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Functional status and therapy for older adults with diffuse large B-cell lymphoma in nursing homes: A population-based study

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Abstract

Objectives: To characterize the prevalence of functional and cognitive impairments, and associations between impairments and treatment among older patients with diffuse large B cell lymphoma (DLBCL) receiving nursing home (NH) care.

Methods: We used the Surveillance, Epidemiology, and End Results-Medicare database to identify beneficiaries diagnosed with DLBCL 2011–2015 who received care in a NH within −120 ~ + 30 days of diagnosis. Multivariable logistic regression was used to compare receipt of chemoimmunotherapy (including multi-agent, anthracycline-containing regimens), 30-day

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Conceptualization: Mengyang Di, Adam J Olszewski, Orestis A Panagiotou. Data curation, formal analysis: Mengyang Di, Adam J Olszewski. Data interpretation, writing-review and editing: all authors. Writing-original draft: Mengyang Di, Adam J Olszewski, Orestis A Panagiotou.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

mortality, and hospitalization between NH and community-dwelling patients, estimating odds ratios (OR) and 95% confidence interval (CI). We also examined overall survival (OS). Among NH patients, we examined receipt of chemoimmunotherapy based on functional and cognitive impairment.

Results: Of the eligible 649 NH patients (median age: 82 years), 45% received chemoimmunotherapy; among the recipients, 47% received multi-agent, anthracycline-containing regimens. Compared with community-dwelling patients, those in a NH were less likely to receive chemoimmunotherapy (OR: 0.34, 95%CI: 0.29–0.41), had higher 30-day mortality (OR: 2.00, 95%CI: 1.43–2.78) and hospitalization (OR: 1.51, 95%CI: 1.18–1.93), and poorer OS (hazard ratio: 1.36, 95%CI: 1.11–1.65). NH patients with severe functional (61%) or any cognitive impairment (48%) were less likely to receive chemoimmunotherapy.

Conclusions: High rates of functional and cognitive impairment and low rates of chemoimmunotherapy were observed among NH residents diagnosed with DLBCL. Further research is needed to better understand the potential role of novel and alternative treatment strategies and patient preferences for treatment to optimize clinical care and outcomes in this high-risk population.

Keywords

chemoimmunotherapy; diffuse large B cell lymphoma; functional and cognitive impairment; geriatric oncology; nursing home

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is a common cancer which is potentially curable with standard chemoimmunotherapy.[1–5] It predominantly affects older patients,[6] who have inferior outcomes compared with younger adults.[7,8] Management of DLBCL in older patients is challenging,[9–13] due to the clinical heterogeneity of this population which ranges from otherwise healthy community-dwelling patients to individuals residing in nursing homes (NH) who have major functional or cognitive impairments. NH residents have been understudied and may face barriers to optimal lymphoma care. Functional and/or cognitive impairments are more prevalent and severe in this population when compared with community-dwelling patients,[14–18] and may consequently decrease their chances to receive standard DLBCL treatment.[19] In addition, various systemic barriers may impair the quality of care for NH residents, including delays in diagnosis and initiation of treatment which adversely affect prognosis of DLBCL,[20–22] as well as increased utilization of healthcare resources, including emergency room visits or hospitalizations for therapy-related toxicities which otherwise could be managed in the outpatient setting.

Clinical management of patients with DLBCL in NHs is further complicated by a lack of standard treatment and established guideline recommendations. Although the National Comprehensive Cancer Network guidelines recommend possible regimens for “very frail patients and patients >80 years of age with comorbidities”,[23] some older adults residing in NHs may not tolerate these attenuated regimens. Selection of suitable candidates for treatment and for specific regimens is a nuanced and multi-dimensional process that involves

careful consideration of patient's age, function, cognition, comorbidities, and preferences.[19] Currently, this process relies on clinical expertise and often lacks standardized, objective assessments (such as physical function and frailty) to assist this complicated treatment decision process.[1]

Given these challenges, survival outcomes may be suboptimal for NH patients with DLBCL. Furthermore, functional and cognitive impairments may deter receipt of treatment and be associated with poorer outcomes,[18,19] yet these associations have not been empirically evaluated in large-scale observational studies. In fact, data to characterize impairments among NH adults with DLBCL only recently became available through the addition of Minimum Data Set (MDS) to Surveillance, Epidemiology, and End Results (SEER)-Medicare database.[24] These data can be leveraged to delineate treatment, outcomes, and trends in current practice patterns and provide insight useful for future investigation to improve outcomes.[25] In this study, we use SEER-Medicare-MDS data to characterize functional and cognitive impairments, patterns of cancer-directed therapy, healthcare utilization, and survival among older NH residents with DLBCL receiving care in the United States. We also explored the association of these impairments with receipt of therapies and patient outcomes.

METHODS

Data source and study population

We used the newly available linkage of the SEER registry (reporting incident cancers from 18 geographic areas covering 34.6% of the United States population) with Medicare claims and MDS; MDS includes direct clinical assessments of beneficiaries receiving care in NHs.[24] We selected patients diagnosed with DLBCL 2011–2015, aged ≥65, with continuous fee-for-service Medicare coverage from 1 year prior to lymphoma diagnosis, until ≥6 months after, 1 month before death, or December 2016, whichever occurred first (Figure S1 and Table S1). We chose 6 months as the minimum observed coverage because all claims-based outcomes of interest in this study (except all-cause mortality, recorded separately) would be observed within this timeframe. We excluded beneficiaries with central nervous system lymphoma, and those started on chemoimmunotherapy >120 days after diagnosis. Patients with DLBCL typically receive treatment shortly after the diagnosis; so the threshold of 120 days minimized potential confounding from initiation of lymphoma-directed therapy for another lymphoma diagnosis.[19] We then identified beneficiaries who had an MDS assessment[26] between −120 and +30 days of DLBCL diagnosis (and before treatment), a definition of NH patients used in previous studies.[19,27] We also variedthe timeframe of MDS assessment by using −90 to +30 and −60 to +30 days, respectively, to examine the robustness of our results in the sensitivity analysis. For beneficiaries with several MDS assessments, we selected the one closest to the time of diagnosis. Beneficiaries without matching MDS assessments were classified as community-dwelling. The study was reviewed by the Brown University Institutional Review Board and was exempt from the regulations regarding the inclusion of human participants in research.

MDS assessment

An MDS assessment is routinely performed at the time of NH admission and then every 3 months, both for patients receiving post-acute care in the NH and for long-stay residents. Reporting of the assessment results to Medicare is mandatory.[24] The assessment covers multiple geriatric domains, including physical and cognitive function. We used Morris activities of daily living (ADL) scale to quantify functional disability in each of the seven activities (bed mobility, transfer, locomotion on unit, dressing, eating, toilet use, and personal hygiene, Table S2).[27] We defined "dependency" for each ADL if the item was scored 3 or 4 on the self-performance scale, or if the ADL activity occurred ≤ twice over the seven-day period of assessment. Based on the count of ADLs with dependency, we classified the overall functional disability as none (0 ADL), moderate (1–4 ADLs), or severe (5–7ADLs).[27]

To characterize cognition, we used Cognitive Function Scale (CFS),[28] constructed based on Brief Interview for Mental Status and Cognitive Performance Scale.[29] We classified cognitive impairment as intact, mild, or moderate to severe, based on a well-validated criterion[28] (Table S3).

Outcomes

Among all patients with DLBCL, we examined the receipt of chemoimmunotherapy (Table S1). Chemoimmunotherapy regimens were identified only among those receiving treatment in the outpatient setting, because specific antineoplastic agents are not available from inpatient Medicare claims.[30,31] Regimens that included anthracycline and comprised ≥4 antineoplastic agents (excluding corticosteroids) were classified as "multi-agent, anthracycline-based" or "intensive". Those without anthracycline or containing <4 agents were considered as "attenuated" (Table S4). To generate a complete list of codes for chemoimmunotherapy drugs for DLBCL, we referenced multiple sources of drug codes (e.g., Centers for Medicare & Medicaid Services, American Academy of Professional Coders) and compared our codes with published studies using Medicare data to examine treatment patterns of B-cell lymphoma[19,30,32]; three lymphoma clinicians (MD, AJO, SFH) experienced in using Medicare claims to study lymphoma treatment also reviewed these codes. To explore potential clinical scenarios where patients did not receive lymphoma treatment, we examined transitioning to hospice within 60 days of diagnosis or inpatient death without recorded chemoimmunotherapy.

Among patients receiving chemoimmunotherapy, we examined outcomes including all-cause mortality and hospitalization within 30 days from the start of treatment.[30,33] These early adverse outcomes reflect immediate poor patient outcomes related to treatment selection, decompensated lymphoma, or other baseline health conditions. We also examined overall survival (OS) among patients receiving treatment in the outpatient setting; we estimated OS from treatment initiation. We used OS over cause-specific survival because it is unequivocal, avoiding potentially inaccurate cause-of-death specification.[34]

Statistical analyses

We used descriptive statistics to evaluate baseline characteristics, reporting medians with interquartile ranges (IQR) for continuous variables and counts with percentages for categorical variables.

We compared each outcome between older adults with DLBCL who had a NH stay and those who did not. We also compared outcomes of patients with: (1) moderate versus no disability, (2) severe versus no disability, (3) mild cognitive impairment versus intact cognition, and (4) moderate to severe cognitive impairment versus intact cognition.

We used multivariable Cox regression model to analyze OS, reporting hazard ratio (HR) with 95% confidence interval (CI). For all categorical outcomes (receipt of any chemoimmunotherapy, receipt of intensive regimens, transition to hospice, inpatient death before recorded therapy, 30-day mortality, and 30-day hospitalization), we used multivariable logistic regression models, reporting odds ratios (OR) and 95% CI. All models were adjusted for age, sex, race, DLBCL stage, comorbidity burden, Medicaid dual coverage, and type of NH stay (for models within the NH population; long- vs. short-term stay; long-term stay defined as >90 consecutive days prior to the diagnosis[27]). In the Cox regression models, we additionally adjusted for type of treatment regimens (intensive vs. attenuated as defined above). We estimated comorbidity burden based on the National Cancer Institute-Charlson comorbidity index, using diagnoses derived from the patient's Medicare claims within 1 year prior to the lymphoma diagnosis. We categorized comorbidity burden as low (index score ≤2), moderate,[3,4] high (≥5), or unknown.[19,35] All covariates were categorical in the regression models to avoid the assumption of linear association with outcomes.

In the sensitivity analyses, we performed the propensity score matching of community-dwelling and NH patients (ratio: 1:1, greedy nearest neighbor with caliper equal to 0.2 standard deviation of the propensity score), based on pre-defined age subgroup (≥65 to <75; ≥75 to <80; ≥80 to <85; or ≥ 85), sex, race, DLBCL stage (I/II, III/IV, unknown), comorbidity index, and Medicaid dual coverage. In the matched population, we compared the receipt of chemoimmunotherapy, early transition to hospice, and inpatient death without recorded lymphoma therapy. We replaced any missing data with "unknown" category (only stage and comorbidities had missingness in approximately 5% patients) and did not exclude any patients due to missingness. Outcome models used conditional logistic regression and reported OR and 95% CI. Given the anticipated small sample sizes in the NH sub-populations defined respectively for the other outcomes (e.g., overall survival and receipt of intensive regimens for patients receiving treatment in the outpatient setting), the performance of regression would most likely be superior to that of matching,[36,37] therefore, we only conducted multivariable regression for all the other outcomes.

To better characterize the experience of older adults with DLBCL in NHs, we used multivariable logistic regression models to evaluate all categorical outcomes according to degree of functional and cognitive impairments at the time of diagnosis. Among patients who received lymphoma-directed therapy in the outpatient setting, we compared OS according to the degree of impairment using multivariable Cox regression models,

including the type of chemotherapy regimen as an additional covariate. We also compared the outcomes of interest between patients with short- and long-stay using similar methods.

All analyses were conducted using R v.3.5.1 (https://www.R-project.org/). *p*-values were two-tailed with a type I error rate $\alpha = 0.05$.

RESULTS

Among 10,226 Medicare beneficiaries with DLBCL, we identified 649 patients receiving NH care during the study period. Their median age was 82 years, 59% were women, 90% were White, and 49% had stage III/IV disease (Table 1). Among these beneficiaries, 143 (22%) were long-stay residents (median age: 84 years, 64% females, 83% White) (Table S5).

Nursing home versus community-dwelling patients

Compared with community-dwelling adults with DLBCL, NH patients were less likely to receive chemoimmunotherapy (45% vs. 74%; adjusted OR, 0.34; 95%CI, 0.29–0.41); when treated, they were less likely to receive multi-agent, anthracycline-based regimens (47% vs. 71%; adjusted OR, 0.51; 95%CI, 0.37–0.72). NH patients were more likely to transition to hospice within 60 days of lymphoma diagnosis (adjusted OR, 2.69; 95%CI, 2.18–3.32) or die in the hospital without recorded treatment (adjusted OR, 2.97; 95% CI, 2.36–3.73). Among chemoimmunotherapy recipients, NH patients had higher rates of 30-day mortality (adjusted OR, 2.00; 95%CI, 1.43–2.78) and hospitalization (adjusted OR, 1.51; 95%CI, 1.18–1.93) than community-dwelling individuals (Figure 1, Figure S2). Among those receiving chemoimmunotherapy in the outpatient setting, NH patients had a shorter median OS than community-dwelling individuals (24.1 vs. 54.7 months, adjusted HR: 1.36, 95% CI: 1.11–1.65) (Figure 2). Results of these comparisons in the matched cohort (total $N = 1290$) were very similar to those from the main analyses shown in Figure 1 (Table S6).

DLBCL therapy and outcomes among patients in nursing homes

Twenty percent of NH patients with DLBCL had moderate disability, while 61% had severe disability. Mild and moderate to severe cognitive impairment was present in 18% and 26% patients respectively (Table S5). Compared with patients with intact function, those with severe disability were less likely to receive chemoimmunotherapy (adjusted OR: 0.57, 95% CI: 0.38–0.87). The distributions of disability for each ADL item among chemoimmunotherapy recipients and non-recipients are shown in Figure S3. Those with severe disability (vs. no disability) were also more likely to transition to hospice shortly after lymphoma diagnosis (adjusted OR: 2.00, 95% CI: 1.15–3.47). Among chemoimmunotherapy recipients, patients with severe disability (vs. no disability) had a higher rate of 30-day hospitalization (adjusted OR: 2.02, 95% CI: 1.10–3.68). There were no statistically significant associations between disability and other categorical outcomes (including receipt of anthracycline-based, multi-agent regimens, inpatient death without recorded treatment, and 30-day mortality) (Table 2).

Compared with those with intact cognition, patients with any cognitive impairment were less likely to receive chemoimmunotherapy (adjusted OR for mild cognitive impairment vs. intact cognition: 0.64, 95% CI: 0.44–0.95; adjusted OR for moderate to severe impairment: 0.31, 95% CI: 0.19–0.50), and more likely to transition to hospice within 60 days of lymphoma diagnosis (adjusted OR for mild impairment: 1.65, 95% CI: 1.06–2.56; adjusted OR for moderate to severe impairment: 1.80, 95% CI: 1.09–2.97). Patients with moderate to severe cognitive impairment (vs. intact cognition) were more likely to die in the hospital without recorded chemoimmunotherapy (adjusted OR: 3.29, 95% CI: 1.95–5.56). Those with mild cognitive impairment (vs. intact cognition) had a higher rate of 30-day hospitalization after therapy (adjusted OR: 2.41, 95% CI: 1.28–4.52). There was no statistically significant association between cognitive impairment and other categorical outcomes (including receipt of anthracycline-based, multi-agent regimen, and 30-day mortality) (Table 2). The associations between receipt of chemoimmunotherapy and functional or cognitive impairment were largely unchanged using different time windows to define pre-treatment MDS assessment (e.g.,−60 to +30 days, or − 90 to +30 days of lymphoma diagnosis; Table S7).

In multivariable Cox models, the association between levels of functional or cognitive impairment and OS was not statistically significant among patients who received lymphoma-directed therapy (Table 3).

Long-stay nursing home residents

Patients with short- and long-stay had similar rates of functional and cognitive impairments, and probabilities of receiving treatment (Table S5). Median OS was lower among long-term residents (19.7 vs. 29.2 months). There was no statistically significant difference in any outcomes of interest between short- and long-stay residents (Table S8).

DISCUSSION

In this population-based study, we used the newly available linkage of SEER-Medicare-MDS databases to describe prevalence of functional and cognitive impairments and treatment patterns among older adults with DLBCL who received care in NHs. We found that less than half of the NH patients with DLBCL received chemoimmunotherapy for this potentially curable cancer, indicating that available treatments may either be unfeasible or not preferred in this population. Our study also revealed significant associations of MDS-based functional and cognitive impairments with receipt of chemoimmunotherapy, but not with the use of multi-agent, anthracycline-based regimens.

Compared with community-dwelling patients, NH adults were significantly less likely to receive chemoimmunotherapy: 45% received chemoimmunotherapy (74% in community-dwelling Medicare patients), and 47% of chemotherapy recipients were prescribed standard multi-agent, anthracycline-based regimens. The low treatment rate could partially be explained by the high prevalence of functional and cognitive impairments (e.g., >60% with 5–7 ADL disabilities). Patients in NHs were more likely to transition to hospice shortly after lymphoma diagnosis or die in the hospital before any recorded chemoimmunotherapy, which could be a result of pre-existing impairments, early goals of care discussions, or

rapid clinical deterioration. Patients' preferences, albeit not observed in this retrospective, claims-based study, may also contribute to low treatment use, as individuals who lost their independence may influence willingness to undergo intensive curative chemotherapy. Qualitative studies are needed to better explore patient and provider decision-making among NH patients with DLBCL, with particular focus on physician attitudes and beliefs about treatment counseling and patient experiences and perspectives on pursuing lymphoma-directed therapy.

Older patients with DLBCL in NH had significantly worse short- and long-term outcomes. Even with treatment, OS was substantially shorter compared with community-dwelling patients, likely due to a combination of lower treatment tolerance and other poor prognostic factors. The low treatment rate, the prevalent risk factors for treatment intolerance (e.g., functional and cognitive impairment),[18,19] and the worse outcomes despite treatment in NH patients with DLBCL, suggest that there may be a role for novel, better tolerated treatment strategies for this population, particularly those with high levels of impairment.

Within the NH population, we found a strong association between functional or cognitive impairment and receipt of chemoimmunotherapy for DLBCL. Although functional and cognitive impairments are known independent predictors for complications related to intensive therapies,[18,19,38] the use of multi-agent, anthracycline-based regimens was similar regardless of the level of impairment among chemoimmunotherapy recipients (Table 2). Although there might be other unobserved factors affecting regimen selection (e.g., logistic concerns, impairment or organ dysfunction leading to high concern of treatment intolerance), this observation suggests that requiring NH care itself may be a consideration for the use of attenuated regimens (as opposed to intensive regimens). This hypothesis is partially supported by findings from hematologists surveyed in the Netherlands, in which over 50% preferred attenuated regimens in older patients with DLBCL if they lived in NH, even without knowing patients' comorbidities, functional, and cognitive status.[39] These results raise concern for possible under- or over-treatment of patients with DLBCL receiving NH care. Both phenomena would be highly undesirable from the perspective of optimal treatment selection, as the importance of multi-dimensional geriatric assessment for treatment planning in DLBCL has been well-established.[19,40,41] Taken together, integrating functional and cognitive assessments (e.g., MDS) into treatment planning might improve regimen selection and treatment outcomes for the NH population.

We also found that length of NH stays prior to DLBCL diagnosis/treatment (short- vs. long-term) was not associated with any short-term outcomes, which might indicate similar risk of therapy-related complications between these two sub-populations. This observation appears to be contradictory to the concept that short-stay patients may have a better chance of receiving and tolerating chemoimmunotherapy, including intensive regimens.[42] It again emphasizes the importance of relying on direct geriatric assessment instead of the type of NH stay during treatment planning.

Our study has several limitations. Firstly, in this retrospective analysis, we were unable to account for unobserved confounders of treatment selection and outcomes, for example, molecular characteristics of lymphoma. We were also unable to adjust for baseline

impairment in the comparisons between NH and community-dwelling patients, which is not available for community-dwelling patients in Medicare data. Secondly, doses of chemoimmunotherapy agents were not discernible from Medicare claims, yet dose attenuations are common in older patients.[43,44] Thirdly, sample sizes were relatively small for some analyses, which may have limited statistical significance testing for some differences that might be clinically meaningful (e.g., early mortality based on functional or cognitive impairments). Fourthly, median time between MDS-based functional/cognitive assessments and initiation of therapy was 40–41 days, so the ascertained functional or cognitive assessments might not represent the exact pre-treatment status when a rapid deterioration due to DLBCL occurred. However, our primary results were not sensitive to specific timeframes for pre-treatment MDS assessment (Table S7). Fifthly, we did not distinguish potential causes of death, as this type of data from the claims database (without the knowledge of specific clinical scenarios) is subject to easy misclassification. However, future research will be important to determine if, for example, patients with short survival are more likely to die from non-lymphoma causes. Sixthly, despite our comprehensive list of chemoimmunotherapy drug codes, some misclassification of types of regimens is still possible. Lastly, considerations on treatment decision-making from physicians and patients were not observed. Qualitative research is needed to better understand this complex decision-making process from the perspectives of both patients and providers.

In this first population-based study characterizing older NH patients with DLBCL, we report high prevalence of functional and cognitive impairments, low use of chemoimmunotherapy (including multi-agent, anthracycline-based regimens), and poor short- and long-term outcomes despite the use of lymphoma-directed therapy. Routinely collected NH assessment data revealed strong associations between receipt of chemoimmunotherapy and functional or cognitive impairment among older NH patients with DLBCL. Further studies are needed to uncover the reasoning behind observed treatment decisions in this population to ultimately optimize outcomes for patients while respecting their individual goals of care. Development of alternative, better tolerated therapies for DLBCL will be critical for improving outcomes in this very high-risk patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CONFLICT OF INTEREST

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Sponsor does not have any role in study concept and design, acquisition of subjects and/or data, analysis and interpretation of data, and preparation of manuscript.

REFERENCES

1. Di M, Huntington SF, Olszewski AJ. Challenges and opportunities in the Management of Diffuse Large B-cell lymphoma in older patients. Oncologist. 2021;26:120–132. [PubMed: 33230948]
2. Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. Blood. 2010;116:2040–2045. [PubMed: 20548096]
3. Cunningham D, Hawkes EA, Jack A, et al. Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone in patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma: a phase 3 comparison of dose intensification with 14-day versus 21-day cycles. Lancet. 2013;381:1817–1826. [PubMed: 23615461]
4. Jakobsen LH, Bøgsted M, Brown PN, et al. Minimal loss of lifetime for patients with diffuse large B-cell lymphoma in remission and event free 24 months after treatment: a Danish population-based study. J Clin Oncol. 2017;35: 778–784. [PubMed: 28095160]
5. Teras LR, DeSantis CE, Cerhan JR, Morton LM, Jemal A, Flowers CR. 2016 US lymphoid malignancy statistics by World Health Organization subtypes. CA Cancer J Clin. 2016;66: 443–459. [PubMed: 27618563]
6. National Cancer Insittute: Surveillance E, and End Results Program. Cancer Stat Facts: NHL — Diffuse Large B-Cell Lymphoma (DLBCL).
7. Zhou Z, Sehn LH, Rademaker AW, et al. An enhanced international prognostic index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era. Blood. 2014;123:837–842. [PubMed: 24264230]
8. Issa DE, van de Schans SA, Chamuleau ME, et al. Trends in incidence, treatment and survival of aggressive B-cell lymphoma in The Netherlands 1989–2010. Haematologica. 2015; 100:525–533. [PubMed: 25512643]
9. Lin RJ, Elko TA, Devlin SM, et al. Impact of geriatric vulnerabilities on allogeneic hematopoietic cell transplantation outcomes in older patients with hematologic malignancies. Bone Marrow Transplant. 2020;55:157–164. [PubMed: 31471572]
10. Nagl L, Koinig K, Hofer F, Stauder R. Comorbidities cluster with impaired functional capacities and depressive mood and predict adverse outcome in older patients with hematological malignancies. Leuk Lymphoma. 2020;61:1954–1964. [PubMed: 32281446]
11. Josting A, Rueffer U, Franklin J, Sieber M, Diehl V, Engert A. Prognostic factors and treatment outcome in primary progressive Hodgkin lymphoma: a report from the German Hodgkin lymphoma study group. Blood. 2000;96:1280–1286. [PubMed: 10942369]

12. Hamlin PA, Satram-Hoang S, Reyes C, Hoang KQ, Guduru SR, Skettino S. Treatment patterns and comparative effectiveness in elderly diffuse large B-cell lymphoma patients: a surveil-lance, epidemiology, and end results-medicare analysis. Oncologist. 2014;19:1249–1257. [PubMed: 25342313]
13. Williams JN, Rai A, Lipscomb J, Koff JL, Nastoupil LJ, Flowers CR. Disease characteristics, patterns of care, and survival in very elderly patients with diffuse large B-cell lymphoma. Cancer. 2015;121:1800–1808. [PubMed: 25675909]
14. Madeira T, Peixoto-Pl acido C, Sousa-Santos N, et al. Association between living setting and malnutrition among older adults: the PEN-3 S study. Nutrition. 2020;73:110660.
15. Papadopoulou SK, Tsintavis P, Potsaki P, Papandreou D. Differences in the prevalence of sarcopenia in community-dwelling, nursing home and hospitalized individuals. A systematic review and meta-analysis. J Nutr Health Aging. 2020;24:83–90. [PubMed: 31886813]
16. Xiao DY, Luo S, O'Brian K, et al. Impact of sarcopenia on treatment tolerance in United States veterans with diffuse large B-cell lymphoma treated with CHOP-based chemotherapy. Am J Hematol. 2016;91:1002–1007. [PubMed: 27356783]
17. Hoffmann F, Kaduszkiewicz H, Glaeske G, van den Bussche H, Koller D. Prevalence of dementia in nursing home and community-dwelling older adults in Germany. Aging Clin Exp Res. 2014;26:555–559. [PubMed: 24647931]
18. Hshieh TT, Jung WF, Grande LJ, et al. Prevalence of cognitive impairment and association with survival among older patients with hematologic cancers. JAMA Oncol. 2018;4:686–693. [PubMed: 29494732]
19. Di M, Keeney T, Belanger E, Panagiotou OA, Olszewski AJ. Global risk indicator and therapy for older patients with diffuse large B-cell lymphoma: a population-based study. JCO Oncol Pract. 2022;18(3):e383–e402. [PubMed: 34846916]
20. Blunt DN, Smyth L, Nagamuthu C, et al. Shorter diagnosis-to-treatment interval in diffuse large B-cell lymphoma is associated with inferior overall survival in a large, population-based registry. J Natl Compr Cancer Netw. 2021;19:719–725.
21. Olszewski AJ, Ollila T, Reagan JL. Time to treatment is an independent prognostic factor in aggressive non-Hodgkin lymphomas. Br J Haematol. 2018;181:495–504. [PubMed: 29687879]
22. Maurer MJ, Ghesquières H, Link BK, et al. Diagnosis-to-treatment interval is an important clinical factor in newly diagnosed diffuse large B-cell lymphoma and has implication for bias in clinical trials. J Clin Oncol. 2018;36:1603–1610. [PubMed: 29672223]
23. National Comprehensive Cancer Network. B Cell Lymphoma (Version 5.2021).
24. Thomas KS, Boyd E, Mariotto AB, Penn DC, Barrett MJ, Warren JL. New opportunities for cancer health Services research: linking the SEER-Medicare data to the nursing home minimum data set. Med Care. 2018;56:e90–e96. [PubMed: 29401187]
25. Werner RM, Konetzka RT. Trends in post-acute care use among Medicare beneficiaries: 2000–2015. JAMA. 2018;319: 1616–1617. [PubMed: 29677292]
26. Services CfMM. Minimum Data Set (MDS) 3.0 Resident Assessment Instrument (RAI) Manual.
27. Panagiotou OA, Keeney T, Ogarek JA, Wulff-Burchfield E, Olszewski AJ, Bélanger E. Prevalence of functional limitations and their associations with systemic cancer therapy among older adults in nursing homes with advanced non-small cell lung cancer. J Geriatr Oncol. 2021;12:765–770. [PubMed: 33610505]
28. Thomas KS, Dosa D, Wysocki A, Mor V. The minimum data set 3.0 cognitive function scale. Med Care. 2017;55:e68–e72. [PubMed: 25763665]
29. Morris JN, Fries BE, Mehr DR, et al. MDS cognitive performance scale. J Gerontol. 1994;49:M174–M182. [PubMed: 8014392]
30. Olszewski AJ, Butera JN, Reagan JL, Castillo JJ. Outcomes of bendamustine- or cyclophosphamide-based first-line chemotherapy in older patients with indolent B-cell lymphoma. Am J Hematol. 2020;95:354–361. [PubMed: 31849108]
31. Olszewski AJ, Dusetzina SB, Trivedi AN, Davidoff AJ. Prescription drug coverage and outcomes of myeloma therapy among Medicare beneficiaries. J Clin Oncol. 2018;36:2879–2886. [PubMed: 30113885]

32. Olszewski AJ, Mantripragada KC, Castillo JJ. Risk factors for early death after rituximab-based Immunochemotherapy in older patients with diffuse large B-cell lymphoma. J Natl Compr Cancer Netw. 2016;14:1121–1129.
33. Egan PC, LeBlanc TW, Olszewski AJ. End-of-life care quality outcomes among Medicare beneficiaries with hematologic malignancies. Blood Adv. 2020;4:3606–3614. [PubMed: 32766855]
34. Black WC, Haggstrom DA, Welch HG. All-cause mortality in randomized trials of cancer screening. J Natl Cancer Inst. 2002; 94:167–173. [PubMed: 11830606]
35. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40: 373–383. [PubMed: 3558716]
36. Senn S, Graf E, Caputo A. Stratification for the propensity score compared with linear regression techniques to assess the effect of treatment or exposure. Stat Med. 2007;26:5529–5544. [PubMed: 18058851]
37. Wilkinson J, Mamas MA, Kontopantelis E. Dataset characteristics affected the performance of propensity score methods for controlling confounding: a simulation study. J Clin Epidemiol. 2022;152:176–184. [PubMed: 36126791]
38. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. BMC Geriatr. 2013;13:64. [PubMed: 23786540]
39. van der Poel MW, Mulder WJ, Ossenkoppele GJ, et al. Factors that influence treatment decision-making in elderly DLBCL patients: a case vignette study. Ann Hematol. 2015;94:1373–1379. [PubMed: 25869027]
40. Tucci A, Martelli M, Rigacci L, et al. Comprehensive geriatric assessment is an essential tool to support treatment decisions in elderly patients with diffuse large B-cell lymphoma: a prospective multicenter evaluation in 173 patients by the lymphoma Italian foundation (FIL). Leuk Lymphoma. 2015;56: 921–926. [PubMed: 25110825]
41. Merli F, Luminari S, Tucci A, et al. Simplified geriatric assessment in older patients with diffuse large B-cell lymphoma: the prospective elderly project of the Fondazione Italiana Linfomi. J Clin Oncol. 2021;39:1214–1222. [PubMed: 33577377]
42. Singh S, Eguchi M, Min SJ, Fischer S. Outcomes of patients with cancer discharged to a skilled nursing facility after acute care hospitalization. J Natl Compr Cancer Netw. 2020;18:856–865.
43. Peyrade F, Jardin F, Thieblemont C, et al. Attenuated immunochemotherapy regimen (R-miniCHOP) in elderly patients older than 80 years with diffuse large B-cell lymphoma: a multicentre, single-arm, phase 2 trial. Lancet Oncol. 2011;12:460–468. [PubMed: 21482186]
44. Peyrade F, Bologna S, Delwail V, et al. Combination of ofatumumab and reduced-dose CHOP for diffuse large B-cell lymphomas in patients aged 80 years or older: an open-label, multicentre, single-arm, phase 2 trial from the LYSA group. Lancet Haematol. 2017;4:e46–e55. [PubMed: 28041583]

Key points

- Older nursing home residents with diffuse large B cell lymphoma have a markedly lower rate of treatment and worse survival compared with community-dwelling beneficiaries.
- There is a strong association between receipt of lymphoma treatment and functional or cognitive impairments among residents with diffuse large B cell lymphoma.
- Receipt of intensive regimens is low, irrespective of levels of impairment.

Why does this paper matter?

The low use of traditional chemoimmunotherapy among older patients with diffuse large B cell lymphoma requiring nursing home care suggests a need for further studies to better understand factors beyond the high baseline impairment (such as patient preferences) affecting lymphoma treatment decisions in this population. The low treatment rate, the prevalent risk factors for intolerance to traditional chemoimmunotherapy, and poor outcomes despite the use of chemoimmunotherapy also reveals a potential role for novel, better tolerated, alternative treatment strategies in this population, especially for patients with high level of impairment.

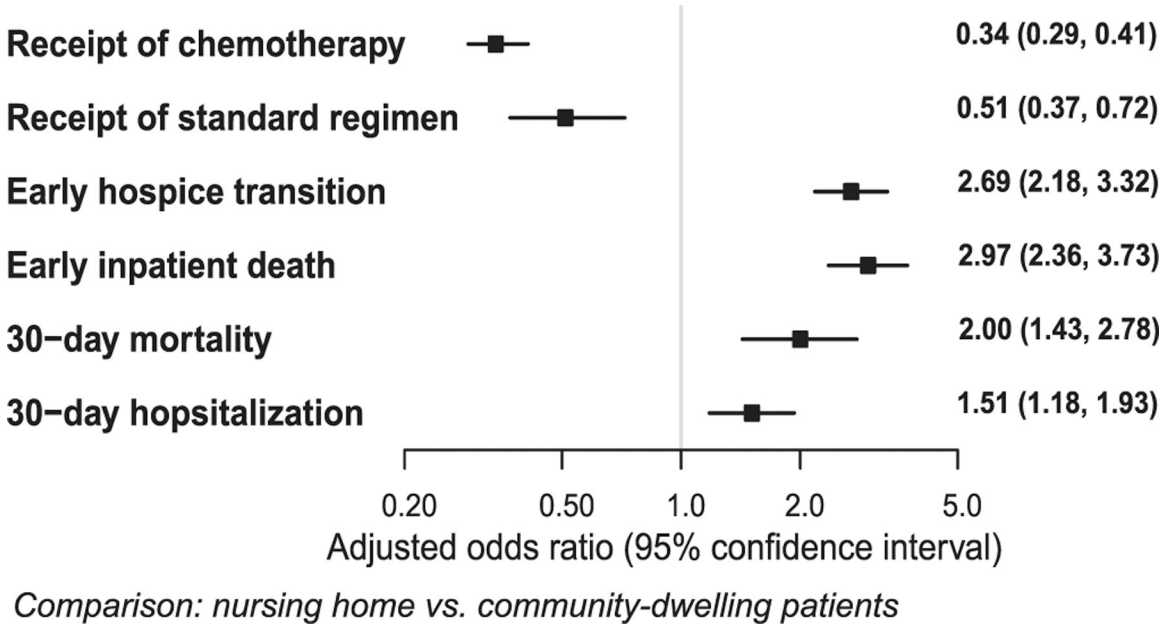

FIGURE 1.

Forest plot of adjusted odds ratios for comparisons between patients in nursing homes and community-dwelling individuals. Standard regimens refer to multi-agent, anthracycline-based regimens. All the models were additionally adjusted for age, sex, race, lymphoma stage at diagnosis, Medicaid dual coverage, and comorbidities.

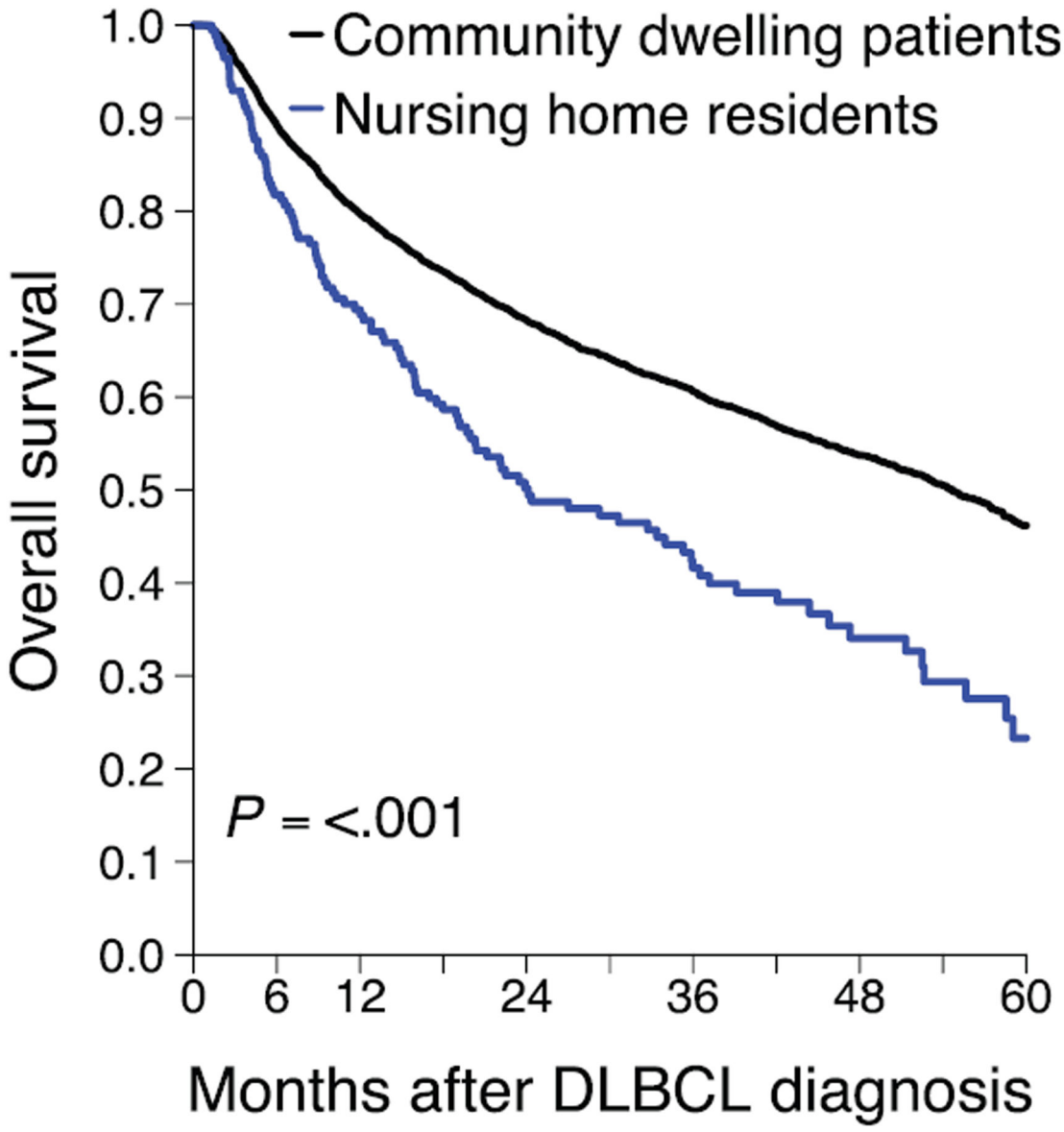

FIGURE 2.

Overall survival between nursing home ($N = 170$) and community dwelling patients ($N = 5222$) who received chemoimmunotherapy in the outpatient setting. p value was estimated based on a multivariable Cox regression model. The model was additionally adjusted for age, sex, race, lymphoma stage at diagnosis, Medicaid dual coverage, comorbidities, and type of chemoimmunotherapy regimen.

TABLE 1

Baseline characteristics and receipt of chemoimmunotherapy in Medicare beneficiaries with diffuse large B cell lymphoma.

	Communitydwelling patients[§] (*N* = 9577)	**Patients in nursing home[§] (*N* = 649)**
Age at diagnosis, year, median (IQR)	77 (71, 83)	82 (76, 87)
Sex, female, *n* (%)	4473 (47)	380 (59)
Race, White, *n* (%)	8149 (85)	582 (90)
Marital status, married, *n* (%)	5278 (55)	217 (33)
Medicaid dual eligibility, *n* (%)	960 (10)	104 (16)
History of congestive heart failure, *n* (%)	903 (9)	187 (29)
History of renal disease, *n* (%)	1122 (12)	170 (26)
Stage of DLBCL, stage III/IV, *n* (%)	5088 (53)	319 (49)
Receipt of chemoimmunotherapy, *n* (%)	7093 (74)	294 (45)
Receipt of intensive regimens, *n* (%)[a]	3700 (71)	79 (47)

Abbreviation: IQR, interquartile range.

[§]Statistically significant difference in every variable (except race) between the community-dwelling and nursing home groups using Chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables (p value <0.01).

[a]Among patients who received any chemoimmunotherapy in the outpatient setting.

TABLE 2

Receipt of chemoimmunotherapy and patient outcomes based on functional and cognitive statuses among nursing home beneficiaries with diffuse large B cell lymphoma.

Outcome	Type of impairment	Degree of impairment	Crude rate, *n* (%)	aOR (95% CI)
Receipt of chemoimmunotherapy	Function	0 ADL	71 (57)	Ref
		1–4 ADLs	60 (47)	0.68 (0.41, 1.13)
		5–7 ADLs	163 (41)	**0.57 (0.38, 0.87)**
	Cognition	Intact	180 (53)	Ref
		Mild	73 (43)	**0.64 (0.44, 0.95)**
		Moderate to severe	30 (25)	**0.31 (0.19, 0.50)**
Receipt of curative regimen[a]	Function	0 ADL	22 (49)	Ref
		1–4 ADLs	19 (53)	1.11 (0.42, 2.94)
		5–7 ADLs	38 (43)	0.69 (0.30, 1.55)
	Cognition	Intact	49 (44)	Ref
		Mild to severe[b]	25 (49)	1.82 (0.89, 3.73)
Transition to hospice	Function	0 ADL	19 (15)	Ref
		1–4 ADLs	31 (24)	1.59 (0.82, 3.06)
		5–7 ADLs	112 (28)	**2.00 (1.15, 3.47)**
	Cognition	Intact	71 (21)	Ref
		Mild	51 (30)	**1.65 (1.06, 2.56)**
		Moderate to severe	39 (33)	**1.80 (1.09, 2.97)**
Inpatient death without recorded therapy	Function	0 ADL	20 (16)	Ref
		1–4 ADLs	24 (19)	1.17 (0.60, 2.28)
		5–7 ADLs	81 (21)	1.28 (0.73, 2.22)
	Cognition	Intact	56 (17)	Ref
		Mild	24 (14)	0.90 (0.53, 1.53)
		Moderate to severe	41 (35)	**3.29 (1.95, 5.56)**
30-day mortality[c]	Function	0–4 ADL[b]	21 (16)	Ref
		5–7 ADLs	32 (20)	1.08 (0.57, 2.08)
	Cognition	Intact	27 (15)	Ref
		Mild to severe[b]	24 (23)	1.70 (0.90, 3.23)

Outcome	Type of impairment	Degree of impairment	Crude rate, *n* (%)	aOR (95% CI)
30-day hospitalization[c]	Function	0 ADL	32 (45)	Ref
		1–4 ADLs	36 (60)	1.88 (0.91, 3.91)
		5–7 ADLs	103 (63)	**2.02 (1.10, 3.68)**
	Cognition	Intact	94 (52)	Ref
		Mild	52 (71)	**2.41 (1.28, 4.53)**
		Moderate to severe	20 (67)	2.03 (0.84, 4.92)

Note: All the models were additionally adjusted for age, sex, race, lymphoma stage at diagnosis, Medicaid dual coverage, comorbidities, and type of nursing home stay. Bold type highlights significant difference between patients with impairment and no impairment.

Abbreviations: ADL, activity of daily living; aOR, adjusted odds ratio; CI, confidence interval; Ref, reference group/level.

[a] In patients who received chemoimmunotherapy in the outpatient setting.

[b] Values combined according to the reporting policy of NCI to protect patient privacy.

[c] In patients who received chemoimmunotherapy; events happening within 30 days of treatment initiation.

TABLE 3

Overall survival based on degree of impairment among nursing home beneficiaries with diffuse large B cell lymphoma who received active therapy.

Population	Covariate	Comparison	*N*	Median OS, m	aHR (95% CI)
Therapy recipients in outpatient setting (model 1)	Functional status	No ADL disabilities	45	23.5	Ref
		1–4 ADL disabilities	36	24.1	0.94 (0.52, 1.69)
		5–7 ADL disabilities	89	23.9	0.99 (0.61, 1.60)
Therapy recipients in outpatient setting (model 2)	Cognitive status	No cognitive impairment	112	27.0	Ref
		Mild cognitive impairment	>35[a]	19.7	1.18 (0.71, 1.99)
		Moderate to severe impairment	>11[a]	19.0	1.11 (0.56, 2.23)

Note: All the models were additionally adjusted for age, sex, race, lymphoma stage at diagnosis, Medicaid dual coverage, comorbidities, type of treatment regimen, and type of nursing home stay. Effects of functional and cognitive impairments were estimated in separate models due to the strong correlation between the two variables.

Abbreviations: ADL, activities of daily living; aHR, adjusted hazard ratio; CI, confidence interval; m, months; OS, overall survival; Ref, reference group/level.

[a]Exact numbers were not reported according to the reporting policy of NCI to protect patient privacy.