Response to Comment on: "A simplified frailty score predicts outcome in curatively treated older patients with classical Hodgkin lymphoma"

We are grateful for Dr. Huangs's insightful comments[1] on our work "A simplified frailty score predicts outcome in curatively treated older patients with classical Hodgkin lymphoma".[2] Overall, we agree that our simplified geriatric model to predict prognosis after doxorubicin-based chemotherapy needs to be tested prospectively and in context with other tools for geriatric assessment (GA). We encourage plans to evaluate it in broader patient populations, including palliatively treated older patients with classical Hodgkin lymphoma (cHL).

We specifically chose to include only patients treated with an adequate dose intensity of doxorubicin. This was done to reflect current treatment standards and avoid the bias inherent in including patients already believed not to benefit from those options. Including the palliatively treated patients would certainly have reduced the outcome of the unfit group of our analysis, but the effect of an *a priori* selected lower treatment intensity would have been difficult to disentangle. More details on the palliatively treated patients from our population-based cohort have been published recently.[3]

We included variables in our retrospective record-based study that are commonly used in GA, such independence in personal activities of daily living (pADL, as assessed prior to onset of lymphoma symptoms), cognitive function, and nutrition (as body mass index [BMI] at diagnosis). A more sophisticated assessment was difficult, as for instance function in instrumental ADL and neurocognitive performance are not captured in routine care and are difficult to estimate retrospectively. Dependence in pADL and BMI were significantly associated with outcome in univariate, but not in multivariable analysis of older cHL patients, but with heterogenous results and without validation in external cohorts. How they contribute to better prognostication remains uncertain. Also important, but less well studied, is the reversible impact that lymphoma may have on frailty. It may be important to determine the level of frailty prior to onset of lymphoma (the host reserve), at diagnosis (host reserve minus deterioration from lymphoma) or during treatment (host reserve minus the irreversible impact of lymphoma but with added treatment toxicity). As disseminated cHL with severe constitutional symptoms may still be curable, GA in lymphoma patients may be more difficult than in for instance, solid tumors.

We derived our model by straight forward Cox regression analysis and dichotomized all variables for simplicity as in other prognostic models used in oncology.[4] This could be refined by, for instance, adding different risk categories for several variables as in the National Comprehensive Cancer Network refinement of the International Prognostic Score for aggressive B-cell lymphomas.[5] We agree that dichotomization at 70 years may be overly simplistic. However, progression-free survival (PFS) was not statistically different for 71-80 year-old patients (hazard ratio [HR] =1.58; 95% confidence interval [CI]: 1.05-2.39; 60-70 years as reference) compared to those >80 years (HR=2.20; 95 % CI: 1.13-4.29). Only 30 patients were over 80 years at diagnosis in the development cohort, and the HR comes with a wide CI. The same limitation applies to stratification within the group with performance status ≥2, or very high comorbidity scores, these are few patients. To address these limitations, we demonstrate that age and comorbidity (both by Cumulative Index Rating Scale in Geriatrics and Charlson Comorbidity Index) could be incorporated as continuous variables in the model and we provide a calculator to estimate outcomes based on actual data.

The c-index for internal validation in the Norwegian cohort is stated in the article, 0.69 for PFS, and 0.70 for overall survival (OS). For the Swedish cohort, the corresponding numbers are 0.66 and 0.64 for PFS and OS respectively.

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Disclosures

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Contributions

All authors contributed equally to writing the comment and approved the final version.

References

1. Huang K. When 'simplified' may be oversimplified: reassessing frailty scoring in elderly Hodgkin lymphoma. Comment on: A simplified frailty score predicts outcome in curatively treated older patients with classical Hodgkin lymphoma. Haematologica. 2025;110(11):2864-2865.
2. Lia K, Jørgensen RRK, Wikman P, et al. A simplified frailty score predicts outcome in curatively treated older patients with classical Hodgkin lymphoma. 2025;110(10):2356-2366.
3. Fosså A, Molin D, Bröckelmann PJ, et al. Brentuximab vedotin monotherapy is a feasible and effective treatment for older patients with classical Hodgkin lymphoma unsuitable for curative chemotherapy: results from the prospective GHSG–NLG phase II BVB trial. Hemasphere. 2025;9(3):e70099.
4. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med. 1993;329(14):987-994.
5. 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(6):837-842.