https://doi.org/10.31925/farmacia.2026.4.19 **ORIGINAL ARTICLE**

LYMPHOVASCULAR INVASION AS A CRITERION FOR SELECTING ADJUVANT CHEMOTHERAPY *VERSUS* SURVEILLANCE IN TESTICULAR SEMINOMA

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Abstract

Testicular seminoma generally has an excellent prognosis, but relapse may occur, highlighting the need for reliable risk stratification factors to guide the choice between adjuvant carboplatin and active surveillance after orchiectomy. This retrospective single-center study evaluated the prognostic role of lymphovascular invasion (LVI) in 60 patients with testicular seminoma treated at the Oncology Institute "Prof. Dr. Ion Chiricuță" in Cluj-Napoca between 2016 and 2021. LVI was defined by lymphatic and/or vascular invasion on histopathology, and associations with stage, progression-free survival (PFS), and overall survival (OS) were assessed. Median age was 37 years; 36 patients had stage I disease, 14 stage II, and 10 stage III. LVI was present in 37 patients and was significantly associated with advanced stage at diagnosis (Fisher's exact test, p = 0.0066; OR = 5.43, 95% CI: 1.42–26.27). However, LVI was not significantly associated with PFS in stage I disease. The estimated 5-year PFS was 88.2% in LVI-positive patients and 89.5% in LVI-negative patients. Similar findings were observed in the overall cohort, with estimated 5-year PFS of 81.1% *versus* 91.3%, respectively. OS differed significantly by stage, with worse survival in stage III disease. Among stage I patients, recurrence occurred in 20.0% of those under surveillance and 9.5% of those receiving adjuvant carboplatin, without a statistically significant difference. These findings suggest that LVI may reflect higher disease burden at diagnosis, but its independent prognostic value in seminoma remains uncertain, and it does not currently justify LVI-based selection for adjuvant carboplatin, given the drug's potential for acute and long-term toxicity.

Rezumat

Seminomul testicular are, în general, un prognostic excelent, însă recidiva poate surveni, ceea ce subliniază necesitatea unor factori fiabili de stratificare a riscului, care să orienteze alegerea între carboplatin adjuvant și supravegherea activă după orhiectomie. Acest studiu retrospectiv unicentric a evaluat rolul prognostic al invaziei limfovasculare (LVI) la 60 de pacienți cu seminom testicular, tratați la Institutul Oncologic „Prof. Dr. Ion Chiricuță" din Cluj-Napoca, între 2016 și 2021. LVI a fost definită prin invazie limfatică și/sau vasculară la examenul histopatologic, fiind analizate asocierile cu stadiul, supraviețuirea fără progresie (PFS) și supraviețuirea globală (OS). Vârsta mediană a fost de 37 de ani; 36 de pacienți au avut boală în stadiul I, 14 în stadiul II și 10 în stadiul III. LVI a fost prezentă la 37 de pacienți și s-a asociat semnificativ cu stadiul avansat la diagnostic (testul exact Fisher, p = 0,0066; OR = 5,43, IC 95%: 1,42–26,27). Cu toate acestea, LVI nu s-a asociat semnificativ cu PFS la pacienții cu boală în stadiul I. Rata estimată a PFS la 5 ani a fost de 88,2% la pacienții cu LVI pozitivă și de 89,5% la cei cu LVI negativă. Rezultate similare au fost observate și în întreaga cohortă, în care ratele estimate ale PFS la 5 ani au fost de 81,1% și, respectiv, 91,3%. Supraviețuirea globală a fost influențată semnificativ de stadiu, fiind mai redusă în stadiul III. Dintre pacienții în stadiul I, recidiva a survenit la 20,0% dintre cei aflați sub supraveghere activă și la 9,5% dintre cei care au primit carboplatin adjuvant, fără o diferență semnificativă statistic. Rezultatele sugerează că LVI poate reflecta o extensie mai mare a bolii la diagnostic, însă valoarea sa prognostică independentă în seminom rămâne incertă și nu justifică, în prezent, selecția pentru carboplatin adjuvant pe baza statusului LVI, având în vedere potențialul de toxicitate acută și pe termen lung al acestui medicament.

Keywords: testicular cancer, germ cell tumors, seminomatous tumors

Introduction

Testicular cancer accounts for only 1–2% of all male malignancies. Still, it remains the most common cancer diagnosed in adolescent and young adult men, particularly between the ages of 15 and 35 years, with an increasing rate in recent decades (1-3). The vast majority of these tumors are testicular germ cell tumors, which are further classified by cellular origin into seminomatous and non-seminomatous subtypes, including embryonal carcinoma, teratoma,

yolk sac tumor, and choriocarcinoma, as well as rarer stromal tumors such as Leydig and Sertoli cell tumors (4). Although seminomatous and non-seminomatous tumors occur at relatively similar rates, seminomatous tumors are reported slightly more frequently in most published series (5-7).

Seminoma is associated with an excellent prognosis, with survival rates approaching 99% in early-stage disease; however, survival may decrease to approximately 70% in patients with advanced stages (8). Moreover, in clinical stage I disease, relapse rates under surveillance are reported to range from approximately 15% to 30%, depending on the presence of associated risk factors. This risk profile has guided post-orchiectomy management strategies, including active surveillance and, in selected patients, adjuvant carboplatin (9). Taken together, these considerations emphasize the need for accurate clinical and pathological risk stratification to balance relapse prevention with the potential adverse effects of chemotherapy.

Established clinicopathological risk factors, including tumor size > 4 cm and rete testis invasion, have shown inconsistent predictive value in patients with stage I testicular seminoma. Although adjuvant carboplatin may be administered either universally or selectively in the presence of these factors, its prognostic value remains controversial, as prospective validation studies are lacking. While larger tumor size has more consistently been associated with an increased risk of relapse, evidence supporting rete testis invasion as an independent predictor has remained inconclusive across multiple studies (10-12).

Lymphovascular invasion (LVI) is an established adverse prognostic marker in non-seminomatous germ cell tumors (13); however, its role in prognostic stratification for seminoma remains supported by limited evidence. Emerging data from recent studies suggest that LVI may contribute to relapse-risk stratification in clinical stage I seminoma and may be associated with an increased risk of recurrence (14). These findings raise the possibility that additional pathological risk stratification models incorporating LVI may emerge in the future to individualize treatment and surveillance strategies better. Furthermore, limited retrospective evidence suggests that vascular invasion may also be associated with a higher clinical stage at diagnosis in seminoma (15). However, its prognostic role in stage II–III seminoma remains insufficiently defined and is not currently incorporated into standard risk stratification models.

Identifying reliable prognostic markers in seminoma is clinically relevant, especially in stage I patients, where the balance between overtreatment and relapse prevention remains challenging. Active surveillance avoids unnecessary treatment-related toxicity in many patients, but requires accurate identification of those at increased risk of recurrence. Conversely, adjuvant treatment may reduce relapse risk but exposes patients to potential acute and long-term adverse effects. Beyond stage I disease, assessing the relationship between LVI and higher stage at diagnosis may also provide insight into patterns of disease spread and help clarify whether LVI reflects a more aggressive biological phenotype in seminoma.

This study aimed to evaluate the prognostic impact of LVI in patients with testicular seminoma. We assessed progression-free survival (PFS) according to LVI status in patients with stage I disease and in the overall cohort. Secondary analyses included overall survival (OS) according to LVI status, the association between LVI and disease stage at diagnosis, OS according to stage group, and PFS among stage I patients managed with surveillance *versus* carboplatin.

Materials and Methods

Study design and patient selection

This was a retrospective, single-center cohort study including patients diagnosed with testicular seminoma at the "Prof. Dr. Ion Chiricuță" Oncology Institute, Cluj-Napoca, Romania, between January 2016 and December 2021. The study period was selected to ensure standardized data availability and sufficient follow-up time for outcome assessment. Clinical and pathological data were collected from institutional medical records.

Patients were eligible for inclusion if they had a confirmed diagnosis of testicular seminoma and available baseline clinicopathological data, including date of diagnosis, disease stage, LVI status, treatment strategy, recurrence status, and survival information. Patients with non-seminomatous germ cell tumors or missing essential data required for survival analysis were excluded.

A total of 60 patients met the eligibility criteria and were included in the final analysis.

Data collection

Clinical and pathological data were retrospectively collected from institutional medical records and pathology reports. Extracted variables included age at diagnosis, date of diagnosis, tumor laterality, TNM classification, serum tumor marker category, disease stage, LVI status, treatment strategy, recurrence or progression status, date of recurrence or progression, vital status, and date of death, when applicable.

Tumors were staged according to the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) TNM classification, 8th edition (2017), including the serum tumor marker (S) category. LVI was defined by the pathology report and was considered positive if lymphatic or vascular invasion, or both, were documented.

Treatment strategy was categorized as active surveillance/follow-up, carboplatin-based adjuvant

chemotherapy, or bleomycin, etoposide, and cisplatin (BEP)-based chemotherapy. For patients with stage I disease, treatment was additionally analyzed as surveillance *versus* carboplatin, when applicable. Dates of recurrence and progression were extracted from institutional medical records. Follow-up assessments were performed according to institutional practice and the treating physician's discretion. Generally, they included clinical evaluation, serum tumor marker assessment (AFP, β-hCG, and LDH), and imaging studies, primarily thoraco-abdomino-pelvic computed tomography (CT). In selected cases with elevated tumor markers and no evidence of disease on CT imaging, positron emission tomography/computed tomography (PET/CT) was performed at the treating physician's discretion. Because of the study's retrospective design, surveillance schedules were not fully standardized and could not be uniformly reconstructed from the medical records. Vital status and date of death, when applicable, were verified using municipal civil registry records. Patients without recurrence, progression, or death were censored at their last documented follow-up. The final follow-up update was performed on April 15, 2026.

Study endpoints

The primary endpoint was PFS, defined as the time from diagnosis to the first documented recurrence, disease progression, or death from any cause, whichever occurred first. Recurrence or progression was primarily determined based on radiologic evidence of new or progressive disease documented in the medical records, including findings on CT or PET/CT when performed. Histopathological confirmation was considered when available. Patients without recurrence, progression, or death were censored at their last documented follow-up. When a patient experienced more than one component event, only the first event was used in the PFS analysis.

The primary analysis evaluated the association between LVI status and PFS in the overall cohort and in the subgroup of patients with stage I disease. Secondary endpoints and analyses included OS, defined as the time from diagnosis to death from any cause or last documented follow-up, the association between LVI status and OS, the association between LVI status and disease stage at diagnosis, OS according to disease stage, and PFS among patients with stage I disease managed with surveillance *versus* carboplatin.

Statistical analysis

Descriptive statistics were used to summarize baseline clinical and pathological characteristics. Continuous variables were reported as median (range), while categorical variables were reported as frequencies and percentages. Associations between categorical variables, including LVI status and disease stage at diagnosis, were assessed using Fisher's exact test. Odds ratios were estimated by conditional maximum likelihood, with exact conditional 95% confidence intervals.

PFS and OS were estimated using the Kaplan-Meier method, and differences between survival curves were assessed using the log-rank test. Five-year PFS and OS rates were estimated from Kaplan-Meier survival curves. PFS was compared by LVI status in the overall cohort and separately among patients with stage I disease. OS was evaluated according to LVI status and disease stage.

Cox proportional hazards regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) for the association between LVI status and PFS. Additional Cox analyses were performed for PFS according to treatment strategy among patients with stage I disease. When Cox regression estimates were unstable due to the absence of events in one comparison group, the results were interpreted using Kaplan-Meier curves and the log-rank test. A two-sided p-value < 0.05 was considered statistically significant. All statistical analyses were performed using R software version 4.5.3 (R Foundation for Statistical Computing, Vienna, Austria). Survival analyses were conducted using the survival and survminer packages.

Results and Discussion

Patient characteristics

A total of 60 patients diagnosed with testicular seminoma were included in the analysis. The annual distribution of diagnosed cases is shown in Figure 1, with a mean of 10 patients diagnosed *per* year during the study period. The median age at diagnosis was 37 years, with a range of 18 to 57 years. Tumor localization was right-sided in 33 patients (55.0%) and left-sided in 26 (43.3%), with laterality not recorded in 1 patient (1.7%).

The distribution of clinical stage is presented in Table I. Most patients were diagnosed with stage I disease (n = 36, 60.0%), followed by stage II (n = 14, 23.3%) and stage III disease (n = 10, 16.7%). According to the serum tumor marker category of the TNM classification, 36 patients (60.0%) were classified as S0, 13 (21.7%) as S1, 7 (11.7%) as S2, 3 (5.0%) as S3, and 1 patient (1.7%) as Sx, as shown in Table II.

Table III summarizes LVI status in the overall cohort and in the stage I subgroup. In the overall cohort, LVI was present in 37 of 60 patients (61.7%). Among patients with stage I disease, LVI was present in 17 of 36 patients (47.2%).

Treatment and therapeutic approach

Treatment strategies in the overall cohort and in the stage I subgroup are summarized in Table IV. In the overall cohort, 23 patients (38.3%) received carboplatin-based chemotherapy, 19 patients (31.7%)

received BEP-based chemotherapy, and 18 patients (30.0%) were managed with follow-up/surveillance. Among patients with stage I disease, 21 patients (58.3%) received carboplatin, and 15 patients (41.7%) were managed with follow-up/surveillance. Radiotherapy to the retroperitoneal lymph nodes was administered to 1 patient (1.7%), and surgical resection of retroperitoneal residual disease/lymph nodes was recorded in 3 patients (5.0%).

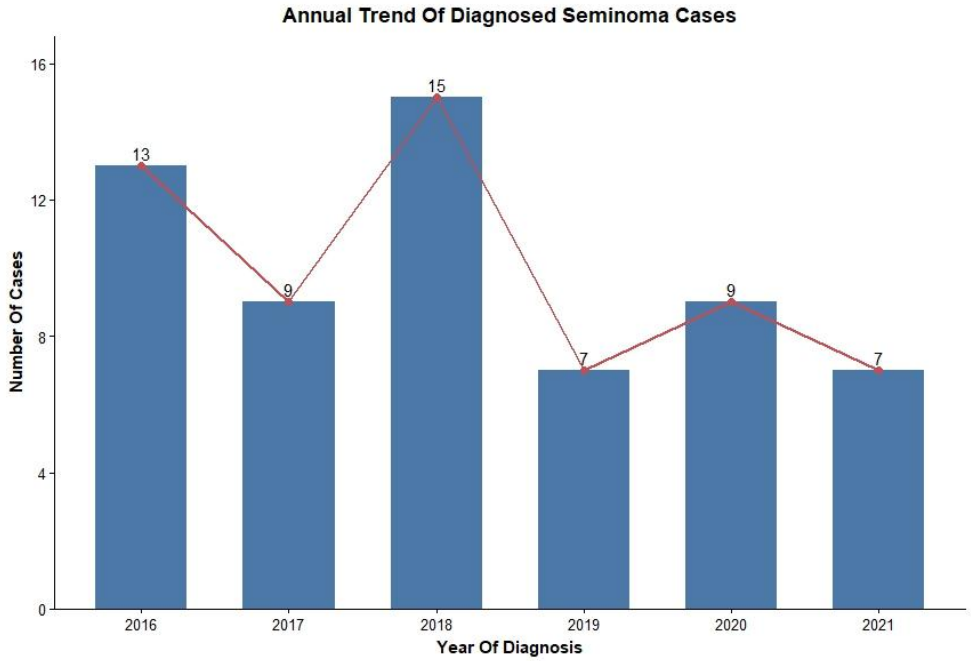

Figure 1.
Annual number of newly diagnosed seminoma cases

Table I
Distribution of Clinical Stage at Diagnosis

Clinical stage	Number of patients (n)	n (%)
Stage I	**36**	**60.0%**
IA	15	25.0%
IB	15	25.0%
IS	5	8.3%
I not specified	1	1.7%
Stage II	**14**	**23.3%**
IIA	6	10.0%
IIB	6	10.0%
IIC	2	3.3%
Stage III	**10**	**16.7%**
IIIA	1	1.7%
IIIB	6	10.0%
IIIC	3	5.0%
Total	**60**	**100.0%**

Table II
Distribution of serum tumor marker levels (S–stage)

S -Serum markers	Number of patients (n)	n (%)
S0	36	60.0%
S1	13	21.7%
S2	7	11.7%
S3	3	5.0%
Sx	1	1.7%

Table III

LVI Status in the Overall Cohort and Stage I Subgroup

LVI status	All stages, n (%)	Stage I, n (%)
Positive	37 (61.7%)	17 (47.2%)
Negative	23 (38.3%)	19 (52.8%)

LVI-lymphovascular invasion; LVI was considered positive when lymphatic invasion (L1), vascular invasion (V1), or both were reported, and negative when neither L1 nor V1 was documented.

Table IV

Treatment Strategy in the Overall Cohort and Stage I Subgroup

Treatment strategy	Overall cohort, n (%)	Stage I subgroup, n (%)
Follow-up/surveillance	18 (30.0%)	15 (41.7%)
Carboplatin	23 (38.3%)	21 (58.3%)
BEP-based chemotherapy	19 (31.7%)	0 (0.0%)
Total	**60 (100.0%)**	**36 (100.0%)**

Association between LVI and Disease Stage

Stage II–III disease was observed in 20 of 37 patients with LVI-positive tumors (54.1%), compared with 4 of 23 patients with LVI-negative tumors (17.4%). LVI positivity was significantly associated with higher odds of stage II–III disease (Fisher's exact test, p = 0.0066; conditional maximum-likelihood OR = 5.43, exact 95% CI: 1.42–26.27).

Survival outcomes

Recurrence and mortality events are summarized in Table V. Overall, recurrence was documented in 7 patients (11.7%), while 6 patients (10.0%) died during follow-up. Among patients with stage I disease, 5 recurrences (13.9%) and 1 death (2.8%) were recorded. Mortality was highest among patients with stage III disease, with 4 deaths among 10 patients (40.0%). According to LVI status, recurrence occurred in 4 LVI-positive patients (10.8%) and 3 LVI-negative patients (13.0%), whereas all deaths occurred in the LVI-positive group (6/37, 16.2%). In the stage I subgroup, recurrence was documented in 3 of 15 patients managed with follow-up/surveillance (20.0%) and in 2 of 21 patients treated with carboplatin (9.5%).

Table V

Recurrence and mortality according to stage, LVI Status, and Stage I treatment

Subgroup	N	Recurrences, n (%)	Deaths, n (%)
All patients	60	7 (11.7%)	6 (10.0%)
Stage I	36	5 (13.9%)	1 (2.8%)
Stage II	14	1 (7.1%)	1 (7.1%)
Stage III	10	1 (10.0%)	4 (40.0%)
LVI positive	37	4 (10.8%)	6 (16.2%)
LVI negative	23	3 (13.0%)	0 (0.0%)
Stage I - Follow-up/surveillance	15	3 (20.0%)	0 (0.0%)
Stage I - Carboplatin	21	2 (9.5%)	1 (4.8%)

Note: Recurrence and death categories are not mutually exclusive; patients who experienced recurrence and subsequently died may be included in both categories.

Survival analyses were performed to assess the prognostic impact of LVI on PFS. In the stage I subgroup, the Kaplan-Meier curves for LVI-positive and LVI-negative patients were largely overlapping, indicating similar PFS between the two groups (Figure 2). The estimated 5-year PFS was 88.2% (95% CI: 74.2-100.0%) in LVI-positive patients and 89.5% (95% CI: 76.7-100.0%) in LVI-negative patients, with no statistically significant difference by log-rank testing (p = 0.872).

In the overall cohort, the Kaplan-Meier curves showed some separation, with numerically lower PFS in the LVI-positive group (Figure 3). The estimated 5-year PFS was 81.1% (95% CI: 69.4-94.7%) in LVI-positive patients and 91.3% (95% CI: 80.5-100.0%) in LVI-negative patients; however, this difference was not statistically significant by the log-rank test (p = 0.356).

Cox regression analysis confirmed the absence of a significant association between LVI status and PFS in both analyses, as shown in Table VI. In the stage I subgroup, LVI status was not significantly associated with PFS (HR = 0.87, 95% CI: 0.17-4.48; p = 0.872). Similarly, in the overall cohort, LVI positivity was not significantly associated with PFS (HR = 1.84, 95% CI: 0.49-6.83; p = 0.364).

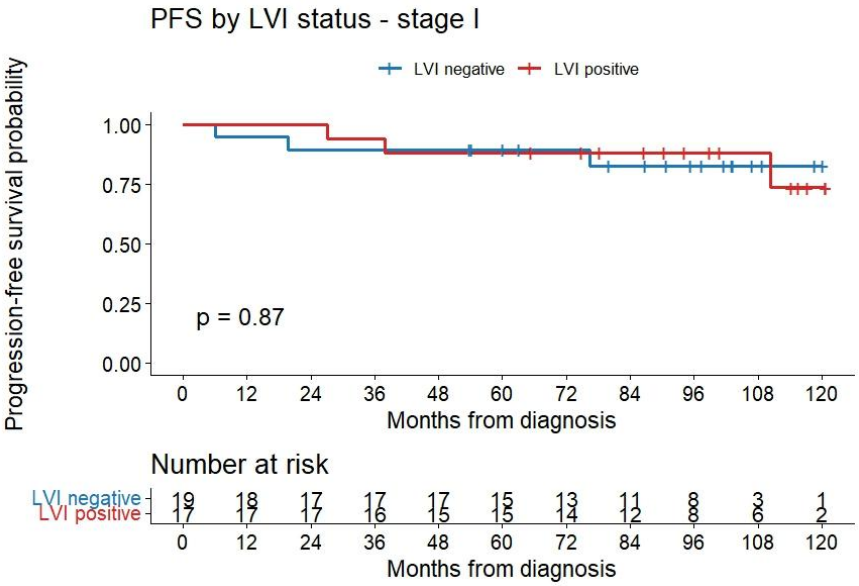

Figure 2.
PFS by LVI Status in Stage I disease

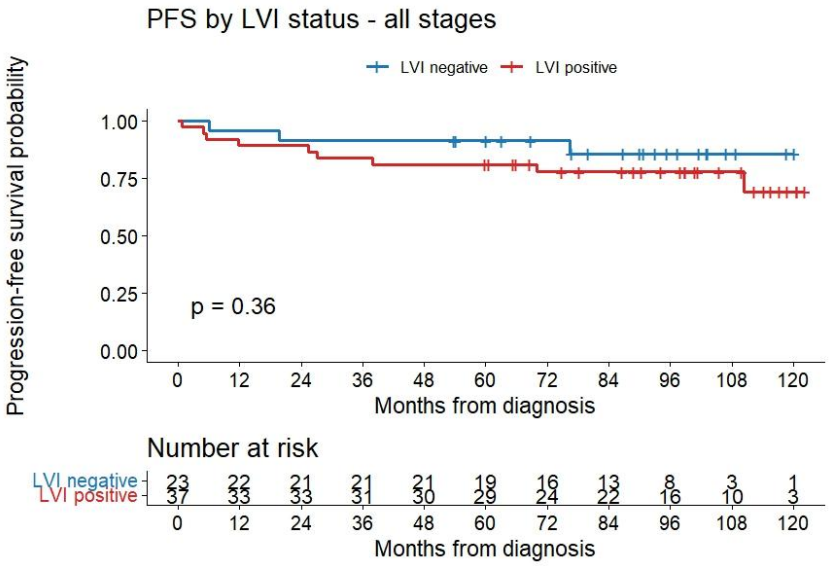

Figure 3.
PFS by LVI Status in the overall cohort

Table VI
Association between LVI Status and PFS

Cohort	LVI status	N	PFS events	5-year PFS (95% CI)	HR	95% CI	Cox p-value	Log-rank p-value
Stage I disease	**LVI negative**	**19**	**3**	**89.5% (76.7-100.0)**	**Reference**	**-**	**-**	**0.872**
Stage I disease	**LVI positive**	**17**	**3**	**88.2% (74.2-100.0)**	**0.87**	**0.17-4.48**	**0.872**	**0.872**
Overall cohort	**LVI negative**	**23**	**3**	**91.3% (80.5-100.0)**	**Reference**	**-**	**-**	**0.356**
Overall cohort	**LVI positive**	**37**	**9**	**81.1% (69.4-94.7)**	**1.84**	**0.49-6.83**	**0.364**	**0.356**

Note: PFS events represent unique patients with at least one component event; only the first event was counted in the time-to-event analysis.

OS for the entire cohort is shown in Figure 4. During follow-up, 6 deaths were recorded among the 60 patients included in the analysis. The 5-year OS rate was 93.3% (95% CI: 87.2-99.9%).

OS was further evaluated according to LVI status (Figure 5). All deaths occurred in the LVI-positive group, with 6 deaths among 37 patients (16.2%), whereas no deaths were observed among LVI-negative patients. The difference between the Kaplan–Meier curves was not statistically significant (log-rank p = 0.065). Given the small number of deaths and the absence of events in the LVI-negative group, Cox regression was not performed because hazard-ratio estimation would have been unstable.

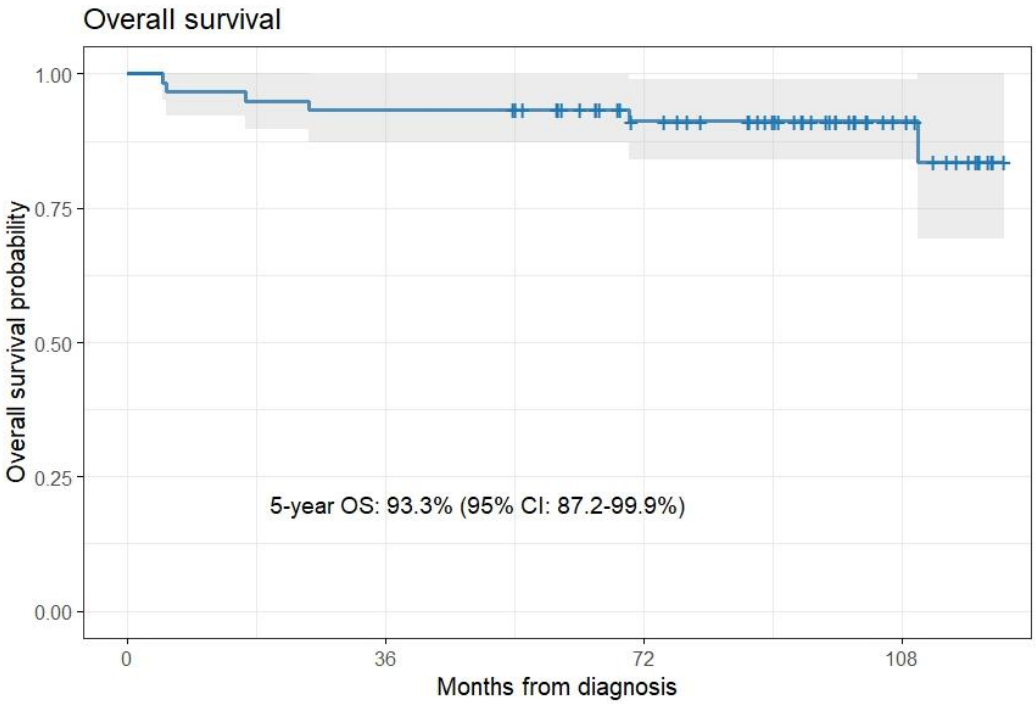

Figure 4.
OS in the entire cohort

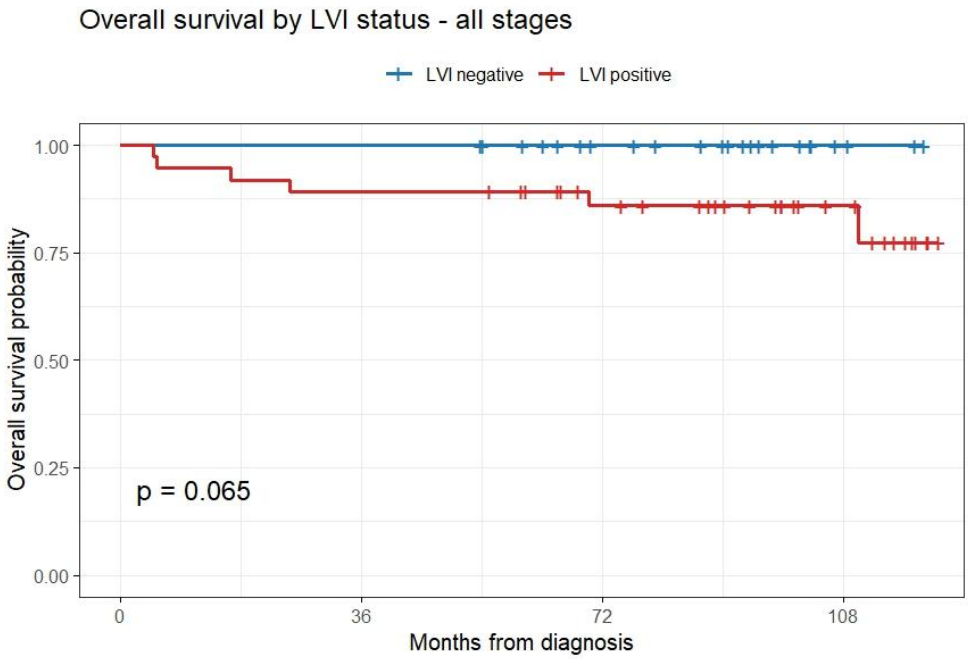

Figure 5.
OS by LVI in the entire cohort

Kaplan-Meier analysis showed a significant difference in OS according to stage group (log-rank p = 0.0006) (Figure 6). The estimated 5-year OS was 100.0% for patients with stage I and stage II disease, compared with 60.0% (95% CI: 36.2-99.5%) for patients with stage III disease (Table VII).

Table VII

Five-Year OS According to Stage Group

Stage group	N	5-year OS (95% CI)
Stage I	**36**	**100.0% (100.0-100.0)**
Stage II	**14**	**100.0% (100.0-100.0)**
Stage III	**10**	**60.0% (36.2-99.5)**

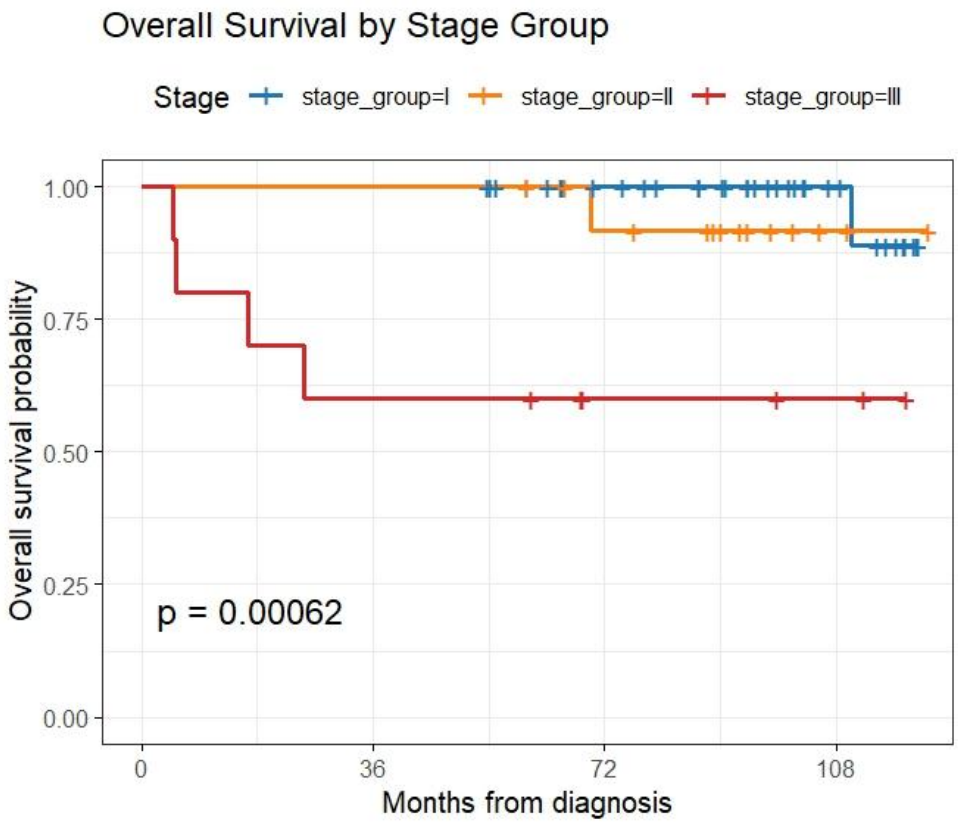

Figure 6.
OS by stage group

Among patients with stage I disease, PFS was compared between those managed with follow-up/surveillance and those treated with carboplatin (Figure 7). The estimated 5-year PFS was 86.7% (95% CI: 71.1-100.0%) in the follow-up/surveillance group and 90.5% (95% CI: 78.8-100.0%) in the carboplatin group. The Kaplan-Meier curves showed numerically better PFS in the carboplatin group; however, the difference was not statistically significant by the log-rank test (p = 0.432). Cox regression analysis showed that carboplatin was associated with a numerically lower risk of PFS events compared with follow-up/surveillance (HR = 0.52, 95% CI: 0.10-2.72), but this association was not statistically significant (p = 0.439) (Table VIII).

Table VIII

PFS by Treatment Strategy in Stage I Disease

Treatment strategy	N	PFS events	5-year PFS (95% CI)	HR	95% CI	Cox p-value	Log-rank p-value
Follow-up/ surveillance	15	3	86.7% (71.1-100.0)	Reference	-	-	0.432
Carboplatin	21	3	90.5% (78.8-100.0)	0.52	0.10-2.72	0.439	0.432

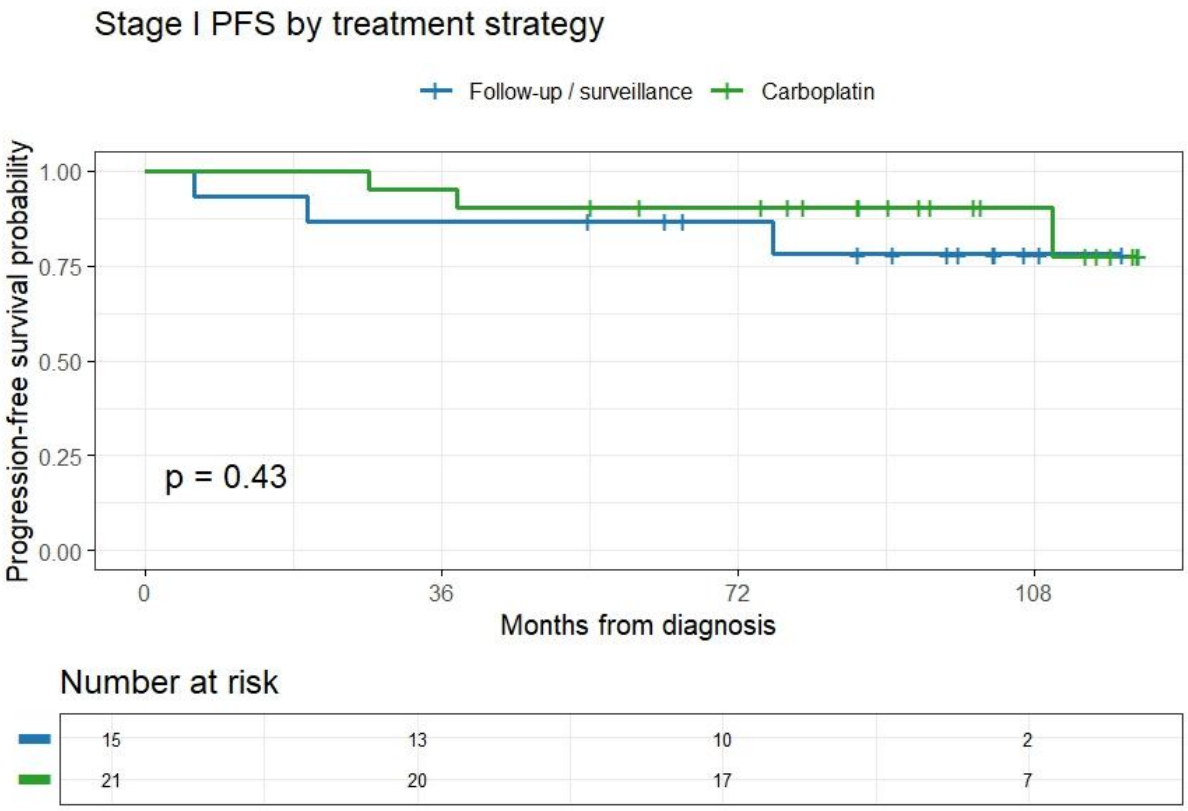

Figure 7.
PFS by treatment strategy in Stage I disease

In this retrospective cohort of 60 patients with testicular seminoma, the mean annual number of diagnosed cases was 10. This reflects institutional case volume rather than population-based incidence. The median age at diagnosis was 37 years, which is consistent with the typical age distribution reported for seminoma (16, 17). Seminomas are most often diagnosed in men aged 25-45 years, and epidemiological data indicate a peak age of occurrence around 35-39 years (18).

In our cohort, stage I disease was the most frequent presentation, accounting for 60.0% of cases, although this proportion was lower than the approximately 80% reported in previous studies of seminoma (19, 20). This difference may be partly related to our institution's tertiary referral pattern, as we may receive a higher proportion of patients with more advanced disease. Additionally, factors such as limited health education and potential delays within the healthcare system may contribute to late presentation and diagnosis at advanced stages in Romania.

The proportion of LVI-positive tumors in our cohort was relatively high, with LVI identified in 61.7% of all patients and in 47.2% of patients with stage I disease. This rate exceeds those reported in previous clinical stage I seminoma cohorts, in which LVI positivity ranged from approximately 10% to 22% (14, 21, 22). Importantly, LVI assessment in seminoma can be challenging and subject to pre-analytical and interpretative variability. A pathology-focused study reported LVI in 20% of seminoma cases, but rates varied markedly according to grossing practice, reaching 46% in specimens grossed by residents *versus* 15% in those grossed by pathology assistants, partly due to tumor displacement artifact that mimics true vascular invasion (23). Therefore, the high LVI rate observed in our cohort may partly reflect a lower proportion of early-stage disease, as well as differences in LVI definitions and variability in pathological reporting.

Despite the high frequency of LVI, LVI status did not significantly influence PFS in either the stage I subgroup or the overall population. Five-year PFS was very similar between LVI-positive and LVI-negative patients with stage I disease. Although PFS was numerically lower among LVI-positive patients in the overall cohort, the difference was not statistically significant. Previous studies have also reported inconsistent results regarding LVI as a relapse-risk factor. Earlier surveillance cohorts suggested that small vessel invasion might be associated with relapse in stage I seminoma. In contrast, the pooled analysis by Warde *et al*. identified tumor size and rete testis invasion, rather than LVI, as the main prognostic factors for relapse (24). In a single-institution Japanese cohort, Kakimoto *et al*. reported that neither vascular invasion nor lymphatic invasion predicted relapse in patients with stage I seminoma

managed with surveillance (25). More recently, Chung *et al*. did not find small vessel invasion to be significantly associated with relapse in a large validation cohort of stage I seminoma patients managed with surveillance (21). Taken together, these findings suggest that LVI alone may not be sufficient to reliably identify patients at higher risk of recurrence or progression in seminoma. This interpretation is supported by emerging risk-adapted approaches that incorporate LVI alongside other clinicopathological features, reflecting ongoing efforts to improve relapse-risk stratification in stage I seminoma (14, 22).

An important finding of our study was the significant association between LVI positivity and a more advanced disease stage at diagnosis. LVI-positive tumors were more frequently observed in patients with stage II-III disease than in those with stage I disease, suggesting that LVI may reflect a more extensive disease presentation at diagnosis. This finding is consistent with previous pathological data, which reported that vascular invasion, together with tumor size, was independently associated with a higher clinical stage in testicular seminoma (15). Although LVI was associated with disease extent at presentation, it did not significantly predict subsequent PFS in our cohort. This apparent discrepancy highlights the need to interpret LVI within the broader clinical and pathological context.

The OS analysis provided additional context. OS in the cohort was favorable, with an estimated 5-year OS of 93.3%, consistent with the generally good prognosis of seminoma (26, 27). The analysis of OS by LVI status should be interpreted with caution. Although all deaths occurred among LVI-positive patients and none were observed in the LVI-negative group, this difference did not reach statistical significance. Moreover, advanced-stage disease was more frequent in the LVI-positive group, and deaths were concentrated among patients with stage III disease. The observed difference in OS may therefore be explained, at least in part, by differences in disease stage rather than by an independent effect of LVI. An adjusted analysis was not considered reliable because of the small number of deaths and the absence of deaths in the LVI-negative group. In contrast, OS differed significantly according to disease stage, with markedly poorer 5-year OS among patients with stage III disease compared with those with stage I or II disease. This finding reinforces the central prognostic role of stage in seminoma and suggests that LVI should be interpreted in relation to disease extent rather than as an isolated prognostic marker.

Management of stage I seminoma has shifted toward risk-adapted strategies, with active surveillance preferred for most patients, adjuvant carboplatin considered in selected cases, and radiotherapy used less often because of long-term toxicity concerns. In this context, tumor size and rete testis invasion have commonly been used to guide risk stratification. However, their prognostic value remains debated, prompting recent efforts to refine or replace these criteria with alternative prognostic models (14, 22). In our cohort, among patients with stage I disease, 15 patients (41.7%) were managed with follow-up/surveillance, whereas 21 patients (58.3%) received carboplatin. The relatively high proportion of stage I patients receiving carboplatin may reflect institutional treatment preferences and perceived relapse risk, particularly given the absence of a universally accepted risk stratification system and the ongoing efforts to refine prognostic models in stage I seminoma. Within this treatment framework, carboplatin-treated patients showed numerically more favorable PFS compared with those managed with surveillance, with estimated 5-year PFS rates of 90.5% and 86.7%, respectively. This result is consistent with previous studies reporting lower relapse rates with adjuvant carboplatin compared with surveillance. In a multicenter study, 5-year disease-free survival was 96.6% in patients receiving carboplatin compared with 83.5% in those managed with surveillance (28). Similarly, the SWENOTECA study reported lower relapse rates with adjuvant carboplatin compared with surveillance in both low-risk and higher-risk patients (29). However, as in previous literature, improved relapse control does not necessarily translate into an OS advantage, and treatment comparisons in retrospective cohorts should be interpreted with caution (27, 30).

Limitations

This study has several limitations. First, it was retrospective and single-center in design, with a relatively small sample size. Second, the number of PFS and OS events was limited, reducing statistical power and resulting in wide confidence intervals. Third, data on established pathological risk factors, including rete testis invasion and tumor size, were not available and therefore could not be incorporated into the analysis. This limited our ability to compare LVI with established risk features in stage I seminoma and may have affected the interpretation of the high LVI rate observed in our cohort. Finally, treatment decisions were not randomized, so comparisons between surveillance and carboplatin in stage I disease may be affected by selection bias.

Strengths

Despite these limitations, the study provides real-world data on the prognostic role of LVI in testicular seminoma. It includes both survival-based analyses and a clinicopathological assessment of the association between LVI and disease stage at diagnosis. In addition, the study contributes data from an Eastern European cohort, a population that remains underrepresented in the seminoma literature.

Conclusions

In testicular seminoma, LVI may offer insight into the extent of disease at diagnosis. Still, in this cohort, it did not reliably distinguish patients at higher risk of recurrence or progression, either overall or among patients with stage I disease. Its prognostic value appears to depend on the broader clinical context and should be considered alongside disease stage, treatment approach, and other pathological factors. Larger studies are needed to determine whether LVI should be included in risk-adapted management strategies for seminoma.

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Availability of data and materials

The datasets analyzed during the current study are not publicly available due to institutional and patient confidentiality restrictions but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Oncology Institute "Prof. Dr. Ion Chiricută" Cluj-Napoca. (approval no. 379/15.04.2026).

AI use disclosure

AI-assisted tools were used solely for language refinement. The authors take full responsibility for the final content of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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