistic Regression	82	1552	20	389	[264, 125, 5, 15]	0.7639 (0.6192–0.8874)	0.3433 (0.1598–0.5675)	0.6822	0.7143	0.75	0.6787	0.1071	0.1875	0.1948
Overall cohort	Logistic Regression	247	8099	62	2025	[1267, 758, 16, 46]	0.7394 (0.6649–0.8104)	0.1606 (0.0926–0.2665)	0.6291	0.6838	0.7419	0.6257	0.0572	0.1062	0.1283

Values represent the performance metrics of the best-performing model according to ROC AUC within each diagnosis period. TN: True Negatives (survival correctly predicted); FP: False Positives (survival incorrectly predicted as death); FN: False Negatives (death incorrectly predicted as survival); TP: True Positives (death correctly predicted); ROC AUC (95% CI): receiver operating characteristic area under the curve with 95% confidence interval; PR AUC (95% CI): precision–recall area under the curve with 95% confidence interval; PPV: positive predictive value (precision for 12-month death); MCC: Matthews correlation coefficient.

Although ROC AUC values suggested moderate discrimination, overall classification performance remained limited, as reflected by low MCC (ranging from 0.0268 to 0.1948) and PR AUC values (ranging from 0.0264 to 0.3433) across all periods. Performance for the minority mortality class also remained challenging, evidenced by low positive predictive values (PPVs) ranging from 0.0277 to 0.1071, consistent with the severe class imbalance expected in 12-month mortality prediction for a cancer type with generally favorable short-term survival. Therefore, the machine learning findings should be interpreted as exploratory and complementary to the conventional survival analyses.

Across all analyzed periods, the dataset exhibited severe class imbalance, reflecting the low incidence of 12-month all-cause mortality in early-onset testicular germ cell tumor patients. Stratified train–test partitioning (80:20 split) successfully preserved the mortality event rate between the training and testing sets. Specifically, the pre-COVID-19 cohort comprised 77 mortality events (out of 3349 training patients) in the training set and 19 events (out of 838 testing patients) in the testing set. During the COVID-19 period, 89 training events (out of 3362 patients) and 22 testing events (out of 841 patients) were evaluated. The 2022–2023 cohort included 82 training events (out of 1634 patients) and 20 testing events (out of 409 patients). Finally, in the overall 2018–2023 cohort, the models were trained on 247 events (out of 8346 patients) and evaluated on 62 events (out of 2087 patients).

3.6. Model Discrimination Based on ROC and PR Analysis

Model discrimination and precision–recall trade-offs are presented in Figure 3. In the pre-COVID-19 cohort, Support Vector Machine showed the highest ROC AUC (0.574), whereas Support Vector Machine and Logistic Regression achieved the highest PR-AUC (0.026) compared to the 0.023 baseline prevalence (Panels A and B). During the COVID-19 period, Logistic Regression yielded the highest ROC AUC (0.764) and PR-AUC (0.167) relative to the 0.026 baseline (Panels C and D). In the 2022–2023 period, Logistic Regression achieved both the highest ROC AUC (0.764) and the highest PR-AUC (0.343) against the 0.049 baseline (Panels E and F). Finally, in the overall cohort, Logistic Regression demonstrated the strongest discrimination (ROC AUC = 0.739), while Gradient Boosting achieved the highest PR-AUC (0.164) compared to the 0.030 baseline (Panels G and H). Overall, while ROC curves suggested moderate discrimination across periods, the precision–recall curves highlight the substantial difficulty in predicting rare 12-month mortality events, as evidenced by modest PR-AUC values despite consistently outperforming random baseline prevalence.

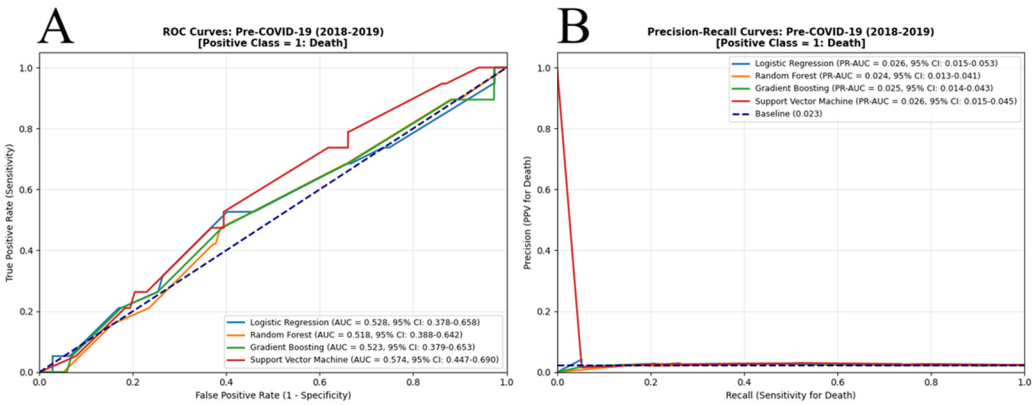


Figure 3. *Cont.*

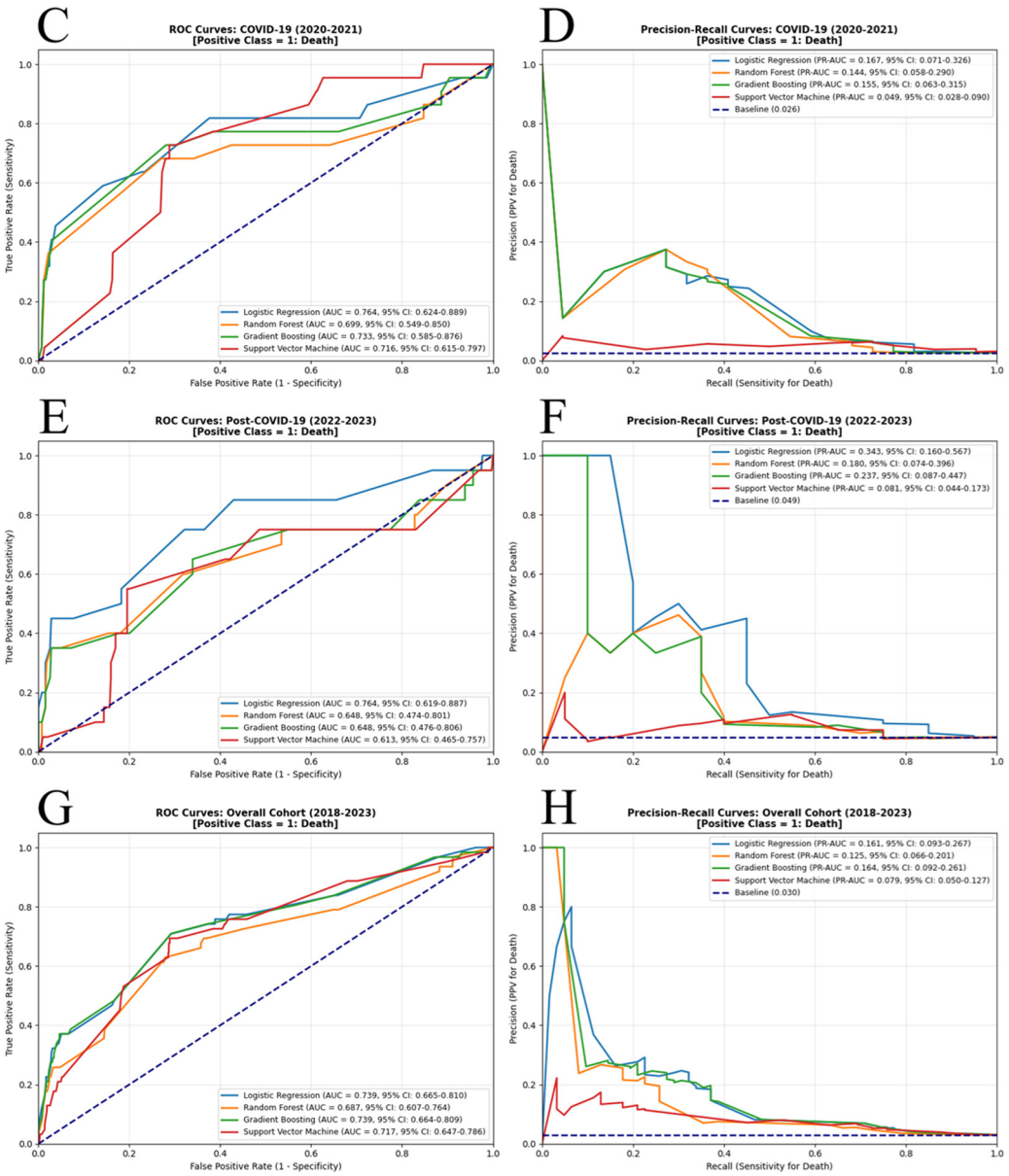


Figure 3. Discrimination and precision–recall performance of machine learning models for 12-month all-cause mortality prediction. Receiver operating characteristic (ROC) curves (left panels: (**A**,**C**,**E**,**G**)) and corresponding precision–recall (PR) curves (right panels: (**B**,**D**,**F**,**H**)) evaluate model performance across diagnosis periods: (**A**,**B**) pre-COVID-19 (2018–2019), (**C**,**D**) COVID-19 (2020–2021), (**E**,**F**) 2022–2023 period, (**G**,**H**) the overall cohort (2018–2023). The positive class corresponds to 12-month all-cause mortality following diagnosis. Diagonal dashed lines in ROC plots represent random chance classification (AUC = 0.50), while horizontal dashed lines in PR plots indicate period-specific baseline prevalence rates: 0.023 (pre-COVID-19), 0.026 (COVID-19), 0.049 (2022–2023), and 0.030 (overall cohort). Area under the curve (AUC) values and 95% confidence intervals (CIs) for each model are presented in the respective panel legends.

4. Discussion

In this population-based SEER study of 13,303 male patients aged 15–49 years, diagnosis during the COVID-19 and 2022–2023 periods was associated with a modestly higher proportion of regional or distant-stage disease than diagnosis before the pandemic. Survival analyses nevertheless identified a higher risk of testicular cancer-specific death in the 2022–2023 cohort. This association was present in the cause-specific Cox model,

remained after accounting for other-cause death in Fine–Gray competing-risk regression, and persisted when follow-up was restricted to 12 months.

The modest shift toward regional or distant-stage disease observed in this study should be interpreted in the broader context of cancer care disruption during the COVID-19 pandemic. Several studies have reported that pandemic-related changes in healthcare delivery, including delayed referrals, reduced diagnostic capacity, and altered patient healthcare-seeking behavior, may have affected cancer diagnosis and staging patterns [11–14]. For testicular germ cell tumors, timely diagnosis is particularly relevant because there is no population-based screening program, and diagnosis depends largely on symptom recognition, clinical examination, scrotal ultrasound, serum tumor marker assessment, and prompt urologic referral [1,2,14]. Previous testicular cancer-specific studies have reported possible stage migration or more advanced presentation during or after the pandemic, although findings have not been entirely uniform [11–13]. Our results are consistent with these observations, but the small absolute difference in regional or distant-stage presentation indicates that the effect should be viewed as a modest population-level signal rather than as evidence of a major deterioration in clinical presentation. This interpretation is particularly relevant in testicular germ cell tumors, where high treatment sensitivity and excellent survival may attenuate the short-term survival impact of modest changes in stage distribution [3–5,15,16].

The survival findings require a more nuanced interpretation than the crude death proportions, which were lowest in the 2022–2023 cohort because that group had the shortest follow-up. After multivariable adjustment, diagnosis during the 2022–2023 period was associated with higher testicular cancer-specific mortality in both cause-specific and competing-risk models. Persistence of the association in the 12-month restricted analysis reduces, but does not eliminate, concern about unequal follow-up. Residual confounding remains likely because SEER does not fully capture serum tumor marker levels, IGCCCG risk classification, metastatic burden, recurrence, chemotherapy regimen, dose intensity, treatment intent, or quality of care. The result should therefore be considered hypothesis-generating and requires confirmation in datasets with detailed clinical staging and treatment information.

Histology remained an important factor associated with disease extent. Non-seminoma histology was associated with higher odds of regional or distant-stage disease compared with seminoma. This finding is consistent with the established clinical distinction between seminoma and non-seminoma, which differ in age distribution, biological behavior, metastatic patterns, treatment sensitivity, and prognosis [1,3,8,17–19]. Population-based analyses have shown that histological composition varies by age and that specific non-seminomatous subtypes may have distinct prognostic implications [3,9,19]. Although our analysis used the broad seminoma versus non-seminoma classification for epidemiological clarity, future studies may provide additional insight by evaluating more detailed histological categories, including embryonal carcinoma, yolk sac tumor, teratoma, choriocarcinoma, and mixed germ cell tumors [3,9,19].

The sociodemographic findings should also be considered within the context of previous testicular cancer disparity research. In this study, married or common-law patients had lower odds of regional or distant-stage disease compared with single or never-married patients. This may reflect differences in social support, symptom recognition, healthcare navigation, or access to timely care, although these mechanisms cannot be directly evaluated using SEER data. Prior population-based work has identified demographic and social determinants, including marital status, race, geography, insurance status, and socioeconomic status, as factors associated with metastatic presentation and cancer-specific mortality in testicular cancer [4,20]. In our cohort, American Indian/Alaska Native race

was associated with higher odds of regional or distant-stage disease compared with White race; however, this subgroup was small, and the finding should be interpreted cautiously.

Registry-recorded treatment characteristics showed only small differences across diagnosis periods. Primary-site surgery was recorded for 95.5% of patients and varied by approximately one percentage point across periods. Chemotherapy was slightly more frequent during the COVID-19 period and less frequent during the 2022–2023 period. These observations may reflect differences in case mix, disease extent, missing-data coding, or clinical decision-making; they do not establish changes in treatment quality or surgical pathways. SEER treatment variables may combine "No" and "Unknown" categories and do not provide regimen, dose, adherence, recurrence, or operative-intent information. Treatment-related results should therefore remain descriptive and should not be interpreted as causal effects.

From a surgical oncology perspective, the available SEER variable is limited to registry-recorded surgery of the primary site. It does not reliably distinguish radical inguinal orchiectomy from testis-sparing surgery, nor does it capture retroperitoneal lymph node dissection, post-chemotherapy residual mass surgery, referral delay, operative intent, or surgical pathology details. Consequently, the data support statements about the frequency of registry-recorded primary-site surgery, but not conclusions about specific surgical pathways or pandemic-related surgical delay. The absence of a period difference in time from diagnosis to treatment also cannot exclude delays before diagnosis, including symptom appraisal, primary-care access, ultrasound, or urologic referral.

The machine learning component provides a complementary and exploratory perspective on short-term mortality prediction. In this study, the models demonstrated moderate discrimination for predicting 12-month all-cause mortality across temporal cohorts, with the highest ROC AUC observed during the COVID-19 period for Logistic Regression. However, the low MCC values and limited mortality-class performance indicate that these models should not be interpreted as clinically deployable prediction tools [7,21]. Rather, they provide an exploratory assessment of whether routinely available registry variables can capture short-term mortality risk patterns in early-onset testicular germ cell tumors. Future studies should include external validation, calibration assessment, and modeling approaches specifically designed for imbalanced outcomes.

This study has several strengths. It used a large, contemporary, population-based SEER cohort with diagnoses through 2023 and focused on early-onset malignant testicular germ cell tumors, a clinically relevant adolescent and young adult population. The analysis evaluated both complete and known-stage distributions, applied Multivariable Logistic Regression, retained deaths recorded at 0 survival months by assigning 0.5 months of follow-up, and supplemented cause-specific Cox regression with Aalen–Johansen cumulative incidence estimates and Fine–Gray competing-risk models. The 12-month restricted analyses provided a more comparable follow-up window across diagnosis periods. The machine learning component was retained as an exploratory secondary analysis and included mortality-class-specific performance metrics appropriate for an imbalanced outcome.

Several limitations should be acknowledged. First, the retrospective registry-based design precludes causal inference regarding the pandemic and the observed outcomes. Second, the 2022–2023 cohort had shorter follow-up, although the principal association with testicular cancer-specific mortality persisted in the 12-month analyses. Fourth, SEER lacks individual-level information on COVID-19 infection, symptom duration, patient and referral delays, serum tumor markers in a form sufficient for complete risk stratification, IGCCCG category, metastatic burden, recurrence, treatment intent, chemotherapy regimen, dose intensity, adherence, and quality of care; therefore, residual confounding cannot be excluded. Fifth, SEER surgery variables do not identify exact surgical procedures or

pathways, and chemotherapy and radiotherapy variables may include unknown status. Sixth, the proportional hazards assumption was not satisfied globally for several adjustment covariates, although diagnosis period showed no evidence of non-proportionality; therefore, period-specific estimates were interpreted cautiously, and competing-risk analysis was emphasized for cancer-specific death. Finally, the machine learning analysis was exploratory and requires external validation, calibration assessment, and evaluation in independent datasets before any clinical application.

In conclusion, early-onset testicular germ cell tumors diagnosed during the COVID-19 period and in 2022–2023 showed a modest population-level shift toward regional or distant-stage presentation. The absolute differences were small, and SEER data do not permit detailed assessment of surgical pathways or delays. Diagnosis during the 2022–2023 period was associated with higher testicular cancer-specific mortality in both cause-specific and Fine–Gray competing-risk analyses, including the 12-month restricted analysis, whereas the 12-month overall mortality association was not statistically significant. These findings are hypothesis-generating and should be interpreted cautiously in view of residual confounding, limited clinical detail, and shorter follow-up in the 2022–2023 cohort. Continued population-based surveillance and validation in clinically detailed datasets are needed.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/surgeries7030097/s1, Supplementary Table S1: Detailed machine learning model performance for 12-month all-cause mortality prediction across diagnosis periods; Software S1: Python source codes and execution scripts for the reported machine learning models and ROC analysis are available at https://github.com/omerecinar/MDPI-Manuscript-Colab-Codes (accessed on 14 May 2026).

Author Contributions: Conceptualization, S.Ü. and Y.A.; methodology, Y.A. and Ö.E.Ç.; software, Y.A. and Ö.E.Ç.; validation, S.Ü., Y.A. and Ö.E.Ç.; formal analysis, Y.A. and Ö.E.Ç.; investigation, S.Ü. and Y.A.; resources, S.Ü. and Y.A.; data curation, Y.A. and Ö.E.Ç.; writing—original draft preparation, Y.A. and S.Ü.; writing—review and editing, S.Ü., Y.A. and Ö.E.Ç.; visualization, Y.A. and Ö.E.Ç.; supervision, S.Ü. and Y.A.; project administration, Y.A.; funding acquisition, not applicable. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Ethical review and approval were waived for this study because it was based on publicly available, de-identified data from the Surveillance, Epidemiology, and End Results (SEER) Program. The study was conducted in accordance with the principles of the Declaration of Helsinki and the SEER Research Data Use Agreement.

Informed Consent Statement: Patient consent was waived because this study used publicly available, de-identified registry data from the SEER Program.

Data Availability Statement: The data used in this study were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the U.S. National Cancer Institute. Case extraction was performed using SEER*Stat software version 9.0.42 from the Incidence—SEER Research Data, 17 Registries, November 2025 Submission, including cases diagnosed from 2000 to 2023. The SEER data are publicly available to registered users through the SEER Program after completion of the SEER Research Data Use Agreement. Python source codes and execution scripts for the machine learning models and ROC analyses are provided as Supplementary Software S1 and are also available at https://github.com/omerecinar/MDPI-Manuscript-Colab-Codes (accessed on 14 May 2026).

Acknowledgments: The authors acknowledge the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute for providing access to the de-identified registry data used in this study. AI-assisted language support was used only for grammar correction and academic language editing.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

AFP	Alpha-fetoprotein
AI	Artificial intelligence
AUC	Area under the curve
CI	Confidence interval
COVID-19	Coronavirus disease 2019
CSS	Cancer-specific survival
EOD	Extent of Disease
hCG	Human chorionic gonadotropin
HR	Hazard ratio
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
LDH	Lactate dehydrogenase
MCC	Matthews correlation coefficient
ML	Machine learning
OR	Odds ratio
OS	Overall survival
SEER	Surveillance, Epidemiology, and End Results
SVM	Support Vector Machine
TGCT	Testicular germ cell tumor

References

1. Travis, L.B.; Feldman, D.R.; Fung, C.; Poynter, J.N.; Lockley, M.; Frazier, A.L. Adolescent and Young Adult Germ Cell Tumors: Epidemiology, Genomics, Treatment, and Survivorship. *J. Clin. Oncol.* **2024**, *42*, 696–706. [CrossRef] [PubMed]
2. Saltzman, A.F.; Cost, N.G. Adolescent and Young Adult Testicular Germ Cell Tumors: Special Considerations. *Adv. Urol.* **2018**, *2018*, 2375176. [CrossRef] [PubMed]
3. Mason, J.B.; Srivastava, A.; Lanzotti, N.J.; Ellis, J.L.; Carlo, H.N.D.; Gearhart, J.P.; Bowen, D.K.; Gupta, M.; Picken, M.M.; Gupta, G.N.; et al. Variations in Germ Cell Tumor Histology by Age and Implications for Cancer-Specific Survival among Pediatric and Adult Males: A Population-Based Study. *Urol. Oncol. Semin. Orig. Investig.* **2024**, *42*, 292.e1–292.e26. [CrossRef] [PubMed]
4. Shah, Y.B.; Goldberg, H.; Hu, B.; Daneshmand, S.; Chandrasekar, T. Metastatic Testicular Cancer Patterns and Predictors: A Contemporary Population-Based SEER Analysis. *Urology* **2023**, *180*, 182–189. [CrossRef] [PubMed]
5. Spermon, J.R.; Witjes, J.A.; Kiemeney, L.A.L.M. Difference in stage and morphology-adjusted survival between young and elderly patients with a testicular germ cell tumor. *Urology* **2002**, *60*, 889–893. [CrossRef] [PubMed]
6. Mangone, L.; Marinelli, F.; Bisceglia, I.; Masini, C.; Palicelli, A.; Morabito, F.; Di Girolamo, S.; Neri, A.; Pinto, C. Incidence and Survival of Testicular Cancers in a Province in Northern Italy and Their Association with Second Tumors. *Biology* **2023**, *12*, 1409. [CrossRef] [PubMed]
7. Yu, H.; Feng, B.; Zhang, Y.; Lyu, J. Development and Validation of a Nomogram for Predicting the Overall Survival of Patients with Testicular Cancer. *Cancer Med.* **2023**, *12*, 15567–15578. [CrossRef] [PubMed]
8. Cano Garcia, C.; Barletta, F.; Incesu, R.B.; Piccinelli, M.L.; Tappero, S.; Panunzio, A.; Tian, Z.; Saad, F.; Shariat, S.F.; Antonelli, A.; et al. Survival of Testicular Pure Teratoma vs. Mixed Germ Cell Tumor Patients in Primary Tumor Specimens across All Stages. *Cancers* **2023**, *15*, 694. [CrossRef] [PubMed]
9. Maringe, C.; Spicer, J.; Morris, M.; Purushotham, A.; Nolte, E.; Sullivan, R.; Rachet, B.; Aggarwal, A. The Impact of the COVID-19 Pandemic on Cancer Deaths Due to Delays in Diagnosis in England, UK: A National, Population-Based, Modelling Study. *Lancet Oncol.* **2020**, *21*, 1023–1034. [CrossRef] [PubMed]
10. Sud, A.; Torr, B.; Jones, M.E.; Broggio, J.; Scott, S.; Loveday, C.; Garrett, A.; Gronthoud, F.; Nicol, D.L.; Jhanji, S.; et al. Effect of Delays in the 2-Week-Wait Cancer Referral Pathway during the COVID-19 Pandemic on Cancer Survival in the UK: A Modelling Study. *Lancet Oncol.* **2020**, *21*, 1035–1044. [CrossRef] [PubMed]
11. Lee-Ying, R.; O'Sullivan, D.E.; Gagnon, R.; Bosma, N.; Stewart, R.N.; Railton, C.; Tilley, D.; Alimohamed, N.; Basappa, N.; Cheng, T.; et al. Stage Migration of Testicular Germ Cell Tumours in Alberta, Canada, during the COVID-19 Pandemic: A Retrospective Cohort Study. *CMAJ Open* **2022**, *10*, E633–E642. [CrossRef] [PubMed]
12. Fagan, M.; Janes, W.C.I.; Andrews, M.; Harvey, D.R.; Warden, G.M.; Organ, M.K.; Johnston, P. Restricted Access and Advanced Disease in Post-Pandemic Testicular Cancer. *Can. Urol. Assoc. J.* **2024**, *18*, 262–267. [CrossRef] [PubMed]

13. Amini, A.; Waxweiler, T.V.; Maroni, P.D.; Kessler, E.R.; Cost, C.R.; Greffe, B.S.; Garrington, T.P.; Liu, A.K.; Cost, N.G. Survival Outcomes of Adolescent and Adult Patients with Non-Seminomatous Testicular Germ-Cell Tumors: A Population-Based Study. *J. Pediatr. Urol.* **2016**, *12*, 405.e1–405.e9. [CrossRef] [PubMed]
14. Yildiz, A.K.; Ozgur, B.C.; Bayraktar, A.; Yazar, V.M.; Doluoglu, O.G. The Effect of the COVID-19 Pandemic on Patients with Testicular Germ Cell Tumor. *Cir. Cir.* **2022**, *90*, 8–14. [CrossRef] [PubMed]
15. Keskin, A.; Yorulmaz, E.M.; Donmez, K.; Ozcan, S.; Kose, O.; Gorgel, S.N.; Akin, Y. Impact of the Coronavirus Disease 2019 (COVID-19) Pandemic on Tumor Stage Progression in Urological Malignancies: A Comparative Study. *Front. Urol.* **2025**, *5*, 1619185. [CrossRef] [PubMed]
16. Kvammen, Ø.; Myklebust, T.; Solberg, A.; Møller, B.; Klepp, O.H.; Fosså, S.D.; Tandstad, T. Long-Term Relative Survival after Diagnosis of Testicular Germ Cell Tumor. *Cancer Epidemiol. Biomark. Prev.* **2016**, *25*, 773–779. [CrossRef] [PubMed]
17. Shrem, N.S.; Wood, L.; Hamilton, R.J.; Kuhathaas, K.; Czaykowski, P.; Roberts, M.; Matthew, A.; Izard, J.P.; Chung, P.; Nappi, L.; et al. Testicular Cancer Survivorship: Long-Term Toxicity and Management. *Can. Urol. Assoc. J.* **2022**, *16*, 257–272. [CrossRef] [PubMed]
18. Haugnes, H.S.; Bosl, G.J.; Boer, H.; Gietema, J.A.; Brydyø, M.; Oldenburg, J.; Dahl, A.A.; Bremnes, R.M.; Fosså, S.D. Long-Term and Late Effects of Germ Cell Testicular Cancer Treatment and Implications for Follow-Up. *J. Clin. Oncol.* **2012**, *30*, 3752–3763. [CrossRef] [PubMed]
19. Xu, P.; Wang, J.; Abudurexiti, M.; Jin, S.; Wu, J.; Shen, Y.; Ye, D. Prognosis of Patients With Testicular Carcinoma Is Dependent on Metastatic Site. *Front. Oncol.* **2020**, *9*, 1495. [CrossRef] [PubMed]
20. Derouen, M.C.; Mujahid, M.; Srinivas, S.; Keegan, T.H.M. Disparities in Adolescent and Young Adult Survival After Testicular Cancer Vary by Histologic Subtype: A Population-Based Study in California 1988–2010. *J. Adolesc. Young Adult Oncol.* **2016**, *5*, 31–40. [CrossRef] [PubMed]
21. Ding, L.; Wang, K.; Zhang, C.; Zhang, Y.; Wang, K.; Li, W.; Wang, J. A Machine Learning Algorithm for Predicting the Risk of Developing to M1b Stage of Patients With Germ Cell Testicular Cancer. *Front. Public Health* **2022**, *10*, 916513. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.