Clinical outcomes in patients diagnosed with extra-nodal Hodgkin lymphoma: a 20-year retrospective analysis of the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database

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Author contributions
Nnawuba K conceived the research project, collected the data & wrote paper; Trikannad Ashwini Kumar AK; Vellanki S and Nzeako T wrote the paper; Robinson S performed the analysis & wrote the paper; Jensen H contributed to data & wrote the paper.

Competing interests
The authors declare no conflicts of interest.

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Abbreviations
ENHL, extra-nodal Hodgkin lymphoma; SEER, the National Cancer Institute’s Surveillance, Epidemiology, and End Results; AYA, adolescent and young adult; HR, hazard ratio; CI, confidence interval.

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Abstract
Background: Hodgkin lymphoma refers to a malignancy of the lymphatic tissue. Extra-nodal Hodgkin lymphoma (ENHL) is a rare variant consisting of Hodgkin lymphoma occurring outside the lymphatic system. Studies investigating the epidemiology associated with ENHL are rare. Methods: 618 ENHL cases were analyzed using the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database (2000–2020). Demographics including sex, race/ethnicity, rural-urban continuum, age group (categorized as adolescent and young adult (AYA) if between years of 15 and 39, and adult if over the age of 40), and living status (alive/deceased) were examined, with survival status as the main outcome. Results: This study included 335 males (54.2%) and 283 females (45.8%). Of this total, 47.9% were in the AYA group. In terms of ethnicity the distribution was 12.5% non-Hispanic Black, 67.5% non-Hispanic White, 5.2% non-Hispanic Asian/Pacific Islander, and 14.9% Hispanic. Bivariate analyses evidenced significant differences in survival by age group with 91.6% in AYA vs. 72.4% in adults (P < 0.001) alive by the end of the study period. Multivariable analyses identified age as a key predictor of survival, as the AYA patients had a lower odds ratio for death (odds ratio = 0.25, P < 0.001). In addition, survival outcomes were also impacted by race, with non-Hispanic Blacks showing higher survival probabilities. Regarding treatment, 27.0% of patients underwent surgery, with 10.2% receiving post-surgery radiation, reducing odds of mortality (odds ratio = 0.32, P = 0.046).

Conclusion: The background research as such, tends to affirm that these two factors – age and race are quite crucial in the prognosis as well as management of ENHL. Compared to adults, AYA patients had significantly lower odds of death, while non-Hispanic Black individuals exhibited reduced survival probabilities. It should be noted that 27.0% of patients underwent surgery with 10.2% receiving post-operative radiation which led to decrease in mortality rates. Thus, these results reiterate the necessity for tailor-made treatment methods according to demographic characteristics to boost patient outcomes effectively. For better ENHL care, future studies could shed light on these disparities and improve treatment regimens as needed.

Keywords: Hodgkin lymphoma; extra nodal disease; SEER; cancer survival
Background

Hodgkin lymphoma is a clonal B-cell hematologic malignancy that typically affects only lymphoid tissue. Extra-nodal involvement, such as in the bone, lung, or liver, occurs in approximately 15% of cases, which is much less common compared to non-Hodgkin lymphomas. To date, few studies worldwide have explored the epidemiology and clinical characteristics of Hodgkin lymphoma with extra-nodal manifestation [1]. A distinctive characteristic of this lymphoma is the scarcity of neoplastic cells, which comprise only about 1% of the cell population. The vast majority of cells are non-neoplastic, primarily composed of T-lymphocytes [2]. It is characterized by Reed-Sternberg cells within a background of inflammatory cells.

While classically described as a nodal disease, extra-nodal occurs in a subset of patients, posing diagnostic and therapeutic challenges. This study examines the demographic characteristics of patients with extra-nodal Hodgkin lymphoma (ENHL) using data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database, spanning from 2000 to 2020. ENHL is a rare form of Hodgkin lymphoma that primarily affects tissues outside of the lymph nodes, representing less than 1% of all Hodgkin lymphoma cases [3]. Understanding the demographic patterns, therapeutic considerations, and prognostic implications of extra nodal Hodgkin lymphoma is paramount for refining risk stratification, guiding treatment decisions, and improving patient outcomes.

Methods

ENHL is typically diagnosed using a combination of clinical symptoms, histopathological examination, imaging studies, laboratory tests, and molecular/genetic studies. All patients diagnosed with ENHL between the years 2000 to 2020 were retrieved from the SEER national database, which contains comprehensive clinical information at the national level but does not allow for patient identification [4]. The SEER database is an authoritative source for cancer statistics in the United States, as it collects deidentified information for incidence, prevalence and survival. This database is accessible to researchers after approval is obtained from the United States National Cancer Institute. The inclusion criteria and clinical variables extracted for this study were: ENHL (International Classification of Diseases code C81.99, site recode, international classification of diseases for oncology (International Classification of Diseases-0-3)/WHO 2008), and age ≥ 15. The SEER database reports age in 5-year increments, and groups 0–5y, 5–10y, and 10–15y were excluded due to extremely small sample size (< 10 patients). Patients were included started at age category 15–20y to include all adults. The demographic characteristics queried included sex, race & ethnicity, median household income, and the rurality of the patient’s residence. Survival status was considered as the main outcome variable. The patients were categorized as either adult (> 40 years of age) or adolescent and young adult (AYA), if between ages 15 and 39 years.

Descriptive statistics were calculated for both the full and analytic samples. Bivariate associations between living status and each demographic characteristic were explored utilizing chi-square tests. In order to assess the impact of different demographic factors on survival while taking into account other variables, multivariable logistic regression was conducted. All data pre-processing and analyses were performed in R Version 4.3.3 (R Core Team 2024); R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/) with statistical significance defined as P < 0.05

Results

Overall patient characteristics for the full sample are summarized in Table 1. The majority of the sample was male (55%) and predominantly white (68%), with most patients (88%) living in very large metropolitan areas and a considerable percentage living in areas with populations exceeding one million individuals (57%). The majority of this 20-year cohort were aged 40 years or more and 71% were alive at the time of the data query.

Patients classified in race/ethnicity or surgery subgroups that were extremely small e.g., non-Hispanic American Indian/Alaska Native and those patients classified as dead due to causes other than this cancer were removed from the analytic sample for bivariate and multivariable analyses. Sample characteristics for the analytic sample are displayed in Table 2.

Bivariate analyses

All analyses (bivariate and multivariable) were conducted using the analytic sample. Table 3 highlights the differences in living status that exist within this cohort due to demographics. Living status differed significantly based upon age group (P < 0.001) and the surgery/radiation sequence the patient received (P = 0.015). Specifically, the AYA cohort had higher rates of survival at the time of sampling (92%) than those in the adult cohort (72%) and those individuals receiving radiation after surgery had higher rates of survival (94%) than those patients who received no radiation or cancer-directed surgery (80%).

Multivariable analyses

We fitted a multivariable logistic model to predict whether a patient was currently alive using age, sex, race, rurality, surgery status, and surgery/radiation sequence as explanatory variables (Table 4). Within this model, the effects of age (P < 0.001) and the surgery/radiation sequence (P = 0.046) were statistically significant. Standardized parameters were obtained by fitting the model on a standardized version of the dataset. 95% confidence intervals (CIs) and P-values were computed using a Wald z-distribution approximation.

In this model, the odds of an individual being dead are 0.25 that of an adult if you are in the AYA group when all other variables are constant (OR = 0.25, P < 0.001). The odds of an individual being dead are 0.32 that of an individual who did not receive radiation and/or cancer-directed surgery if you did receive radiation after surgery when all other variables are constant (OR = 0.32, P = 0.046).

In Figure 1, a flowchart highlighting the rate of living patients by age group and the surgery/radiation sequence for ENHL begins with patient categorization into age groups: under AYA (15–39) & adults ≥40. Following diagnosis, treatment pathways converge into either surgery first or radiation first. For surgery-first patients, successful surgery leads to radiation, while unsuccessful surgery prompts alternative treatments. Radiation-first patients proceed to surgery if radiation is effective; otherwise, the treatment plan is reassessed.

Discussion

Epidemiological studies have provided valuable insights into the demographic variations in the incidence of ENHL. The analysis of 618 ENHL cases from the SEER database (2000–2020) highlights several important demographic trends and their implications for prognosis and treatment.

The study sample included 335 males (54.2%) and 283 females (45.8%), with nearly half of the patients (47.9%) falling into the AYA age group (15–39 years). This slight male predominance is consistent with previous studies on classic Hodgkin lymphoma and may be influenced by biological and environmental factors that warrant further investigation [1]. Racial and ethnic demographics revealed that the majority of the sample were non-Hispanic Whites (67.5%), followed by non-Hispanic Blacks (12.5%), Hispanics (14.9%), and non-Hispanic Asians or Pacific Islanders (5.2%). These variations reflect broader epidemiological trends in lymphoma incidence, underscoring the importance of considering race and ethnicity in disease management and research.

The bivariate analyses showed differences in living status by age group, with a higher survival rate in the AYA group (91.6%) compared to adults (72.4%) (P < 0.001, 95% CI: [13.0%, 25.3%]). Multivariable analyses further demonstrated lower odds of death (OR = 0.25, P <
Table 1 Sample characteristics for the full sample (N = 733)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>402 (54.8)</td>
</tr>
<tr>
<td>Female</td>
<td>331 (45.2)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Hispanic (all races)</td>
<td>111 (15.1)</td>
</tr>
<tr>
<td>Non-Hispanic American Indian /Alaska Native</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Non-Hispanic Asian or Pacific Islander</td>
<td>33 (4.5)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>90 (12.3)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>497 (67.8)</td>
</tr>
<tr>
<td>Non-Hispanic unknown race</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td><strong>Rural-urban continuum</strong></td>
<td></td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. ≥ 1 million</td>
<td>414 (56.5)</td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. between 250k and 1 million</td>
<td>180 (24.6)</td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. &lt; 250k</td>
<td>53 (7.2)</td>
</tr>
<tr>
<td>Nonmetropolitan areas adjacent to a metropolitan area</td>
<td>62 (8.5)</td>
</tr>
<tr>
<td>Nonmetropolitan areas not adjacent to a metropolitan area</td>
<td>24 (3.3)</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
</tr>
<tr>
<td>AYA i.e., ≤ 39 y.o.</td>
<td>312 (42.6)</td>
</tr>
<tr>
<td>Adult i.e., &gt; 40 y.o.</td>
<td>421 (57.4)</td>
</tr>
<tr>
<td><strong>Surgery status</strong></td>
<td></td>
</tr>
<tr>
<td>Surgery performed</td>
<td>200 (27.3)</td>
</tr>
<tr>
<td>Surgery recommended but not performed for unknown reason</td>
<td>18 (2.5)</td>
</tr>
<tr>
<td>Surgery not recommended</td>
<td>513 (70.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td><strong>Surgery/radiation sequence</strong></td>
<td></td>
</tr>
<tr>
<td>No radiation and/or cancer-directed surgery</td>
<td>664 (90.6)</td>
</tr>
<tr>
<td>Radiation after surgery</td>
<td>67 (9.1)</td>
</tr>
<tr>
<td>Radiation before and after surgery</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Radiation before surgery</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td><strong>Living status</strong></td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>517 (70.5)</td>
</tr>
<tr>
<td>Dead</td>
<td>120 (16.4)</td>
</tr>
<tr>
<td>Dead (due to causes other than this cancer)</td>
<td>96 (13.1)</td>
</tr>
</tbody>
</table>

AYA, adolescent and young adult.

Table 2 Sample characteristics for the analytic sample (N = 618)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>335 (54.2)</td>
</tr>
<tr>
<td>Female</td>
<td>283 (45.8)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Hispanic (all races)</td>
<td>92 (14.9)</td>
</tr>
<tr>
<td>Non-Hispanic Asian or Pacific Islander</td>
<td>32 (5.2)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>77 (12.5)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>417 (67.5)</td>
</tr>
<tr>
<td><strong>Rural-urban continuum</strong></td>
<td></td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. ≥ 1 million</td>
<td>358 (57.9)</td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. between 250k and 1 million</td>
<td>156 (25.2)</td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. &lt; 250k</td>
<td>36 (5.8)</td>
</tr>
<tr>
<td>Nonmetropolitan areas adjacent to a metropolitan area</td>
<td>46 (7.4)</td>
</tr>
<tr>
<td>Nonmetropolitan areas not adjacent to a metropolitan area</td>
<td>22 (3.6)</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
</tr>
<tr>
<td>AYA i.e., ≤ 39 y.o.</td>
<td>296 (47.9)</td>
</tr>
<tr>
<td>Adult i.e., &gt; 40 y.o.</td>
<td>322 (52.1)</td>
</tr>
<tr>
<td><strong>Surgery status</strong></td>
<td></td>
</tr>
<tr>
<td>Surgery performed</td>
<td>167 (27.0)</td>
</tr>
<tr>
<td>Surgery not recommended</td>
<td>451 (73.0)</td>
</tr>
<tr>
<td><strong>Surgery/radiation sequence</strong></td>
<td></td>
</tr>
<tr>
<td>No radiation and/or cancer-directed surgery</td>
<td>555 (89.8)</td>
</tr>
<tr>
<td>Radiation after surgery</td>
<td>63 (10.2)</td>
</tr>
<tr>
<td><strong>Living status</strong></td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>504 (81.6)</td>
</tr>
<tr>
<td>Dead</td>
<td>114 (18.4)</td>
</tr>
</tbody>
</table>

AYA, adolescent and young adult.
Table 3 Bivariate analysis of demographics by living status

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Alive (N = 504)</th>
<th>Dead (N = 114)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.070</td>
</tr>
<tr>
<td>Male (N = 335)</td>
<td>264 (78.8)*</td>
<td>71 (21.2)</td>
<td></td>
</tr>
<tr>
<td>Female (N = 283)</td>
<td>240 (84.8)</td>
<td>43 (15.2)</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td>0.220</td>
</tr>
<tr>
<td>Hispanic (all races) (N = 92)</td>
<td>72 (78.3)</td>
<td>20 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic Asian or Pacific Islander (N = 32)</td>
<td>27 (84.4)</td>
<td>5 (15.6)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic Black (N = 77)</td>
<td>69 (89.6)</td>
<td>8 (10.4)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White (N = 417)</td>
<td>336 (80.6)</td>
<td>81 (19.4)</td>
<td></td>
</tr>
<tr>
<td>Rural-urban continuum</td>
<td></td>
<td></td>
<td>0.764</td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. ≥ 1 million (N = 358)</td>
<td>297 (83.0)</td>
<td>61 (17.0)</td>
<td></td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. between 250k and 1 million (N = 156)</td>
<td>126 (80.8)</td>
<td>30 (19.2)</td>
<td></td>
</tr>
<tr>
<td>Metropolitan areas w/ pop. &lt; 250k (N = 36)</td>
<td>27 (75.0)</td>
<td>9 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Nonmetropolitan areas adjacent to a metropolitan area (N = 46)</td>
<td>36 (78.3)</td>
<td>10 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Nonmetropolitan areas not adjacent to a metropolitan area (N = 22)</td>
<td>18 (81.8)</td>
<td>4 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AYA i.e., ≤ 39 y.o. (N = 296)</td>
<td>271 (91.6)</td>
<td>25 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Adult i.e., &gt; 40 y.o. (N = 322)</td>
<td>233 (72.4)</td>
<td>89 (27.6)</td>
<td></td>
</tr>
<tr>
<td>Surgery status</td>
<td></td>
<td></td>
<td>0.440</td>
</tr>
<tr>
<td>Surgery performed (N = 167)</td>
<td>140 (83.8)</td>
<td>27 (16.2)</td>
<td></td>
</tr>
<tr>
<td>Surgery not recommended (N = 451)</td>
<td>364 (80.7)</td>
<td>87 (19.3)</td>
<td></td>
</tr>
<tr>
<td>Surgery/radiation sequence</td>
<td></td>
<td></td>
<td>0.015</td>
</tr>
<tr>
<td>No radiation and/or cancer-directed surgery (N = 555)</td>
<td>445 (80.2)</td>
<td>110 (19.8)</td>
<td></td>
</tr>
<tr>
<td>Radiation after surgery (N = 63)</td>
<td>59 (93.7)</td>
<td>4 (6.3)</td>
<td></td>
</tr>
</tbody>
</table>

*P-value for demographic survival differences utilizing a χ² test if assumptions are met otherwise the P-value for demographic differences is computed for the χ² test using a Monte Carlo test with 10,000 replicates. *Values throughout reflect N (%) of each row variable that are alive and dead respectively e.g., 264 individuals among the 335 males (78.8%) are alive. AYA, adolescent and young adult.

Table 4 Multivariable logistic regression results

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.68</td>
<td>[0.24, 1.79]</td>
</tr>
<tr>
<td>Age group [AYA]</td>
<td>0.25</td>
<td>[0.15, 0.39]*</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.41</td>
<td>[0.91, 2.19]</td>
</tr>
<tr>
<td>Race/ethnicity [non-Hispanic Asian or Pacific Islander]</td>
<td>0.87</td>
<td>[0.26, 2.58]</td>
</tr>
<tr>
<td>Race/ethnicity [non-Hispanic Black]</td>
<td>0.36</td>
<td>[0.14, 0.87]</td>
</tr>
<tr>
<td>Race/ethnicity [non-Hispanic White]</td>
<td>0.79</td>
<td>[0.45, 1.44]</td>
</tr>
<tr>
<td>Rural-urban continuum [metropolitan w/ pop. ≥ 1 million]</td>
<td>0.57</td>
<td>[0.25, 1.40]</td>
</tr>
<tr>
<td>Rural-urban continuum [metropolitan w/ pop. 250k to 1 million]</td>
<td>0.72</td>
<td>[0.30, 1.86]</td>
</tr>
<tr>
<td>Rural-urban continuum [nonmetropolitan, metropolitan adjacent]</td>
<td>0.84</td>
<td>[0.28, 2.52]</td>
</tr>
<tr>
<td>Rural-urban continuum [nonmetropolitan, not metropolitan adjacent]</td>
<td>0.59</td>
<td>[0.14, 2.27]</td>
</tr>
<tr>
<td>Surgery status [surgery performed]</td>
<td>1.01</td>
<td>[0.58, 1.71]</td>
</tr>
<tr>
<td>Surgery/radiation sequence [radiation after surgery]</td>
<td>0.32</td>
<td>[0.09, 0.89]*</td>
</tr>
</tbody>
</table>

AYA, adolescent and young adult; CI, confidence interval.

Figure 1 Flowchart highlighting rate of living patients by age group and surgery/radiation sequence. AYA, adolescent and young adult.
In our study we did not collect time to event data and this difference needs to be seen in context. This also might align with the findings from Hodgkin lymphoma, which is sometimes mistakenly considered predominantly an adult malignancy. This misconception may stem from its bimodal age distribution, which shows a high incidence in young adults (ages 20–34) and another peak in older adults (over 55). The average age at diagnosis is 39 years, emphasizing age as a vital prognostic indicator [1].

In a previous retrospective analysis, the clinical characteristics of patients with involvement in various extra nodal sites were compared, and the authors discovered that the median age of patients with lung involvement (31 years) was higher than that of patients with involvement in other extra nodal sites [6]. Additionally, patients with bone involvement were predominantly female (P = 0.026), while those with involvement in other sites were predominantly male. Another study of extra nodal involvement in Hodgkin lymphoma patients demonstrated male predominance aligning with the gender distribution typically observed in classic Hodgkin lymphoma cases, suggesting that men are slightly more likely to develop extra-nodal involvement [1]. This trend may point to underlying biological or environmental factors that predispose men to this form of the disease more than women. However, in the latter study, bone was the most frequently compromised extra nodal site, affecting an equal number of men and women (50% of extra-nodal patients) [1].

While men with Hodgkin lymphoma are slightly more likely to develop extra-nodal involvement than women, the overall impact of gender on specific sites of extra nodal involvement and histological subtypes appears minimal. Further studies are needed to explore the reasons behind this gender disparity and to determine if specific treatment strategies should be tailored accordingly. The prognostic implications of extra nodal involvement in Hodgkin lymphoma remain debated. Some studies associate extra nodal disease with poorer outcomes, particularly in advanced-stage Hodgkin lymphoma, while others suggest that extra nodal involvement may not independently predict prognosis but rather reflect disease biology and stage at presentation.

Understanding racial differences in the prevalence and outcomes of ENHL is critical for developing targeted treatment strategies and improving patient outcomes. In our study, race impacted survival, with non-Hispanic Blacks showing a higher survival probability. Previous studies have highlighted several factors contributing to these disparities, including genetic predispositions, socioeconomic status, access to healthcare, and biological variations in various other cancers. Genetic factors may play a significant role in the prevalence and outcomes of ENHL across different racial groups. Epigenetics is often cited as a potential mediator between environmental exposure and health outcomes, yet it is not formally explored in many studies. Epigenetics is frequently mentioned as a possible link between environmental exposure and health outcomes, but it is not often thoroughly examined. For instance, Hu et al. analyzed data from 255,128 female breast cancer cases in the California SEER database and discovered that adults exposed to higher levels of PM10 and PM2.5 experienced significantly shorter survival times compared to those in lower exposure areas [7]. Their research also found that Black individuals had higher PM2.5 exposure levels (> 15.04 g/m³) compared to White individuals (41.9% vs. 33.1%), as well as those living in highly urbanized areas (51.7%) versus less urbanized areas (39.65%). Additionally, Black females had nearly twice the adjusted hazard ratio (HR) for death due to breast cancer compared to White females (HR 1.9, 95% CI 1.8–2.0). Even after adjusting for confounding variables and air pollution exposure, Black women still had higher death rates from breast cancer (adjusted HR 1.6, 95% CI 1.5–1.7). The extent to which air pollution may have contributed to disparities in breast cancer mortality rates was not quantified. The authors also suggested that DNA methylation could play a role, although it was not measured in this study.

These studies highlight the need for further research linking environmental factors, epigenetics, and racial disparities in health. Biological differences among racial groups may also contribute to variations in ENHL prevalence and outcomes, as they’ve been shown to do in other cancers [7, 8]. African American or non-Hispanic Black women in breast cancer, for example, often face barriers such as lack of insurance, lower rates of early diagnosis, and reduced access to advanced treatment options, leading to worse prognoses compared to their White counterparts [9]. Additionally, lifestyle factors such as diet, smoking, and alcohol consumption may vary across racial groups, potentially impacting disease incidence and outcomes [10]. As no prior studies specifically addressing racial differences in the prevalence and outcomes of ENHL were found in the literature review, insights from research on racial differences in other cancers, such as breast cancer, or more general racial/ethnic disparities in health, might need to be considered for now. Future studies should continue to explore these factors to develop more effective interventions and reduce racial disparities in ENHL.

Optimal management of ENHL involves a multidisciplinary approach, including chemotherapy, radiotherapy, and targeted agents such as brentuximab vedotin. Treatment decisions are influenced by disease extent, histological subtype, and patient characteristics. Consolidative radiotherapy may offer survival benefits in localized extra nodal disease, while systemic therapy remains central for disseminated ENHL. In our study 27.0% underwent surgery, while 73.0% did not. Among surgical cases, 10.2% received post-surgery radiation therapy. Patients who received radiation after surgery had lower odds of death (OR = 0.32, P = 0.046).

Emerging treatments show promise, particularly in relapsed or refractory cases. Standard Hodgkin lymphoma treatment protocols, including chemotherapy and primary/adjuvant radiotherapy, remain effective for ENHL. Chemotherapy and primary and/or adjuvant radiotherapy provide excellent local and systemic control for Hodgkin lymphoma. The presence of nodal disease in the neck does not affect outcomes when combined modality therapy is utilized. Despite the unique anatomical location of extra nodal lesions, standard Hodgkin lymphoma treatment protocols remain effective in promoting disease-free survival [11]. Combined modality therapy, such as involved field radiotherapy with ABVD chemotherapy, has demonstrated excellent outcomes, achieved complete remission and prevented disease recurrence [12].

Conclusion
This 20-year retrospective study enriches our understanding of ENHL demographics, emphasizing the significance of age and race in prognostic assessments and treatment strategies. The demographic patterns observed in extra nodal Hodgkin lymphoma reflect a complex interplay of host factors, tumor biology, and environmental influences. Recognizing these variations is crucial for optimizing risk stratification, tailoring treatment algorithms, and advancing our understanding of disease pathogenesis. Future collaborative research efforts are essential to elucidate the intricate nuances of ENHL and foster personalized therapeutic approaches.

References


