

ORIGINAL PAPER

Haematological Malignancy – Clinical

SENIOR-IPI: An easily applicable prognostic index for first-line large B-cell lymphomas patients >80 years treated with curative intent

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Summary

Using LYmphoma Study Association clinical trials combining 438 first-line large B-cell lymphomas (LBCL) patients >80 years old, we defined SENIOR-IPI, an easily applicable prognostic index for this elderly population treated with an anti-CD20-miniCHOP (cyclophosphamide, doxorubicin, vincristine and prednisone)-based regimen. SENIOR-International Prognostic Index (SENIOR-IPI) takes into account accessible variables (number of aaIPI predictors, lactate dehydrogenase > 3x Upper Limit of Normal (LDH >3x ULN), albumin <35 g/L and number of years over 80) and segregates patients into four risk categories. In the training cohort, SENIOR-IPI performed better than IPI, age-adjusted IPI (aaIPI) and National Comprehensive Cancer Network IPI (NCCN-IPI) for progression-free survival (PFS) and overall survival (OS). The validation cohort included 195 patients from the real-world REal world all dAta in LYmphoma and Survival in Adults (REALYSA) cohort and confirmed better performance of SENIOR-IPI than IPI, aaIPI and NCCN-IPI both for PFS (C-index 0.66 vs. 0.61, 0.64 and 0.61 respectively) and OS (C-index 0.67 vs. 0.59, 0.62 and 0.61 respectively). Restricted mean survival times at 2 and 5 years were also evaluated: at 2 years, 10 additional SENIOR-IPI points led to 3.7 and 3.6 months of survival lost, respectively, in the training and validation cohorts. Overall, SENIOR-IPI is an easily applicable and reproducible prognostic index, using only readily available clinical and biological data, which better stratifies prognosis of LBCL patients >80 years old fit for age-adapted immunochemotherapy than IPI, aaIPI and NCCN-IPI.

KEYWORDS

elderly, large B-cell lymphoma, prognostic index

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common form of adult lymphoma, accounting for approximately 30%–40% of non-Hodgkin lymphoma cases.¹ Large B-cell lymphomas (LBCL) comprise DLBCL, high-grade B lymphoma (HGBL) and mediastinal grey zone lymphoma. The median age at diagnosis is 67 years² and

a third of patients are over 75 years old. The worldwide annual incidence is increasing, alongside the ageing of the worldwide population.³ Indeed, as the number of people >80 increased threefold between 1980 and 2010,⁴ LBCL is expected to become even more prevalent in this subpopulation. Many of these patients are in a physical condition that enables them to be candidates for treatment with curative intent.

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However, the optimal treatment of these very elderly patients remains understudied, with clinical trials rarely including patients >80 years old. A meta-analysis of 41 phase II/III clinical trials in DLBCL in the post-Rituximab era showed that only 6 included patients >80 years old.⁵ In part due to this, there is a lack of prognostic index for first-line treatment of these patients.

Standard prognostic indexes in LBCL do not sufficiently stratify elderly patients, notably as low risk. Indeed, neither revised IPI (R-IPI) for patients treated with rituximab⁶ nor NCCN-IPI with four risk categories⁷ regard patients above 60 as low risk. A modified three-category NCCN-IPI for patients older than 60 has been published with better discrimination between risk groups, but has not yet been validated in other cohorts.⁸ A recent study showed that most clinical prognostic models failed to accurately predict patient outcomes in patients over 60 years old.⁹

Efforts have been made to elaborate specific prognostic indexes for older LBCL patients, but these studies have included variable ages (≥ 65) and heterogeneous treatment options, including palliative care.^{10,11} Furthermore, to take into account the frailties specific to this elderly population, these models have included geriatric scales,^{10,11} which tend to be difficult to apply in routine clinical practice. We believe that a simple prognostic index developed specifically for very elderly LBCL >80 years old treated with curative intent would better stratify these patients and highlight those for whom a geriatric assessment is essential, thus using physicians' time more efficiently.

To address these issues, we developed SENIOR-IPI, an internationally applicable, straightforward prognostic index for LBCL patients >80 years old treated with anti-CD20 + miniCHOP (cyclophosphamide, doxorubicin, vincristine and prednisone).¹²

METHODS

Patients

The French LYmphoma Study Association and Lymphoma Academic Research Organization (LYSA/LYSARC) have organized three clinical trials in first-line LBCL patients >80 years old: LNH 03-7B using rituximab-miniCHOP,¹² LNH09-7B using ofatumumab-miniCHOP¹³ and SENIOR evaluating R-miniCHOP versus R-miniCHOP + lenalidomide.¹⁴ Both the standard and experimental arms of SENIOR were included. A brief summary of these trials is provided in [Supporting Information](#). Four hundred and ten patients had all data to calculate SENIOR-IPI (complete data training cohort, $n=410$). Missing values for 28 patients were imputed and results for the training cohort with imputed estimates ($n=438$) are presented in [Supporting Information](#). The external validation set included patients >80 years old from the prospective real-world REALYSA cohort (NCT03869619, inclusion 2018–2023)¹⁵ who were

treated with R-miniCHOP in first line. One hundred and forty patients had all data to calculate SENIOR-IPI (complete data validation cohort, $n=140$). Missing values for 55 patients were imputed and results for the validation cohort with imputed estimates ($n=195$) are presented in [Supporting Information](#).

Statistical methods

Prognostic value of each candidate predictor for SENIOR-IPI was evaluated by Cox proportional hazard models on overall survival (OS) and progression-free survival (PFS). For continuous covariates, splines were used to check for linearity. Dichotomized versions of continuous covariates, using either previously suggested cut-offs or distribution characteristics, were also evaluated in the training set.

Missing data in baseline parameters were imputed separately for the training and validation cohorts by the Multiple Imputation by Chained Equations (MICE) algorithm.¹⁶ Two hundred imputed datasets were generated for each cohort and analysed separately. Further details concerning statistical modelling, including covariate categorization, stratification procedures, interaction testing and pooling methods are available in the [Supporting Information—Supplementary Methods](#).

Briefly, SENIOR-IPI definition was performed in two steps. First, the established IPI, aaIPI and NCCN-IPI scores and their components were compared to derive an optimal score. Second, significant candidate covariates in univariate analyses were sequentially added following a stepwise ascending manner. Variable selection was based on the D1 statistics¹⁷ comparing the nested models including the candidate covariates or not. The variable providing the lowest D1 statistics p -value was included in the further model and the procedure was reiterated until no variable reached a p -value threshold of 0.05. Additional information is provided in [Supporting Information—Supplementary Methods](#).

PFS censored at 2 years (PFS2Y) was the primary endpoint to build the prognostic score, as in this elderly population, PFS2Y more specifically reflects lymphoma-related outcomes. OS and PFS at 2 and 5 years were estimated by the Kaplan–Meier method and median follow-up by the reverse Kaplan–Meier approach.¹⁸

C-Index was the primary criterion used to evaluate and compare the discrimination performances between the prognostic models.¹⁹ SENIOR-IPI calibration properties were also evaluated on the validation cohort following guidance of the Stratos initiative.²⁰ All c-index comparisons are provided in [Supporting Information—Supplementary Methods](#).

Restricted mean survival times (RMSTs) at 2 or 5 years were also evaluated by the pseudo-observation approach²¹ to quantify the mean survival time lost according to the prognostic score.

TABLE 1 Main clinical and biological characteristics of overall, training and validation cohorts.

	Overall (<i>n</i> = 550)	Training (<i>n</i> = 410)	Validation (<i>n</i> = 140)	<i>p</i> -value
Gender				
Female (%)	304 (55.3)	239 (58.3)	65 (46.4)	0.019
Male (%)	246 (44.7)	171 (41.7)	75 (53.6)	
Age				
Mean (SD)	84.1 (3.4)	83.9 (3.4)	84.6 (3.3)	0.030
80–84 (%)	340 (61.8)	265 (64.6)	75 (53.6)	
85–89 (%)	161 (29.3)	110 (26.8)	51 (36.4)	
90+ (%)	49 (8.9)	35 (8.5)	14 (10.0)	
ECOG (%)				
0–1	401 (72.9)	299 (72.9)	102 (72.9)	1.000
2–4	149 (27.1)	111 (27.1)	38 (27.1)	
Ann Arbor stage (%)				
1–2	110 (20)	80 (19.5)	30 (21.4)	0.714
3–4	440 (80)	330 (80.5)	110 (78.6)	
LDH (%)				
≤ULN	181 (32.9)	143 (34.9)	38 (27.1)	0.100
>ULN	319 (58.0)	227 (55.4)	92 (65.7)	
>3× ULN	50 (9.1)	40 (9.8)	10 (7.1)	
Extra-nodal sites (%)				
0–1	307 (55.8)	233 (56.8)	74 (52.9)	0.472
≥2	243 (44.2)	177 (43.2)	66 (47.1)	
NCCN extra-nodal sites (%)				
No	381 (69.3)	291 (71.0)	90 (64.3)	0.169
Yes	169 (30.7)	119 (29.0)	50 (35.7)	
Albumin <35 g/L (%)				
No	311 (56.5)	234 (57.1)	77 (55.0)	0.743
Yes	239 (43.5)	176 (42.9)	63 (45.0)	

Abbreviations: ECOG, Eastern Cooperative Oncology Group; SD, standard deviation.

RESULTS

Patients

Table 1 shows main characteristics of the complete data training (*n* = 410) and validation (*n* = 140) cohorts. Patient characteristics for the cohorts with imputed estimates for missing values (training: *n* = 438; validation: *n* = 195) are reported in [Supporting Information](#). Training and validation cohorts were overall comparable, although the clinical trial training cohort was younger than the real-world validation cohort (83.9 vs. 84.6 years old, *p* = 0.030) and contained more men (53.6% vs. 41.7%, *p* = 0.019), perhaps reflecting the higher proportion of women who live past 80 years old in real-world conditions. Of note, 27 of 195 patients in the validation cohort were reported as HGBL not otherwise specified (NOS) or HGBL with MYC Proto-Oncogene (MYC) and B-cell lymphoma (BCL)2 and/or BCL6 rearrangement. In the training cohort, only SENIOR reported Fluorescence

in situ hybridization (FISH) data, with 11 patients reported as DLBCL with double or triple hit.

Median follow-up in the training cohort and validation cohort was 28.9 and 26.1 months respectively.

One hundred and sixty-three deaths were observed in the training cohort during follow-up: cause of death was known for 88.9% of these patients. Lymphoma, concurrent illness and treatment toxicity accounted for 57.1%, 13.5% and 8% of known deaths respectively. Causes of death were only known for 55 patients in the validation cohort: of these, lymphoma was listed as cause of death for 22 patients (42.3%) and toxicity for 4 patients (7.7%).

SENIOR-IPI design

In the 200 imputed datasets of the training cohort, NCCN-IPI performed better than IPI and aaIPI for PFS2Y (C-index 0.62 vs. 0.60 for IPI and aaIPI). The superiority of NCCN-IPI

was linked to the LDH $>3\times$ ULN threshold, suggesting an intermediate model including components common to aaIPI with the addition of LDH $>3\times$ ULN. This intermediate model proved statistically superior to aaIPI (D1 statistics, $p=3.1\times 10^{-5}$). Next, among candidate predictors with prognostic value in univariate analysis, continuous age value and albumin <35 g/L had the best additional prognostic value compared to aaIPI + 'LDH $>3\times$ ULN' (D1 statistics vs. aaIPI + 'LDH $>3\times$ ULN', $p=2.0\times 10^{-4}$, C-index 0.66). No other candidate predictor added significant prognostic value (Supporting Information—Supplementary Methods).

SENIOR-IPI score was defined as (age in years >80) + $6\times$ aaIPI index + $6\times$ ('LDH $>3\times$ ULN') + $6\times$ ('Albumin <35 g/L'). Weighting coefficients of 6 are based on Cox model coefficients. A web-based calculator to facilitate SENIOR-IPI calculation has been made freely available (<https://senior-ipi-dev.bolt.host/>).

Overall, the index varied between 0 and 40, suggesting patient segmentation in four classes, by tens, to facilitate reproducibility. SENIOR-IPI >40 is theoretically possible but marginal and included in the ≥ 30 risk category. In the training cohort, risk class distribution was as follows: 0–9 (low risk); 19%, 10–19 (low-intermediate risk); 40.2%, 20–29 (intermediate-high risk); 32.4%, and ≥ 30 (high risk); 8.3% (Figure S1 and Table S1). In the validation cohort, distribution among the four SENIOR-IPI classes was not statistically significantly different ($p=0.348$; Figure S1 and Table S1).

Tables S1 and S2 show the distribution of SENIOR-IPI, aaIPI, IPI, R-IPI and NCCN-IPI among complete data and imputed data cohorts respectively.

SENIOR-IPI performance

In the training cohort, SENIOR-IPI performed better for PFS than IPI, aaIPI and NCCN-IPI (C-index 0.65 vs. 0.59, 0.6 and 0.59, respectively), at 2 years (Figure 1A–D) and at 5 years (Figure S2). SENIOR-IPI also performed better for OS than IPI, aaIPI and NCCN-IPI (C-index 0.67 vs. 0.6, 0.62 and 0.61, respectively), at 2 years (Figure 1E–H) and at 5 years (Figure S2). This was confirmed in the validation set, showing better performance of SENIOR-IPI than IPI, aaIPI and NCCN-IPI for PFS (C-index 0.66 vs. 0.61, 0.64 and 0.61 respectively), at 2 years (Figure 2A–D) and at 5 years (Figure S3) as well as for OS (C-index 0.67 vs. 0.59, 0.62 and 0.61 respectively), at 2 years (Figure 2E–H) and at 5 years (Figure S3). Similar results were also observed on imputed data in both cohorts (Figures S4 and S5).

Statistical comparison of c-indexes was performed on both imputed and complete data validation cohorts. For the complete data validation cohort, statistical superiority of SENIOR-IPI was confirmed compared to IPI and R-IPI for PFS at 24 months, and compared to aaIPI, IPI and R-IPI for OS at 24 months (Supporting Information). Calibration was also studied on the validation cohort with strong results (Supporting Information).

Characteristics of the SENIOR-IPI risk groups

SENIOR-IPI uncovered heterogeneity among known prognostic indexes. Focusing on aaIPI (Figure 3A), aaIPI 1 patients were split between low and low-intermediate SENIOR-IPI groups, and a minority was allocated into the high-intermediate group. AaIPI 2 patients were allocated into low-intermediate and high-intermediate SENIOR-IPI groups, with a minority into the high-risk group. All aaIPI 3 patients had either high or high-intermediate SENIOR-IPI scores. Results were similar in the validation cohort (Figure 3B). Alluvial plots for allocation from IPI and NCCN-IPI into SENIOR-IPI are shown in Figures S6 and S7.

Known causes of death according to SENIOR-IPI risk category are shown in Table S3. In the training cohort, high-risk SENIOR-IPI were more highly represented in deaths linked to treatment toxicity (7 of 13 patients) than in deaths linked to lymphoma (9 of 93 patients), suggesting that high-risk SENIOR-IPI might benefit from less toxic chemotherapy-free regimens. Cause of death was known for fewer patients in the validation cohort; however, only four deaths were reported due to toxicity and all four were in the high-intermediate SENIOR-IPI group. On the other hand, 7 (31.8%) of 22 deaths due to lymphoma were high-risk SENIOR-IPI, highlighting the fact that SENIOR-IPI also evaluates tumour aggressivity, notably through LDH and aaIPI predictors.

Of note, patients who had not been able to receive at least one cycle of immunochemotherapy were initially excluded from the study ($n=13$). All 13 were enrolled in a clinical trial (LNH09-7B or SENIOR) and discontinued treatment via the trial during prephase. Reasons for trial discontinuation were altered performance status, concomitant pulmonary embolism or infection, and investigator's choice. Twelve of these 13 patients had complete data to calculate their SENIOR-IPI: 9 (69%) were high-intermediate or high-risk, with 33% being in the high-risk category (data not shown), a notably higher percentage than in the study cohorts, highlighting the potential impact of SENIOR-IPI in first-line decision-making. Eight patients went on to receive R-miniCHOP-based regimen off-trial (outcome data not available). Four did not receive further treatment: two died, one had concurrent illness and one presented delirium due to corticosteroids in prephase.

Increased SENIOR-IPI leads to significant loss of survival

We performed RMST at 2 and 5 years and analysed the impact of additional SENIOR-IPI points leading to a change in risk category. At 2 years, compared to the low-risk SENIOR-IPI category, low-intermediate, high-intermediate and high-risk lose 1.8, 5.2 and 11.1 months of survival respectively. This was confirmed in the validation cohort, with 2.5,

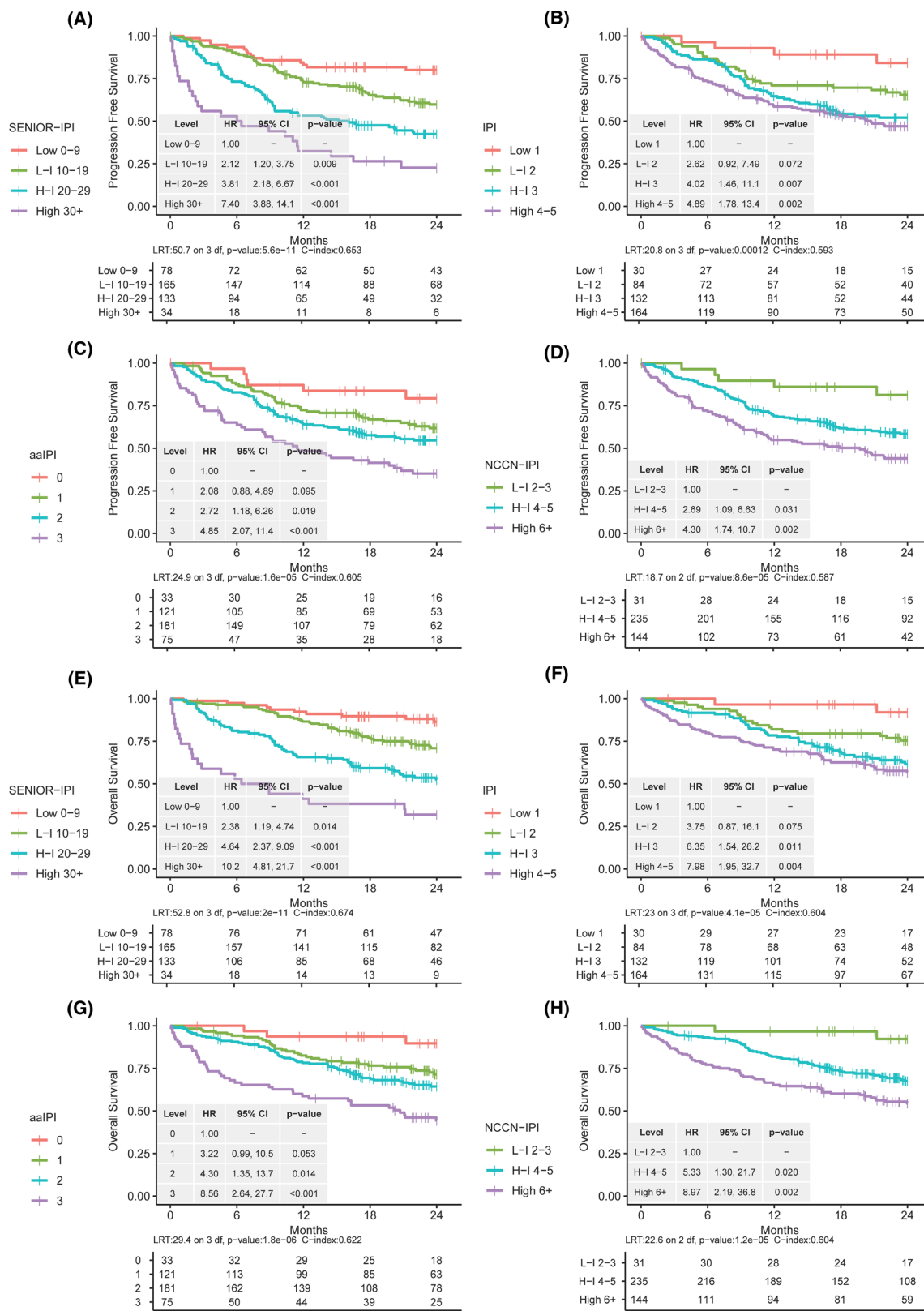


FIGURE 1 SENIOR-IPI performs better than other established prognostic indexes for progression-free survival and overall survival at 2 years in the training cohort. Kaplan-Meier progression-free survival curves for SENIOR-IPI (A), IPI (B), aaIPI (C) and NCCN-IPI (D). Kaplan-Meier overall survival curves for SENIOR-IPI (E), IPI (F), aaIPI (G) and NCCN-IPI (H). Hazard ratios and statistics tests were obtained from univariate Cox models stratified by study arm, with each prognostic index. Hazard ratios are estimated by taking the low-risk category as reference. df, degrees of freedom; LRT, log-likelihood ratio test.

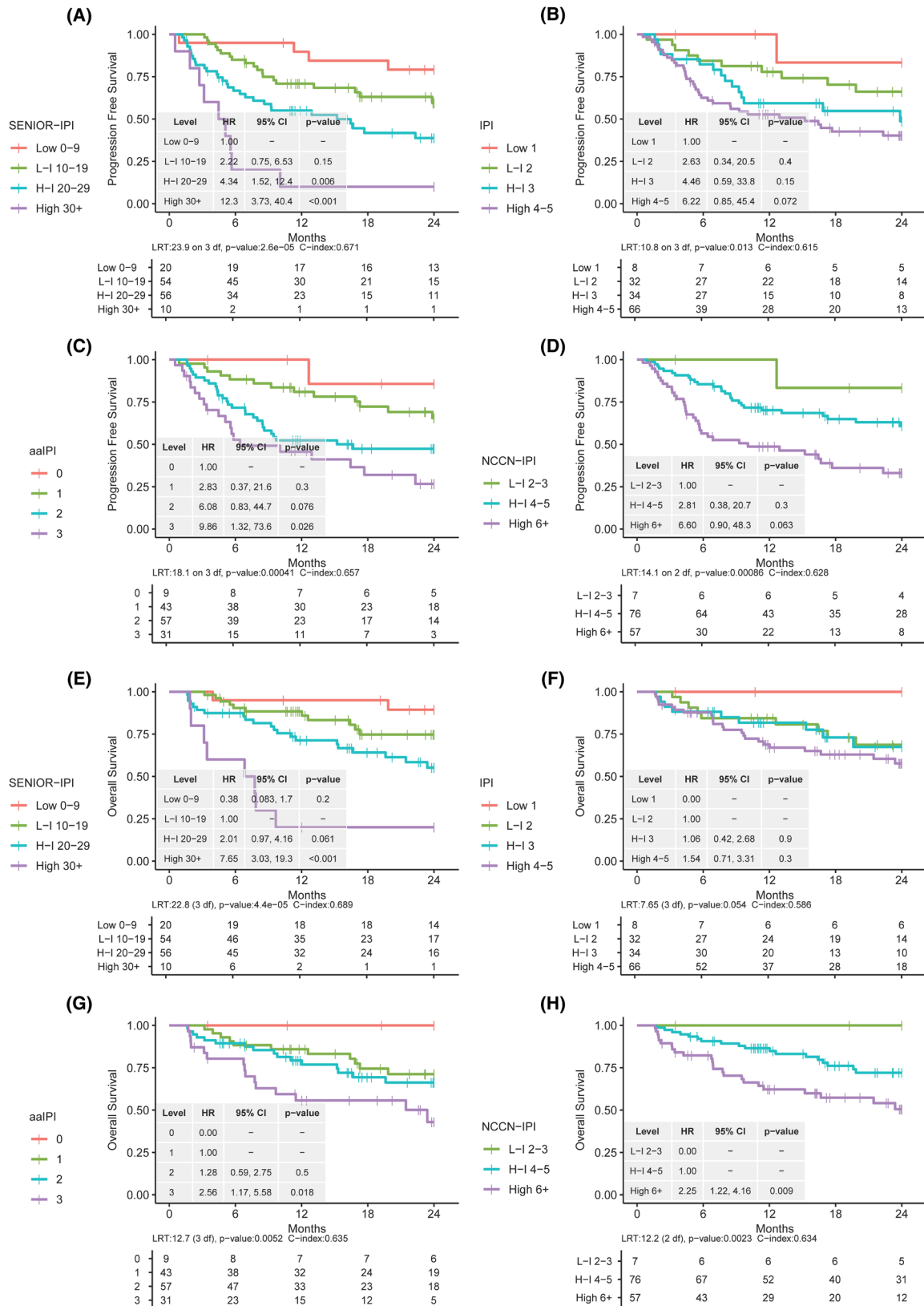


FIGURE 2 Better performance of SENIOR-IPI for progression-free survival and overall survival (OS) at 2 years confirmed in the validation cohort. Kaplan-Meier progression-free survival curves for SENIOR-IPI (A), IPI (B), aaIPI (C) and NCCN-IPI (D). Kaplan-Meier OS curves for SENIOR-IPI (E), IPI (F), aaIPI (G) and NCCN-IPI (H). Hazard ratios and statistical tests were obtained from univariate Cox models with each prognostic index. Hazard ratios are estimated by taking the low-risk category as reference except for the OS analyses where the reference is the low-intermediate category. df, degrees of freedom; LRT, log-likelihood ratio test.

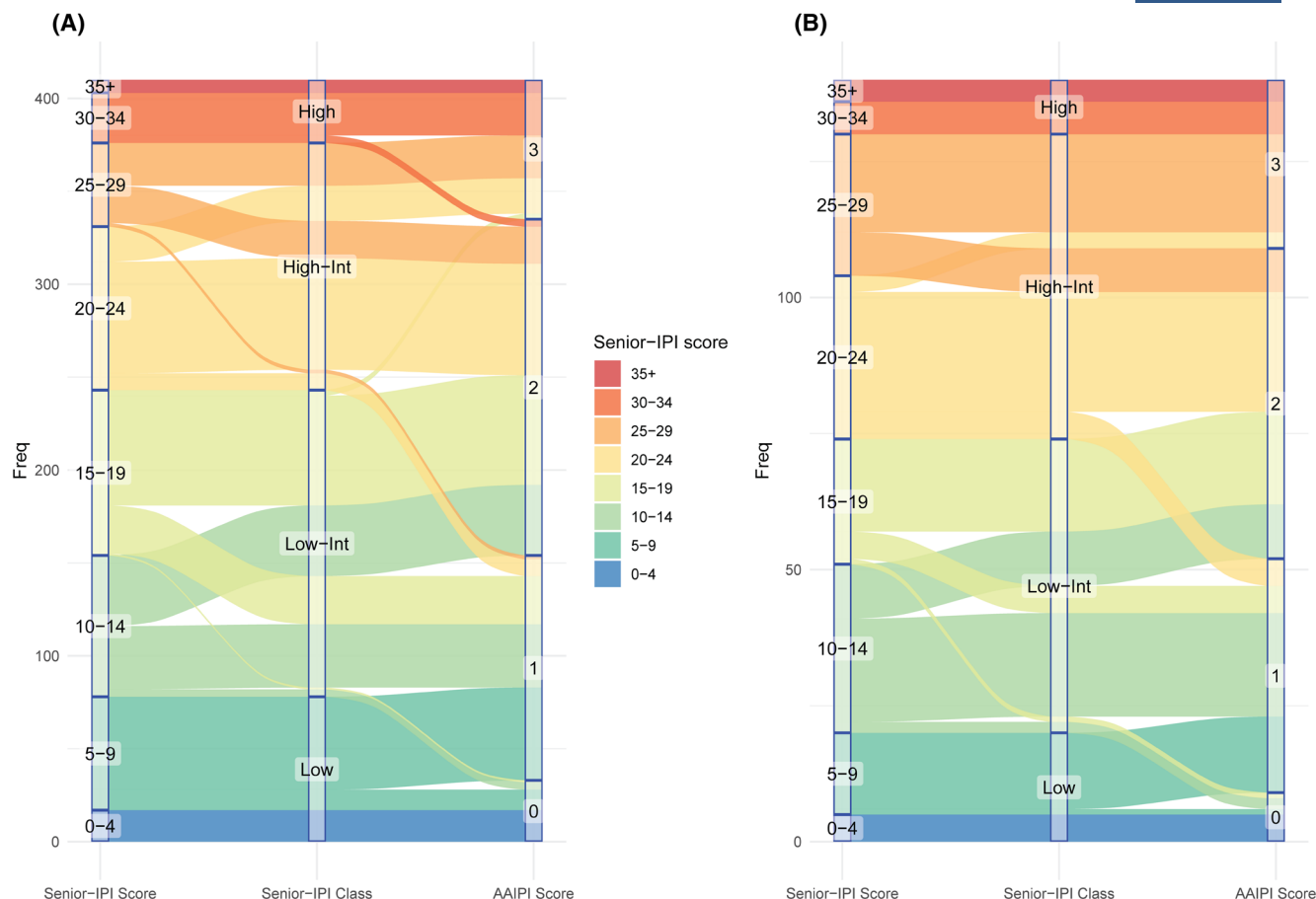


FIGURE 3 Alluvial plots for SENIOR-IPI versus aaIPI in training (A) and validation (B) cohorts. SENIOR-IPI risk categories are shown in the middle section (low, low-intermediate, high-intermediate and high) and are further detailed on the left-hand side, dividing each risk category into two parts based on SENIOR-IPI score. aaIPI score is shown in the right-hand side.

5.04 and 14.45 months of survival lost. At 5 years, changing baseline SENIOR-IPI risk category leads to a range of 10–29 months of average survival lost in the training cohort and 10.7–36.8 months of average survival lost in the validation cohort.

DISCUSSION

SENIOR-IPI is an easily applicable prognostic index, using only clinical and biological data available in routine clinical practice. A freely available web calculator has been developed in order to help clinicians rapidly assess patients' SENIOR-IPI. Of note, this model is based on patients treated with curative intent and might not be applicable to ineligible patients.

We have shown that SENIOR-IPI outperforms currently used IPI, aaIPI and NCCN-IPI in LBCL patients >80 years of age treated in first line. Although the absolute differences in *c*-indexes were quantitatively moderate, even this incremental improvement is of clinical importance, especially in the heterogeneous population of elderly LBCL patients, for whom improved risk stratification may help to better support individualized therapeutic strategies.

SENIOR-IPI was tested and validated in independent cohorts, with strong calibration data, highlighting its robustness. Data imputation was performed to estimate missing data (mostly albumin), and analyses showed similar performance and calibration results in complete and imputed datasets highlighting the strength of SENIOR-IPI. Furthermore, SENIOR-IPI was also recently validated in three pooled international cohorts, where its superiority to IPI, aaIPI and NCCN-IPI in LBCL patients >80 years was confirmed,²² suggesting the model's global applicability. A recently published study comparing prognostic models in a large cohort of DLBCL patients over 60 years old showed that aaIPI performed more accurately in this population than IPI, R-IPI and NCCN-IPI,⁹ validating the choice of comparator indexes.

In designing the SENIOR-IPI, only albumin <35 g/L had additional prognostic value when added to number of complete years over 80 years old + number of aaIPI predictors + LDH >3× ULN. Albumin has been shown to be a surrogate marker for malnutrition and its prognostic impact has been shown in many studies with the same threshold used here of 35 g/L.^{23–25} This, in addition to its availability in daily practice, made it an excellent candidate predictor for SENIOR IPI. Age was integrated as a continuous variable, as none of

the tested age thresholds were more performant. This can be related to the exponential increase in mortality for these age groups: for example, yearly death rates in the French male population increase from 5% at 80 years old to 15% at 90 years old (Figure S8).

Although several geriatric assessments have been tested in clinical trials for patients with LBCL, they were voluntarily not included in SENIOR-IPI as their heterogeneity and lack of consistent use in routine clinical practice would have diminished the applicability of SENIOR-IPI. This was evident even in the construction of this study: only a minority of patients in the validation cohort had the same geriatric index data as in the test cohort. Although SENIOR-IPI does not pretend to evaluate patient fitness as thoroughly as the previously published Elderly Prognostic Index (EPI)¹⁰ or Geriatric Prognostic Index (GPI),¹¹ it does have the benefit of being established on cohorts of patients >80 years old, whereas the EPI and GPI, respectively, studied patients older than 65 and 70. Nevertheless, a performance comparison of these indexes to see whether albumin is a sufficient approximation of patient fitness in this setting would have been interesting. Geriatric assessments were not able to be included either in the recent, large, population-based study published by Jelcic and colleagues due to the same challenges in recovering these data retrospectively.⁹

Another limit of an easily applicable score in routine clinical practice is that molecular characterizations are not taken into account. While these have shown significant prognostic impact, the complexity and delay involved are not currently compatible with daily clinical practice.^{26,27} Elderly DLBCL patients specifically tend to be of MCD genetic subtype and ABC gene-expression profiling, with an increased expression of *VH4-34 IgH* gene.^{28–30} These analyses would be interesting ancillary studies of elderly DLBCL cohorts. Nevertheless, IPI maintains its prognostic impact even in the era of more sophisticated prognostic values.³¹

With the increasingly ageing LBCL population, help in treatment decision-making for this frail population is essential. Mortality rates remain high in elderly LBCL patients treated with R-miniCHOP^{12–14}; conversely, in some selected elderly patients, standard R-CHOP appears feasible with better outcomes than R-miniCHOP,³² suggesting that appropriate age-adapted chemotherapy is still a challenge. SENIOR-IPI evaluates tumour aggressivity via LDH and aaIPI predictors, but our cause of death data in high-risk patients suggests that patient fitness is also approximated via albumin and age. SENIOR-IPI could therefore potentially aid clinicians to select elderly patients eligible for standard immunochemotherapy: either low-risk patients with normal albumin levels and non-dose-limiting age or in well-selected higher risk patients when the elevated SENIOR-IPI is due to tumour aggressivity. In these case-by-case decisions, we highly recommend performing a thorough geriatric evaluation to ensure patient eligibility, as SENIOR-IPI is not a tool designed for geriatric assessment.

In an attempt to improve prognosis and reduce toxicity, chemo-free options for elderly LBCL are becoming

increasingly present in the front-line clinical trial setting. Rituximab, ibrutinib and lenalidomide combination in unfit patients >70 showed efficacy similar to that of R-miniCHOP with acceptable toxicity,³³ leading to a phase 3 trial (NCT05179733). Preliminary results from an LYSA phase 2 trial studying the efficacy of tafasitamab, lenalidomide and rituximab treatment in first-line DLBCL patients >80 years old were recently shown.³⁴ Bispecific antibodies (mosunetuzumab-polatuzumab, r-polatuzumab-glofitamab) are also enticing options for frail first-line DLBCL patients.^{35,36} Although SENIOR-IPI was only evaluated in the R-miniCHOP setting, it could potentially help select high-risk patients who might benefit the most from chemo-free treatment, notably when the high risk is mostly driven by low albumin and extreme age. Indeed, in the study conducted by Vodicka and colleagues, SENIOR-IPI also performed better than IPI, aaIPI and NCCN-IPI in a subcohort of patients >80 treated with chemo-free regimens.²²

SENIOR-IPI's straightforward applicability makes it suitable for use in a prospective clinical trial in order to confirm whether it may help treatment decision-making in elderly patients, particularly in identifying patients most appropriate for standard-of-care R-miniCHOP, those who could tolerate and benefit from standard R-CHOP and those who may be better candidates for less toxic chemotherapy-free regimens.

AUTHOR CONTRIBUTIONS

Aurelien Belot: Methodology; writing – review and editing; validation. **Hervé Tilly:** Data curation; writing – review and editing. **Fabrice Jardin:** Conceptualization; supervision; data curation; writing – review and editing. **Fanny Cherblanc:** Data curation; writing – review and editing. **Hervé Ghesquière:** Data curation; writing – review and editing. **Lucie Oberic:** Data curation; writing – review and editing. **Corinne Haïoun:** Data curation; writing – review and editing. **Jean-Philippe Jais:** Methodology; writing – original draft; formal analysis; data curation; conceptualization. **Sydney Dubois:** Conceptualization; investigation; writing – original draft; formal analysis; data curation.

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CONFLICT OF INTEREST STATEMENT

The authors have no relevant conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

A freely available online calculator has been developed. Extensive supplementary data are made available and additional data are available upon request.

PATIENT CONSENT STATEMENT

All four studies were approved by ethics committees before patient enrolment and patients signed their written informed consent at time of inclusion. Studies were registered on clinicaltrials.gov under the references: NCT03869619 (REALYSA), NCT01087424 (LNH 03-7B), NCT01195714 (LNH 09-7B) and NCT02128061 (SENIOR). LYSARC's data reuse projects are described on the LYSARC website (<https://lymphoma-research-experts.org/lysa/i-am-participating-or-have-participated-in-a-clinical-trial/>). The rights of patients regarding the reuse of their data are explicitly stated. As mentioned in the information note, patients included in the REALYSA cohort were informed of the specific project through the LYSARC webpage (SENIOR IPI: Prognostic score for patients with diffuse large B-cell lymphomas over 80 years of age—Lymphoma Research Experts).

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SUPPORTING INFORMATION

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

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