A prognostic index predicting survival in transformed Waldenström macroglobulinemia

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Supplementary Appendix

Supplement to: Durot E, Kanagaratnam L, Zanwar S et al. A prognostic index predicting survival in transformed Waldenström macroglobulinemia.

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Supplementary Methods

Patients and data collection for development of the prognostic model

Fifteen variables were considered as covariates for model building. These covariates were: sex, number of lines of treatment for WM, rituximab exposure for the treatment of WM, time to transformation, and at time of HT: age, Eastern Cooperative Oncology Group (ECOG) performance status (PS, 0-4), presence of B symptoms (defined as recurrent fever, nights sweats, or > 10% weight loss), extranodal involvement, Ann Arbor stage (I-IV), leucocytes, hemoglobin and platelets counts, and serum albumin, LDH and β2-microglobulin levels. Extranodal involvement at HT was confirmed by the site of biopsy.

Training and validation cohorts

The training and the validation cohorts were formed consecutively. After development of the prognostic model and the scoring system, other centers were contacted to provide data from patients with transformed WM so that the validation cohort was independent. The inclusion criteria for the validation set were similar to those for the training set.

End point

Given the reported poor survival after HT in transformed WM ranging from 1.5 to 3 years[1-3] and the fact that the majority of events, mainly deaths, occur in the first 2 years following the diagnosis of DLBCL[4], 2-year survival after HT was chosen as the main end point for statistical analyses.

Statistical methods

Descriptive statistics included all clinical and demographic characteristics. Continuous variables were expressed as median and range and categorical variables as number and percentages.

Log-linearity and the proportional hazards assumptions were checked. When the log-linearity assumption was not verified, continuous variables were converted into categorical form according to thresholds used in clinical practice or literature data determined before analyzes.

The C-index estimates the proportion of all pairs of patients in whom prediction and outcome are concordant and takes values from 0.5 (no discrimination) to 1.0 (perfect discrimination).

The Harrell's C-index and the May and Hosmer test for goodness-of-fit were used to assess discrimination and calibration in the validation cohort, as was done in the training cohort.

References

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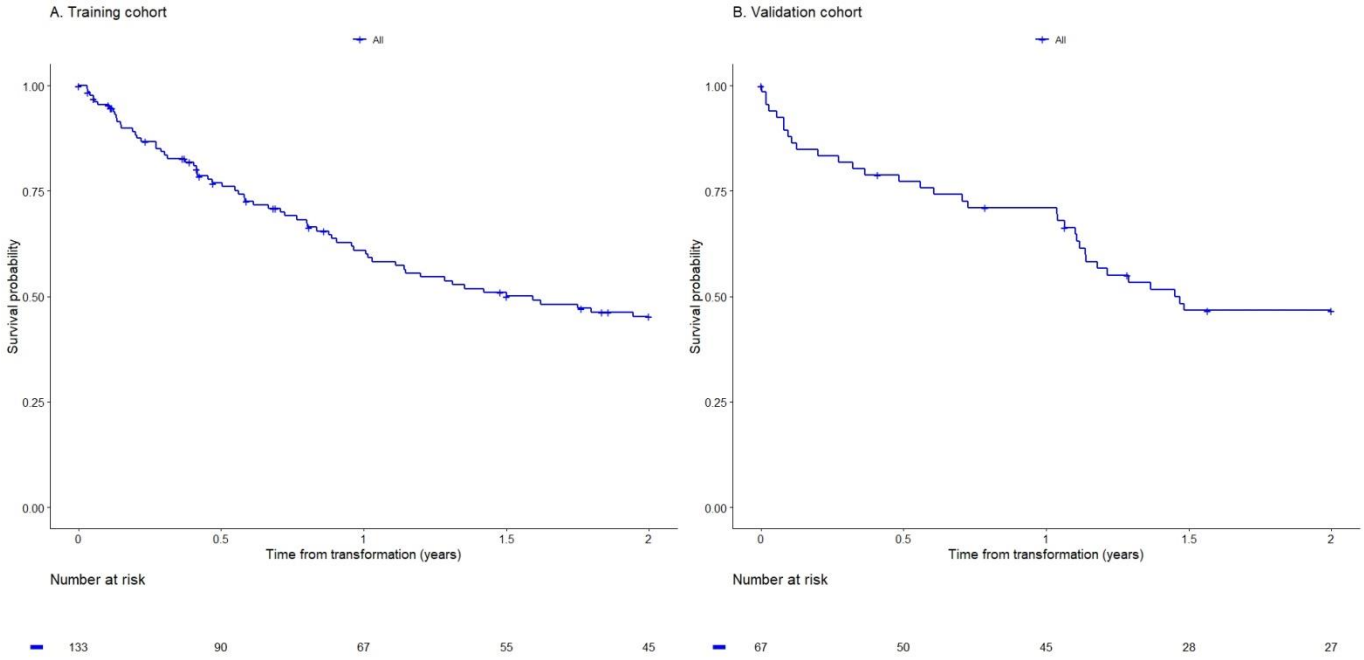
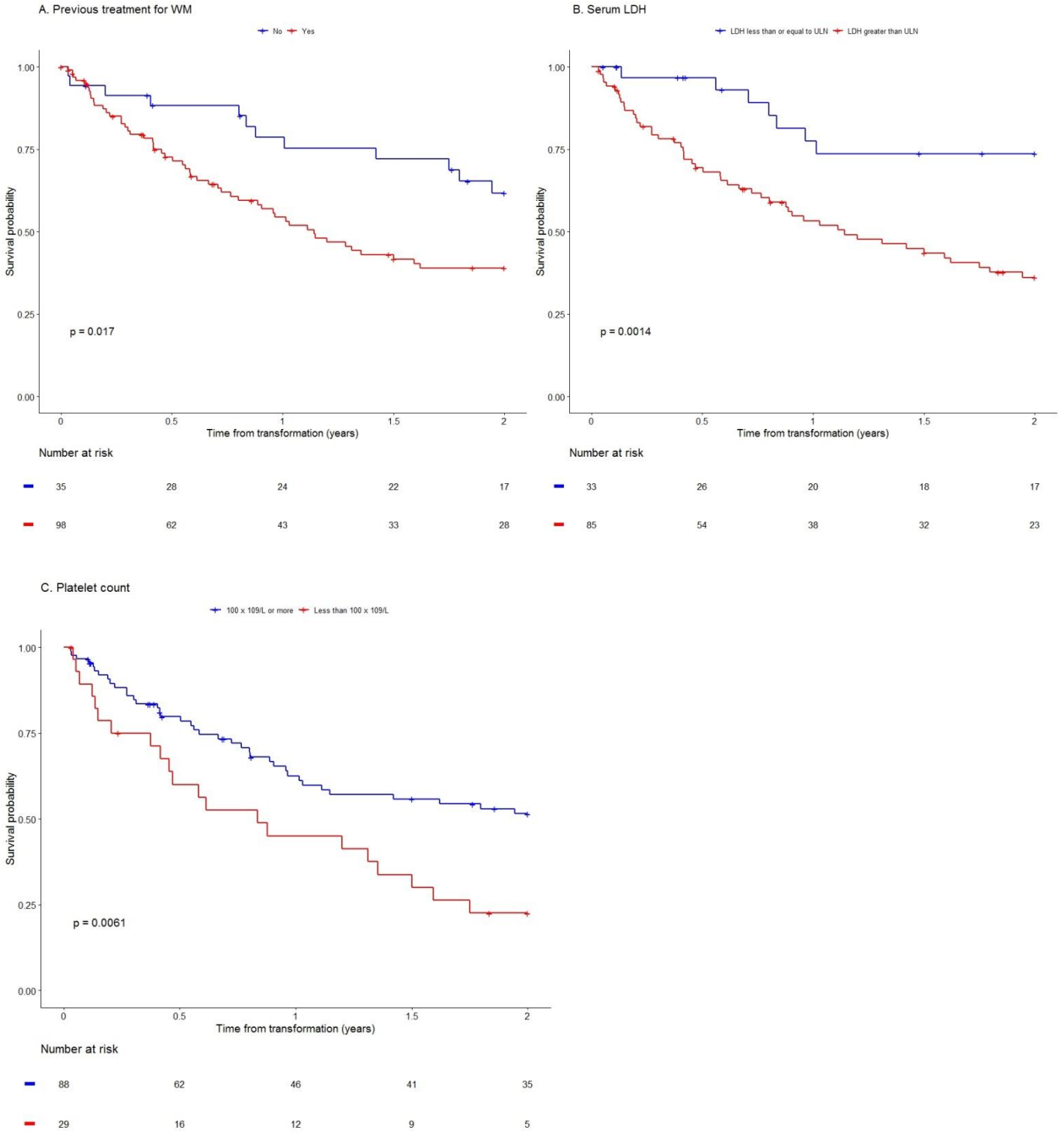
Supplementary Table 1. Accrual of patients

Center	Training set (n = 133)	Validation set (n = 67)
FILO centers (France and Belgium)	**80**	**8**
Lens	10	
Pitié Salpêtrière, Paris	9	
Poitiers	8	
Toulouse		8
Lyon (Léon Bérard)	7	
Strasbourg	7	
Henri Mondor, Créteil	5	
Reims	5	
Rouen	5	
Amiens	3	
Besançon	3	
Bruxelles	3	
Versailles	3	
Clermont-Ferrand	2	
Cochin, Paris	2	
Grenoble	2	
Saint-Louis, Paris	2	
Argenteuil	2	
Le Mans	1	
Nancy	1	
Dana Farber Cancer Institute, Boston, MA, USA	**36**	
University College London Hospitals, London, UK	**13**	
Nieuwegein, The Netherlands	**4**	
Mayo Clinic, Rochester, MN, USA		**27**
University Hospital and IBSAL, Salamanca, Spain		**15**
National and Kapodistrian University of Athens, Greece		**14**
Academical Medical Center, Amsterdam, The Netherlands		**3**

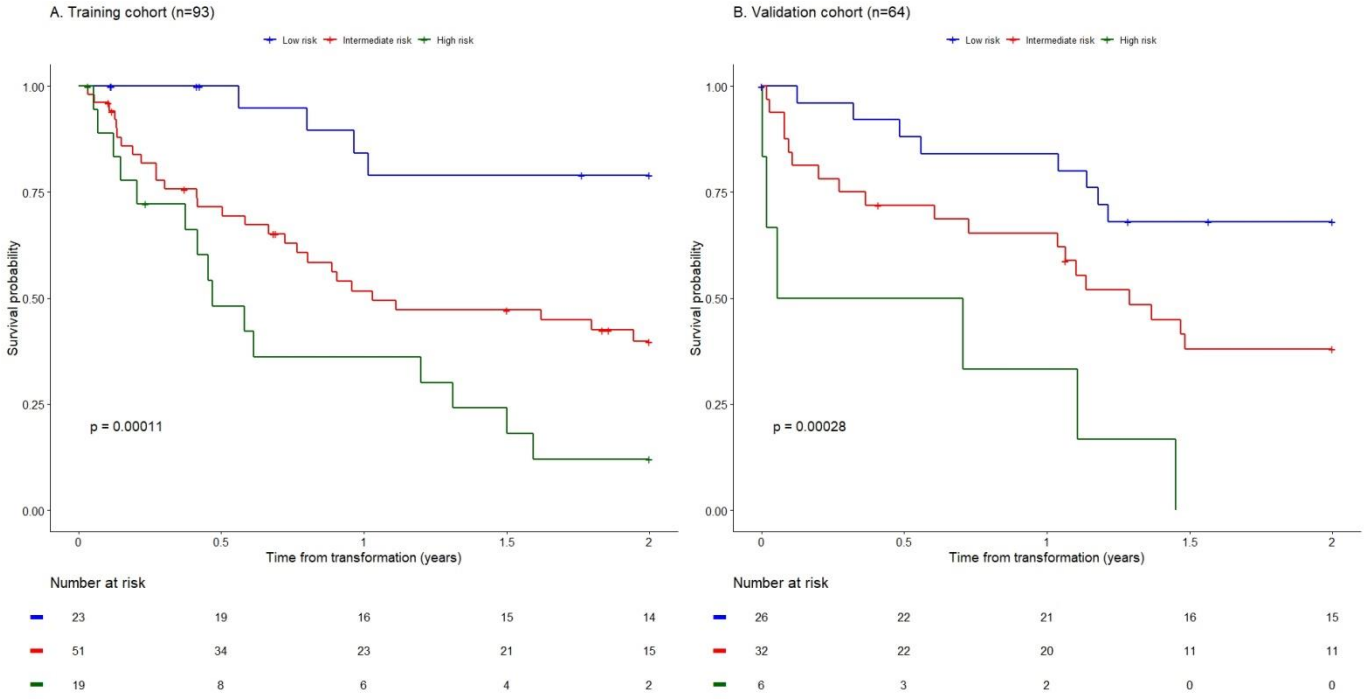
Supplementary Figure 1. Kaplan-Meier curves of survival after transformation. The median OS after HT was 19 months (95% CI 12-31 months) in the training cohort (A) and 18 months (95% CI 13-NR months) in the validation cohort (B).



Supplementary Figure 2. Kaplan-Meier curves of survival after transformation stratified by (A) previous treatment for WM, (B) LDH level at transformation, and (C) platelet count at transformation.



Supplementary Figure 3. Kaplan-Meier curves of survival after transformation according to subgroups defined by the tWIPI after exclusion of patients with concurrent disease. (A) Training cohort. (B) Validation cohort.



Supplementary Table 2. The transformed Waldenström International Prognostic Index: outcome and relative risk of death according to risk group after exclusion of patients with concurrent disease. (A) Training cohort. (B) Validation cohort.

(A) Training cohort (n = 93)

Risk group	Score	No. of patients (%)	Median survival, months	HR	95% CI
Low	0-1	23 (25)	NR	1.0	NA
Intermediate	2-3	51 (55)	12.3	4.2	1.5-11.9
High	4	19 (20)	5.6	8.4	2.8-25.5

HR, hazard ratio; CI, confidence interval; NR, not reached; NA, not applicable

Harrell's C-index: 0.75 (95% CI = [0.65-0.85])
The May and Hosmer goodness-of-fit test: P value > 0.8 for each stratum

(B) Validation cohort (n = 64)

Risk group	Score	No. of patients (%)	Median survival, months	HR	95% CI
Low	0-1	26 (41)	NR	1.0	NA
Intermediate	2-3	32 (50)	15.5	2.5	1.1-5.6
High	4	6 (9)	4.6	7.5	2.6-22.0

HR, hazard ratio; CI, confidence interval; NR, not reached; NA, not applicable

Harrell's C-index: 0.81 (95% CI = [0.65-0.93])
The May and Hosmer goodness-of-fit test: P value > 0.4 for each stratum

Supplementary Table 3. Outcome according to risk group as defined by the IPI and R-IPI in 99 patients with data available for tWIPI and IPI

Risk group	Number of IPI factors	Distribution of patients, %	2-year OS, %	HR	95% CI
Standard IPI					
Low risk	0-1	8	75	1.0	NA
Low-intermediate	2	17	52.9	2.5	0.5-11.7
High-intermediate	3	33	39.4	3.3	0.8-13.9
High	4-5	41	46.3	3.4	0.8-14.3
Revised IPI					
Very good	0	1	100	NA	NA
Good	1-2	24	58.3	NA	NA
Poor	3-4-5	74	43.2	NA	NA

IPI, International Prognostic Index; OS, overall survival; HR, hazard ratio; CI, confidence interval; NA, not applicable.

Supplementary Figure 4. Kaplan-Meier curve of survival after transformation according to MYD88 L265P mutation status.