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Survival from Diagnosis Early Mortality and Recorded Systemic Therapy Lines in a Turkish Small Cell Lung Cancer Analytic Cohort

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Abstract

Background/Objectives: We described survival from diagnosis, early mortality, and recorded systemic therapy lines and explored the association between baseline brain metastases and mortality in a Turkish small cell lung cancer (SCLC) cohort. **Methods:** This retrospective single-center study included 131 eligible adults. Observed diagnoses ranged from 12 August 2009 to 23 May 2023. All included patients had died by follow-up ascertainment. Additional brain-metastasis analyses and calendar-period comparisons were exploratory and post hoc. Treatment calendar details, immunotherapy exposure, and cranial radiotherapy details were unavailable. **Results:** Median overall survival (OS) was 10.41 months (95% confidence interval [CI], 8.74–13.04); 30- and 90-day mortality were 5.3% and 12.2%. First-line platinum–etoposide was recorded in 99 patients (75.6%). Of 22 limited-stage patients, 21 received concurrent thoracic chemoradiotherapy with curative intent; one patient could not start anticancer therapy after pneumonia and rapid clinical deterioration. Within extensive-stage disease, the unadjusted brain-metastasis hazard ratio (HR) was 1.67 (95% CI, 0.98–2.86; $p = 0.061$), the log-rank p value was 0.059, and the adjusted HR was 1.98 (95% CI, 1.07–3.66; $p = 0.029$). A 5000-replicate bootstrap gave a percentile 95% CI of 1.10–4.87 and a bias-corrected and accelerated (BCa) 95% CI of 0.84–3.79. The original full-cohort brain-metastasis p value was 0.033 and became 0.099 after Bonferroni or Holm adjustment across three baseline findings. **Conclusions:** The analyses suggested a possible association between baseline brain metastases and higher mortality, but the original full-cohort association did not meet the significance threshold after Holm correction. Sparse exposure and unmeasured confounding make this finding hypothesis-generating. Clinic-based referral selection may limit generalizability.

Keywords: small cell lung cancer; survival from diagnosis; early mortality; brain metastases; recorded systemic therapy lines; retrospective analytic cohort

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1. Introduction

Small cell lung cancer (SCLC) combines rapid progression with early dissemination and frequent relapse. Its clinical course remains heterogeneous despite the apparently uniform diagnostic label. Disease extent and fitness for treatment influence both management and prognosis, while routine hospital populations include patients who would not enter therapeutic trials [1–3].

Treatment has changed substantially during the period surrounding this cohort. Adding atezolizumab or durvalumab to platinum–etoposide improved survival in extensive-stage SCLC, and consolidation durvalumab improved outcomes in selected patients with limited-stage disease after concurrent chemoradiotherapy [4–6]. The American Society of Clinical Oncology (ASCO) rapid recommendation update incorporated important changes in limited-stage and relapsed disease [7]. More recent randomized evidence from DeLLphi-304 and IMforte further expanded the therapeutic context in relapsed and maintenance settings [8,9]. These advances make the timing and composition of historical cohorts essential to their interpretation.

Routine-care studies complement trials by describing who reaches treatment and how patients fare outside narrowly specified eligibility criteria. In the prospective German Tumour Registry Lung Cancer (TLK) cohort, only half of patients with extensive-stage disease received second-line treatment, illustrating attrition that cannot be captured by studying later-line participants alone [10]. Diagnosis-based cohorts can additionally capture deaths before or shortly after initial treatment decisions. Reporting early mortality alongside median survival therefore describes a clinically relevant part of the disease course, although its causes cannot be inferred from vital status alone.

We aimed to describe survival from diagnosis, 30- and 90-day mortality. We also explored the association between baseline brain metastases and mortality.

2. Materials and Methods

2.1. Setting and Participants

This retrospective single-center cohort was assembled at the Medical Oncology Clinic of Recep Tayyip Erdogan University Faculty of Medicine Training and Research Hospital, Rize, Türkiye. Eligibility required age 18 years or older, histologically or cytologically confirmed SCLC diagnosed between 1 January 2008 and 31 December 2024, and sufficient records to establish the diagnosis date and survival status. All consecutive patients meeting these criteria were included, and inclusion was independent of whether a patient had died. Of the 139 records screened, four duplicate records and four records with uncertain pathological diagnosis and/or insufficient essential clinical information were excluded, leaving 131 eligible patients for analysis. Observed diagnoses ranged from 12 August 2009 to 23 May 2023 (Supplementary Table S1).

Source materials were electronic and paper clinical records, pathology and imaging reports, and treatment records. Deaths were primarily documented in hospital records. A small minority lacking a death date in those records were verified through the Turkish Death Notification System (Ölüm Bildirim Sistemi, ÖBS). Vital status was last verified and the analytic records were locked in September 2026, reported at month precision. The data lock was the final ÖBS verification, not the latest death date. Death was not an eligibility requirement. All 131 included patients had a recorded death date; the latest was 17 April 2026, and no included patient was alive, lost to follow-up, or censored at ascertainment. Reporting was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and applicable Reporting of Studies Conducted Using Observational Routinely Collected Health Data (RECORD) items [11,12].

2.2. Variables and Outcomes

The primary outcome was overall survival (OS) from the recorded date of SCLC diagnosis to death from any cause. Early mortality was death within 30 or 90 days, inclusive, from the same origin. All included patients had a death event, and none was censored in the main analysis. Calendar-based potential follow-up opportunity was defined as the interval from diagnosis to administrative data lock, with years calculated as days/(30.44 × 12); it

is not observed survival. Because ascertainment was reported at month precision, potential follow-up was reported approximately to one decimal place in years, to September 2026. Reverse Kaplan–Meier median follow-up was not estimable: reversing the status of 131 deaths yielded no events. Cause-specific mortality and progression-free survival were not evaluated.

Baseline variables were age at diagnosis, sex, limited- or extensive-stage classification, brain metastases, liver metastases, and pleural effusion at diagnosis. Baseline stage was determined using diagnosis-time clinical notes and computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) reports; the later metastatic progression did not change the baseline stage. General metastasis fields that could include findings developing during follow-up were not used as baseline exposures. Brain and liver metastases and pleural effusion were assessed during pretreatment staging in all 131 patients. CT/PET reports were reviewed for liver metastases and pleural effusion. All 131 patients underwent pretreatment brain MRI. A uniform tumor-node-metastasis (TNM) staging edition was unavailable, and cytological confirmation was not available for all effusions. Prophylactic cranial irradiation (PCI) and therapeutic brain-radiotherapy details remained unavailable.

2.3. Statistical Analysis

The study size was the available final analytic cohort; no retrospective power calculation was used. Continuous variables were summarized by median and interquartile range (IQR) and categorical variables by counts and percentages. Kaplan–Meier estimates used log–log 95% confidence intervals (CIs) based on Greenwood variance. Because the retained cohort had no censoring, fixed-time Kaplan–Meier estimates equal the empirical survival proportions; exact binomial intervals are also reported in the Supplementary Materials. Stage and extensive-stage brain-metastasis curves were compared with two-sided log-rank tests. Early-mortality proportions used exact binomial 95% CIs.

Cox regression used Efron handling of ties. The basic model included age per 10 years, sex, and stage. Brain metastases, liver metastases, and pleural effusion were added separately; the three site-specific models were treated as one exploratory family for Bonferroni and Holm multiplicity adjustments. Covariates were not selected through univariable screening or stepwise procedures. Hazard ratios (HRs) describe conditional associations, not treatment effects or validated predictions. All tests were two-sided; raw and multiplicity-adjusted p values are distinguished.

Scaled Schoenfeld residuals and associated tests assessed proportional hazards [13]. Nonproportionality for age prompted an interaction between age per decade and log time relative to 12 months. Thus $HR_{age}(t) = exp\{\beta_{age} + \beta_{interaction} \times log[t/(12 \times 30.44)]\}$, where t is risk-set time in days, and the age main-effect HR refers to 12 months. A three-degree-of-freedom natural spline did not improve the fit over linear age ($p = 0.599$).

Post hoc analyses added the linear diagnosis year to the time-varying-age brain model, restricted this model to extensive-stage disease, and applied administrative censoring at $36 \times 30.44 = 1095.84$ days. Deaths at or before the boundary were events; later observations were censored. The 36-month analysis retained all patients and assessed the long tail, which overlaps the earlier diagnosis years. Leave-one-out diagnostics did not define exclusions. Additional analyses compared three calendar periods, calculated extensive-stage unadjusted and adjusted brain-metastasis HRs and a log-rank test, used 5000 patient-level bootstrap replicates to calculate percentile and bias-corrected and accelerated (BCa) 95% CIs for the adjusted extensive-stage model [14], and clarified treatment and early-mortality denominators. Firth-penalized Cox regression was added as a complementary sensitivity

analysis for the adjusted extensive-stage model, retaining the covariates and time-varying age effect and using Breslow ties with profile penalized-likelihood confidence intervals [15].

2.4. Ethics

The study was approved by the Recep Tayyip Erdogan University Health Sciences Ethics Committee on 1 September 2026 (decision number 2026/174). Research-specific record review, extraction, curation, and vital-status verification were undertaken in September 2026 after approval. No research-specific patient contact or additional procedures occurred. Individual informed consent was not obtained, being specified as such in the ethics-approved retrospective study protocol.

2.5. Use of Artificial-Intelligence-Assisted Tools

During manuscript preparation, OpenAI Codex (GPT-6.0 Astra model; OpenAI) was used to assist with the development and checking of R analysis code, and ChatGPT was used for language editing and secondary consistency checks across tables and manuscript text. The authors retain full responsibility for the analyses, interpretation, and the manuscript itself.

3. Results

3.1. Cohort Characteristics

The cohort included 131 patients. Median age was 63 years (IQR, 58–69; range, 39–88), and 123 patients (93.9%) were male. Extensive-stage disease was recorded in 109 patients (83.2%) and limited-stage disease in 22 (16.8%). All eight women were in the extensive-stage group. Baseline brain metastases were present in 16 patients (12.2%), liver metastases in 12 (9.2%), and pleural effusion in eight (6.1%); all positive baseline findings occurred in extensive-stage disease (Table 1). Later metastatic findings were kept separate from the verified baseline stage and baseline metastatic status.

Table 1. Baseline characteristics.

Characteristic	Overall $n = 131$	Limited Stage $n = 22$	Extensive Stage $n = 109$
Age, years, median (IQR)	63 (58–69)	62 (60–67.25)	63 (57–70)
Male sex, *n* (%)	123 (93.9)	22 (100)	101 (92.7)
Female sex, *n* (%)	8 (6.1)	0	8 (7.3)
Brain metastases at diagnosis, *n* (%)	16 (12.2)	0	16 (14.7)
Liver metastases at diagnosis, *n* (%)	12 (9.2)	0	12 (11.0)
Pleural effusion at diagnosis, *n* (%)	8 (6.1)	0	8 (7.3)

IQR, interquartile range. Limited and extensive stage accounted for 16.8% and 83.2% of the full cohort. Pleural effusion was not assumed to be cytologically malignant for all patients.

3.2. Description by Diagnosis Period

Patients were grouped into 2009–2013 ($n = 19$), 2014–2018 ($n = 75$), and 2019–2023 ($n = 37$). Recorded stage distribution and baseline brain-metastasis prevalence were similar across periods, whereas first-line platinum–etoposide entries increased from 57.9% to 89.2%. Median OS was 27.53, 11.43, and 7.88 months, respectively (log-rank $p < 0.001$). This descriptive temporal pattern is not interpreted as a treatment-era effect because detailed referral patterns, imaging practice by period, performance status, and actual treatment exposure were unavailable (Supplementary Table S2).

3.3. Recorded Systemic Therapy Lines

A first-line platinum–etoposide regimen was recorded in 99 patients (75.6% of the cohort; 81.1% of 122 patients with a recorded first-line regimen). Other platinum doublets were recorded in 16 patients: platinum–paclitaxel ($n = 9$), platinum–docetaxel ($n = 3$), platinum–gemcitabine ($n = 3$), and platinum–vinorelbine ($n = 1$). Five patients had a non-platinum single agent and two had platinum monotherapy. Nine patients did not receive first-line systemic therapy because of poor performance status. Among patients with and without a recorded first-line regimen, 90-day mortality was 12/122 (9.8%) and 4/9 (44.4%), respectively (Fisher $p = 0.013$). This descriptive contrast is confounded by fitness, treatment selection, and early death. In the limited-stage group, 21/22 patients (95.5%) received concurrent thoracic chemoradiotherapy with curative intent. One patient could not start systemic therapy or radiotherapy (RT) after pneumonia followed by rapid clinical deterioration and died within 90 days of diagnosis. PCI status was not systematically available.

A second-line regimen was documented in 60/131 patients (45.8%), 56/122 patients with a recorded first-line treatment (45.9%), 47/109 extensive-stage patients (43.1%), and 43/101 extensive-stage patients with a recorded first-line treatment (42.6%). Among the 16 patients with baseline brain metastases, 13 had recorded platinum–etoposide, one another platinum doublet, and two no recorded first-line treatment; 30- and 90-day deaths numbered 3 and 4, respectively (Table 2; Supplementary Table S3).

Table 2. Recorded systemic therapy lines by disease stage.

Characteristic	Overall $n = 131$	Limited Stage $n = 22$	Extensive Stage $n = 109$
First-line platinum–etoposide	99 (75.6; 81.1)	9 (40.9; 42.9)	90 (82.6; 89.1)
First-line other platinum doublets	16 (12.2; 13.1)	10 (45.5; 47.6)	6 (5.5; 5.9)
First-line non-platinum single agents	5 (3.8; 4.1)	1 (4.5; 4.8)	4 (3.7; 4.0)
First-line platinum monotherapy	2 (1.5; 1.6)	1 (4.5; 4.8)	1 (0.9; 1.0)
No recorded first-line treatment	9 (6.9)	1 (4.5)	8 (7.3)
Documented second-line regimen	60 (45.8)	13 (59.1)	47 (43.1)
Documented third-line regimen	19 (14.5)	6 (27.3)	13 (11.9)
Documented fourth-line regimen	11 (8.4)	3 (13.6)	8 (7.3)
Documented fifth-line regimen	1 (0.8)	0 (0.0)	1 (0.9)
Documented sixth-line regimen	1 (0.8)	0 (0.0)	1 (0.9)
Recorded first-line treatment	122 (93.1)	21 (95.5)	101 (92.7)
Second-line regimen among first-line treated	56/122 (45.9)	13/21 (61.9)	43/101 (42.6)

For the first four first-line regimen rows, values are *n* (% of full column; % among patients with a recorded first-line regimen), using recorded-first-line denominators of 122 overall, 21 limited stage, and 101 extensive stage. Other rows use the full column unless a denominator is shown. 'No recorded first-line treatment' denotes that first-line systemic therapy was not administered.

3.4. Survival and Early Mortality

Median OS was 10.41 months (95% CI, 8.74–13.04). Survival at 6, 12, and 24 months was 70.2%, 43.5%, and 19.8%, respectively. Seven patients died within 30 days (5.3%; 95% CI, 2.2–10.7) and 16 within 90 days (12.2%; 7.1–19.1) (Table 3). With no censoring, the fixed-time Kaplan–Meier estimates equaled the empirical proportions; log–log Greenwood and exact-binomial intervals were nearly identical (Supplementary Table S4). Calendar-based median potential follow-up opportunity to September 2026 was approximately 9.7 years, reported at the precision supported by the ascertainment month; this is not an observed survival or reverse Kaplan–Meier estimate (Supplementary Table S1). Figure 1 displays 36 months, while the estimates use complete observed follow-up.

Table 3. Overall survival and early mortality.

Outcome	Overall	Limited Stage	Extensive Stage
Patients/deaths	131/131	22/22	109/109
Median OS, months (95% CI)	10.41 (8.74–13.04)	8.16 (3.71–18.36)	11.30 (8.94–13.53)
6-month OS, % (95% CI)	70.2 (61.6–77.3)	54.5 (32.1–72.4)	73.4 (64.0–80.7)
12-month OS, % (95% CI)	43.5 (34.9–51.8)	36.4 (17.4–55.7)	45.0 (35.5–54.0)
24-month OS, % (95% CI)	19.8 (13.5–27.1)	22.7 (8.3–41.4)	19.3 (12.5–27.1)
30-day mortality, *n*/*N*; % (95% CI)	7/131; 5.3 (2.2–10.7)	0/22; 0.0 (0.0–15.4)	7/109; 6.4 (2.6–12.8)
90-day mortality, *n*/*N*; % (95% CI)	16/131; 12.2 (7.1–19.1)	5/22; 22.7 (7.8–45.4)	11/109; 10.1 (5.1–17.3)

OS, overall survival; CI, confidence interval. OS uses Kaplan–Meier estimation with log–log 95% CIs; early mortality uses exact binomial 95% CIs and inclusive day thresholds. The stage log-rank test uses complete follow-up: $\chi^2 = 0.562$, 1 degree of freedom, $p = 0.453$.

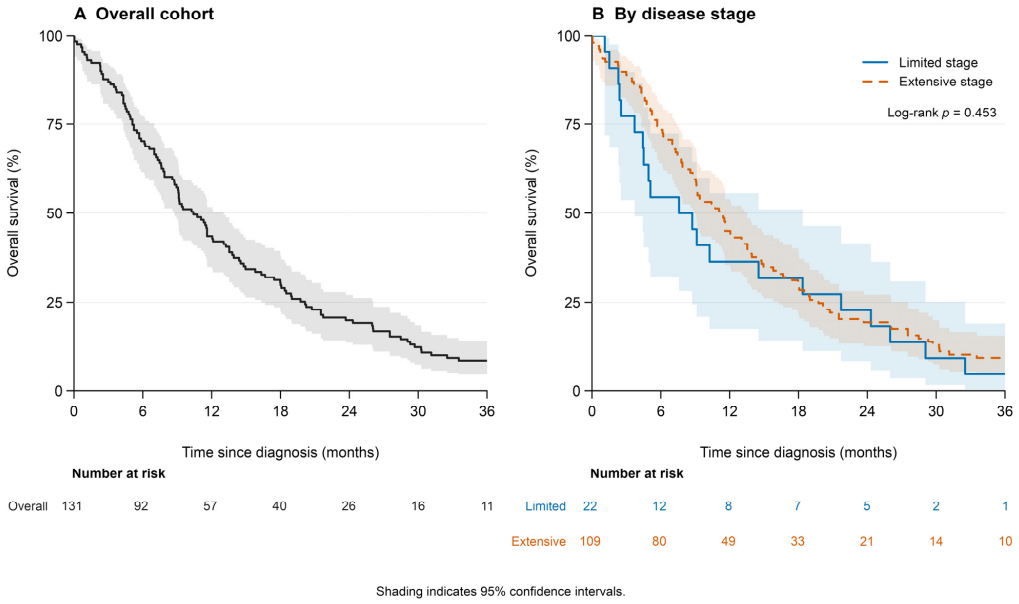


Figure 1. Overall survival in the retained analytic cohort and according to recorded disease stage. Kaplan–Meier estimates are shown for (**A**) all 131 records and (**B**) limited-stage ($n = 22$) and extensive-stage ($n = 109$) records. Shading indicates log–log 95% CIs. The display is limited to 36 months; the log-rank test uses complete observed follow-up. All retained records carried a death event. Late estimates, especially for limited-stage disease (12, 8, and 7 patients at risk at 6, 12, and 18 months), are imprecise and should be interpreted cautiously.

Median survival was 8.16 months (95% CI, 3.71–18.36) for limited-stage disease and 11.30 months (8.94–13.53) for extensive-stage disease. The log-rank test yielded $p = 0.453$.

3.5. Baseline Associations and Model Diagnostics

In the basic Cox model, HRs were 0.91 per 10-year age increase (95% CI, 0.75–1.11), 0.49 for female versus male sex (0.23–1.04), and 0.92 for extensive versus limited stage (0.57–1.46). In separate models, baseline brain metastases had HR 1.91 (1.05–3.47; raw $p = 0.033$), liver metastases HR 1.46 (0.80–2.69), and pleural effusion HR 0.59 (0.26–1.35). Across this three-comparison family, the brain-metastasis p value was 0.099 after either Bonferroni or Holm adjustment and did not meet a family-wise 0.05 threshold (Table 4; Supplementary Table S5).

The proportional-hazards test indicated time-varying age effects in the basic and brain models and a time-varying pleural-effusion effect. In the brain model, age HRs per decade at 1, 3, 6, 12, and 24 months were 1.54, 1.22, 1.06, 0.91, and 0.79, respectively; the

12-month value is the model's age main effect. These risk-set-specific estimates do not imply a protective causal effect of older age. The spline comparison ($p = 0.599$) gave no evidence that a nonlinear age function improved the fit. The brain term showed no detected proportional-hazards departure ($p = 0.609$), while the pleural-effusion term did ($p = 0.013$), limiting the interpretation of a single pleural HR.

Table 4. Adjusted associations with overall survival.

Variable	Model	HR (95% CI)	*p* Value
Age per 10 years	Basic	0.91 (0.75–1.11)	0.365
Female versus male	Basic	0.49 (0.23–1.04)	0.063
Extensive versus limited stage	Basic	0.92 (0.57–1.46)	0.713
Baseline brain metastases	Basic + indicated finding	1.91 (1.05–3.47)	0.033
Baseline liver metastases	Basic + indicated finding	1.46 (0.80–2.69)	0.219
Baseline pleural effusion	Basic + indicated finding	0.59 (0.26–1.35)	0.213

HR, hazard ratio; CI, confidence interval. $N = 131$ and deaths =131 in each model. The basic model includes age/10, sex, and stage. Brain, liver, and pleural findings are added in three separate models; their reference is absence. Models do not jointly adjust for all three findings. These are conventional constant-coefficient estimates. Age and pleural-effusion terms showed nonproportionality; time-varying-age analyses and full diagnostics are in the Supplementary Materials. *p* values are unadjusted for multiple comparisons.

In the 109 extensive-stage records, brain metastases were present in 16 and absent in 93; all records carried an event. The unadjusted HR was 1.67 (95% CI, 0.98–2.86; $p = 0.061$), and the log-rank test yielded chi-square = 3.569 ($p = 0.059$). Adjustment for age, sex, diagnosis year, and time-varying age gave HR 1.98 (1.07–3.66; $p = 0.029$). In a 5000-replicate patient-level bootstrap, 4997 models were estimable and the percentile 95% CI was 1.10–4.87; the BCa 95% CI was 0.84–3.79. The complementary Firth model yielded HR 2.01 (profile penalized-likelihood 95% CI, 1.07–3.61; $p = 0.032$). The BCa interval included unity, indicating sensitivity to the interval method. These findings remain exploratory given sparse exposure and unmeasured confounding (Figure 2; Supplementary Tables S5 and S6).

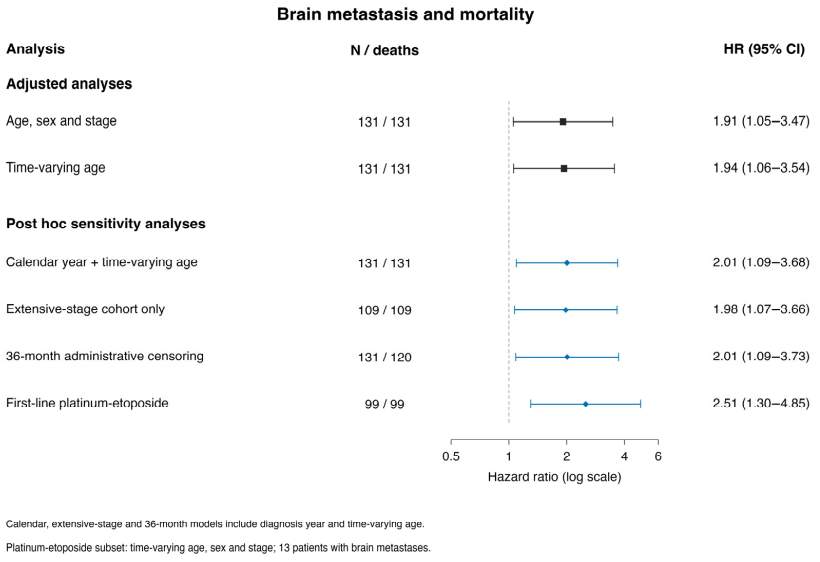


Figure 2. Adjusted associations between baseline brain metastases and OS. The age-sex-stage model was the original adjusted model. All other displayed models were post hoc sensitivity analyses in overlapping populations. The recorded platinum–etoposide subset is treatment-restricted and subject to selection after the diagnosis-based time origin. Raw *p* values are reported in Supplementary

Table S6; no displayed interval is multiplicity-adjusted. Across the original brain, liver, and pleural family, the brain-metastasis p value was 0.099 after Bonferroni or Holm adjustment.

The treatment-restricted analysis included 99 records with first-line platinum–etoposide, including 13 with brain metastases. Its adjusted HR was 2.51 (95% CI, 1.30–4.85; $p = 0.006$). Because treatment began after the survival time origin and precise start dates were unavailable, this post hoc subset analysis conditions on survival and clinical selection before treatment. It is neither an independent replication of the full-cohort result nor an estimate of platinum–etoposide effectiveness.

3.6. Absolute Survival by Brain-Metastasis Status Within Extensive-Stage Disease

Within the 109 extensive-stage records, median OS was 7.10 months (95% CI, 2.30–10.41) with brain metastases and 11.60 months (9.17–14.39) without. Twelve-month survival was 18.8% and 49.5%, respectively. The unadjusted HR was 1.67, and the two-sided log-rank p value was 0.059. Only three brain-positive patients remained at risk at 12 months, so late estimates are imprecise (Figure 3; Supplementary Table S7).

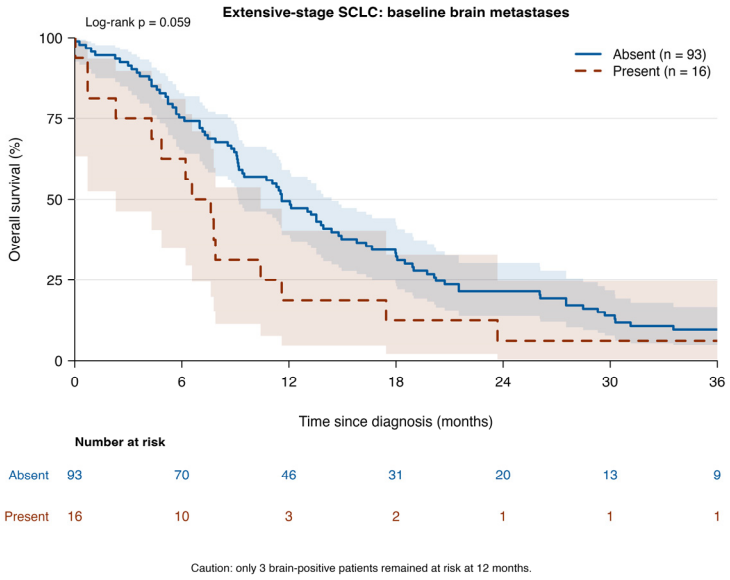


Figure 3. Overall survival by baseline brain-metastasis status within extensive-stage disease. Curves include 93 records without and 16 with baseline brain metastases; all carried a recorded death. The two-sided log-rank test yielded chi-square = 3.569 and $p = 0.059$. Numbers at risk are shown immediately before each time point. The display is limited to 36 months; analyses use complete observed follow-up. Only three brain-positive patients remained at risk at 12 months, and late estimates should be interpreted cautiously.

4. Discussion

This study describes diagnosis-based survival, early mortality, and recorded systemic therapy in a consecutive, eligible single-center SCLC cohort. All 131 patients had died at ascertainment. Median OS was 10.41 months, and 90-day mortality was 12.2%. The brain-metastasis analyses were exploratory.

Turkish real-world studies provide context for these outcomes. A Turkish Oncology Group cohort of 213 patients receiving first-line atezolizumab plus chemotherapy reported a median OS of 11.9 months and identified performance status and metastatic burden as important prognostic factors [16]. A limited-stage series from northeastern Türkiye, treated predominantly with curative intent, reported a median OS of 13.9 months and emphasized concurrent chemoradiotherapy and radiation dose [17]. Our cohort encompasses an earlier

and broader clinical period, with survival measured from diagnosis. Differences in patient selection, treatment setting, and survival time origin therefore limit direct comparison with these studies and contemporary randomized cohorts [4–6,10,16,17].

The analyses suggested a possible association between baseline brain metastases and higher mortality. However, the original full-cohort association did not meet the significance threshold after Holm correction. The BCa interval for the adjusted extensive-stage model also included unity. Given the small subgroup and potential residual confounding, this finding remains hypothesis-generating and requires confirmation.

The platinum–etoposide subgroup yielded an exploratory HR of 2.51. However, patients had to survive from diagnosis to treatment and be selected for therapy to enter this subgroup. The estimate consequently reflects a selected population within the same cohort and cannot independently confirm the association or establish a treatment effect. Treatment timing was unavailable, precluding landmark or time-dependent analyses.

Median OS was numerically shorter in limited-stage than in extensive-stage disease, although the difference was not statistically significant. Of the 22 limited-stage patients, 21 received concurrent thoracic chemoradiotherapy with curative intent. Systemic treatment included other platinum doublets in 10 patients and platinum–etoposide in nine. Despite the predominantly curative treatment intent, the available clinical characteristics do not adequately explain the observed stage ordering. Small numbers, differences in patient fitness, regimen selection, and treatment delivery limit interpretation. A population-based Manitoba study also associated pretreatment performance status with survival among chemotherapy-treated limited-stage patients [18].

Anatomical extent nevertheless remains prognostically relevant: Vlăsceanu et al. reported progressively poorer survival with increasing pathological T category in a surgically selected non-small-cell lung cancer (NSCLC) cohort [19]. This comparison does not establish a biological explanation for our stage ordering. Rare, prolonged survival is also documented in SCLC, including 5- to 18-year survivors in a 1714-patient series [20]. Our small long-term risk sets therefore require caution and do not demonstrate a reversal of the usual stage–prognosis relationship.

Ninety-day mortality was higher among patients who did not receive first-line systemic therapy than among those who did: 4/9 versus 12/122. This difference does not establish a treatment benefit, as clinical fitness and acute illness may influence both treatment eligibility and early mortality. Patients must also survive long enough to initiate therapy. The limited-stage patient who remained untreated developed pneumonia and rapid clinical deterioration, precluding anticancer treatment. This case illustrates how acute illness may contribute to both treatment non-initiation and early death.

Median OS declined across the 2009–2013, 2014–2018, and 2019–2023 periods despite broadly similar distributions of stage and baseline brain metastases. Differences in referral patterns, patient fitness, imaging practices, and treatment timing could not be evaluated, preventing attribution of this pattern to changes in quality of care. The 36-month sensitivity analysis did not resolve these uncertainties because the calendar period overlapped with the long survival tail. Recorded platinum–etoposide documentation increased over the same periods in which survival declined. The available age and stage summaries do not establish the proposed case-mix explanation.

These historical findings provide a diagnosis-based reference for early mortality and attrition across recorded systemic therapy lines, not an estimate of contemporary immunotherapy outcomes. Randomized evidence established survival gains with immunotherapy-based approaches [4–6], but differences in eligibility, treatment exposure, and survival time origin preclude direct efficacy comparisons. Future institutional evaluations should capture those treatment details explicitly.

The estimates for female sex and pleural effusion were also unstable. Only eight women and eight patients with pleural effusion were included, all with extensive-stage disease. Pleural effusion additionally violated the proportional-hazards assumption (Supplementary Table S8). These findings do not support reliable prognostic inference.

Strengths and Limitations

Strengths include consecutive patient inclusion, a common diagnosis-based survival time origin, and explicit assessment of early mortality. Model diagnostics, time-specific age estimates (Supplementary Table S9), leave-one-out analyses (Supplementary Table S10), bootstrap assessment of uncertainty, and multiplicity adjustment helped characterize the robustness of the survival associations.

The single-center, clinic-based referral setting may limit generalizability to the wider SCLC population, while small subgroups limit precision. Important prognostic factors could not be incorporated into the analyses, including numerical performance-status scores, comorbidities, lactate dehydrogenase (LDH) and other laboratory parameters, weight loss, complete baseline metastatic burden, and smoking history. Poorer performance status and greater comorbidity were associated with lower one-year survival in a national SCLC cohort [21]. Their omission leaves potential for residual confounding despite adjustment for age and other covariates. Residual confounding may affect the brain metastasis, stage, and diagnosis-year coefficients; adjustment for the available covariates cannot recover missing clinical fitness or treatment exposure.

Patient-level imaging dates, a uniform TNM edition, and cytological confirmation of malignant pleural effusion were not systematically available. Differences in assessment over the prolonged study period may therefore have affected baseline classification.

Immunotherapy exposure, systemic treatment dose intensity, PCI, and therapeutic brain radiotherapy could not be evaluated. Causes of death were not adjudicated; pneumonia in the untreated limited-stage patient therefore cannot be regarded as a confirmed cause of death. Multiple post hoc analyses also involved overlapping patients. Together, these limitations preclude causal treatment conclusions and independent prognostic validation.

Future studies should systematically assess baseline prognostic factors, treatment initiation and completion, and radiotherapy exposure to clarify the associations observed here.

5. Conclusions

In this SCLC cohort, early mortality was more frequent among patients who did not receive first-line systemic therapy, and survival varied across calendar periods. The analyses suggested a possible association between baseline brain metastases and higher mortality, but the original full-cohort association did not meet the significance threshold after Holm correction. These findings remain exploratory and require confirmation in larger cohorts with more complete clinical and treatment data.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm15229083/s1, Figure S1: Kaplan–Meier estimates across complete observed follow-up. Table S1: Cohort Screening and Ascertainment Information. Table S2: Description by Diagnosis Period. Table S3: Treatment Context and Early Mortality. Table S4: Fixed Time Survival Estimators. Table S5: Extensive Stage Brain Metastasis and Multiplicity Analyses. Table S6: Brain metastasis association across analyses. Table S7: Survival by baseline brain metastasis status within extensive-stage disease. Table S8: Selected proportional hazards diagnostics. Table S9: Time specific age associations. Table S10: Calendar period and influence diagnostics.

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Data Availability Statement: Aggregate results and the reporting checklist accompany the revision. Individual-level clinical records are not publicly posted because they contain sensitive health information. Additional clinical details not established from the available source review were not imputed.

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Abbreviations

ASCO	American Society of Clinical Oncology
BCa	Bias-corrected and accelerated
CI	Confidence interval
CT	Computed tomography
HR	Hazard ratio
IQR	Interquartile range
LDH	Lactate dehydrogenase
MRI	Magnetic resonance imaging
OS	Overall survival
ÖBS	Ölüm Bildirim Sistemi (Turkish Death Notification System)
PCI	Prophylactic cranial irradiation
PET	Positron emission tomography
RECORD	Reporting of Studies Conducted Using Observational Routinely Collected Health Data
RT	Radiotherapy
SCLC	Small cell lung cancer
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TLK	Tumour Registry Lung Cancer
TNM	Tumor-node-metastasis

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