

Independent Prognostic Value of Flow Cytometry (FCM) in Myelodysplastic Syndromes (MDS) - Composition of a Prognostic FCM-Score for Overall Survival

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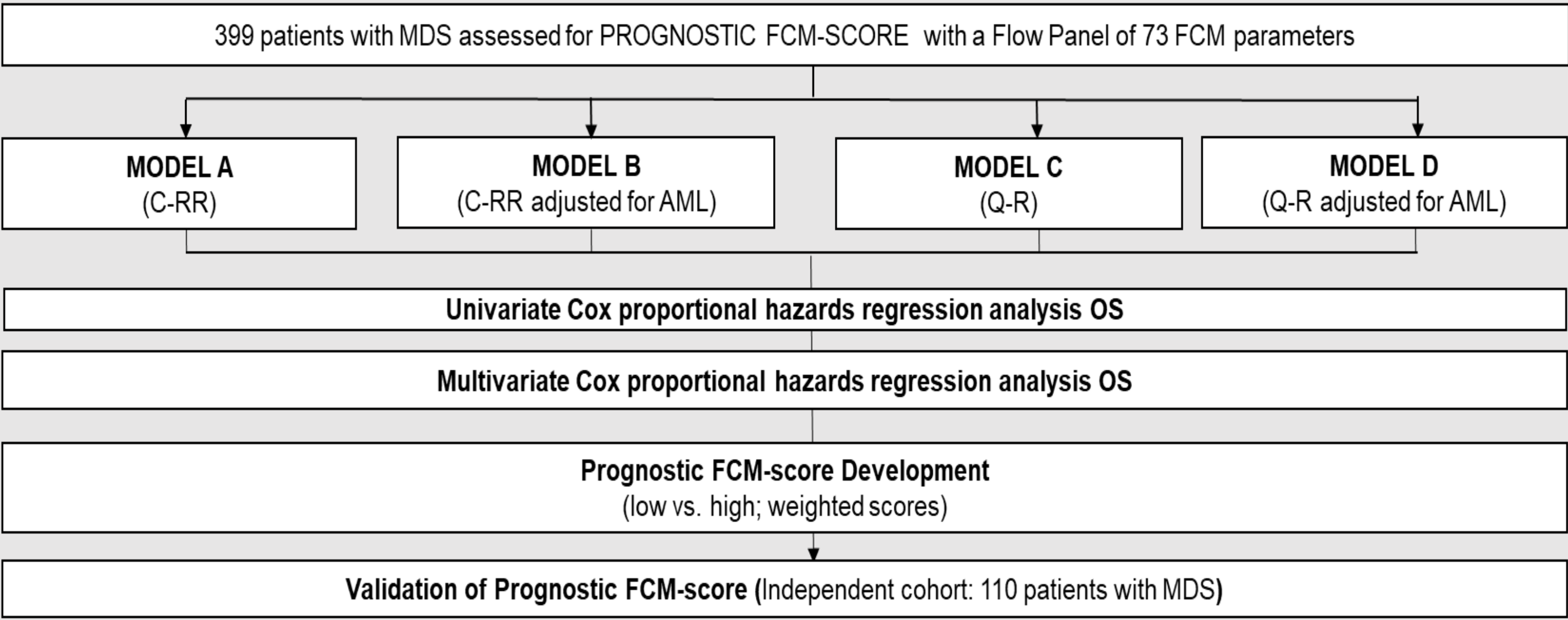
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AIMS

Flow cytometry (FCM) as recommended by European LeukemiaNet (ELN), is a co-criterion in MDS diagnostics. Could the FCM diagnostic parameters discriminate MDS patients with better overall survival (OS)? We aim to develop a prognostic marker panel for survival for MDS patients using manually gated flow cytometry data from a large cohort of individuals and to validate the performance of the prognostic FCM score in an independent cohort of MDS patients.

METHODS

Development of the MDS Prognostic FCM-score following an Adaptive signature design



CONCLUSION

- We have generated two novel prognostic scores based on distinct FCM characteristics which could predict overall survival in MDS patients.
- FCM-score A and B discriminate best MDS patients with better overall survival outperforming IPSS-R as well as Ogata, FCSS and iFS scores in both the training and validation cohort.
- FCM-score A and B includes the following flow parameters: progenitor cells (CD45-MFI, lyPC), granulocytes (CD33, CD15, SSC ratio (gran/ly), ratio ly/gran), lymphocytes (CD19+) and plasmacytoid dendritic cells measured in a laboratory.
- Currently, we are designing a biocomputational automatic pipeline to automatically gate the flow parameters.

Prognostic FCM-score A and B parameters

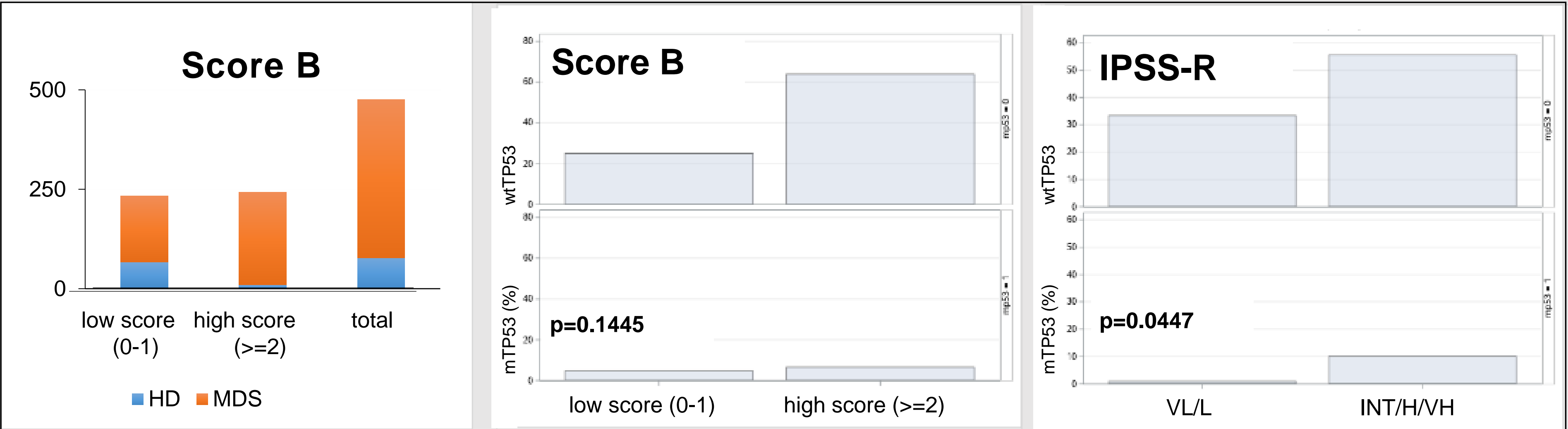
Parameter	Reference Ranges (DD)*
PC: CD45 MFI-ratio (Ly/PC)	>7.0 (>7.5)
PC: lyPC (%)	<5.0% (Ogata)
Granulo: CD33 MFI	>6600 (>29.75)
Granulo: CD15 MFI	<1500 (<61.85)
Granulo: SSC-ratio (gran/ly)	<6.0 (Ogata)
Granulo: Ly/Gran-ratio (%)	>1.0 (FCSS)
Lympho: CD19 (%)	<3,>15.0 (<1.47, >19.40)
Plasmacytic dendritic cells (%)	>1 % (>0.36 %)

* Lab-specific ranges. Amsterdam UMC-VUMC lab-specific reference ranges were given in parentheses. Abbreviations: PC progenitor cells, Granulo granulocytes, Lympho lymphocytes.

Prediction capability (ROC-analysis)

ROC Model	Mann-Whitney			
	Area	SD	95% Wald CI	
Model	0.7284	0.0276	0.6742	0.7825
age	0.4592	0.0296	0.4012	0.5171
sex	0.4699	0.0263	0.1483	0.5214
Score A	0.6913	0.0283	0.6358	0.7468
Score B	0.6998	0.0271	0.6466	0.7529
IPSS-R	0.6180	0.0309	0.5574	0.6786

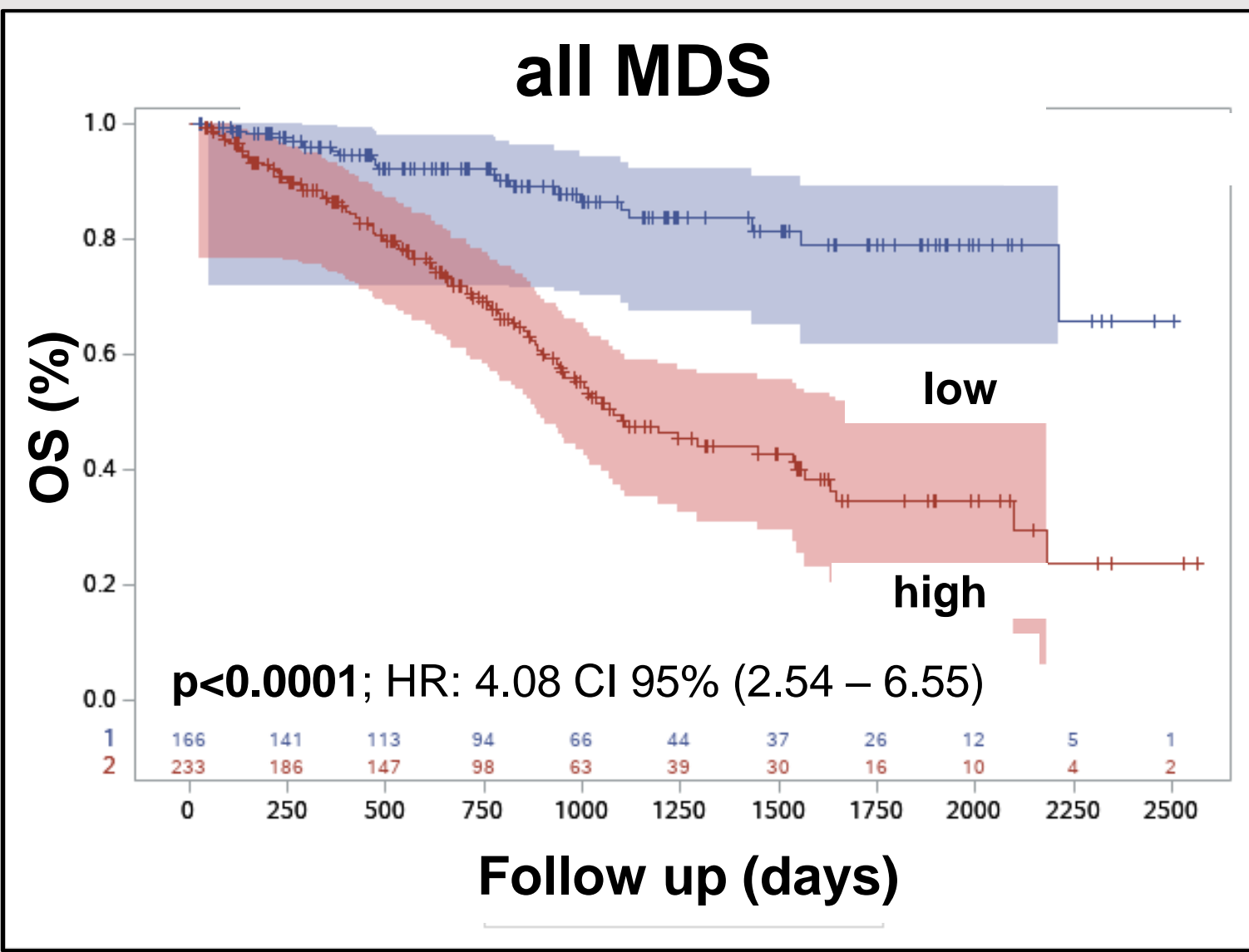
Reliability testing Healthy donors vs. MDS



Healthy donors show mostly a low Score B. There is no significant difference in the distribution of TP53 mutations in low vs. high Score B but for lower vs. higher IPSS-R

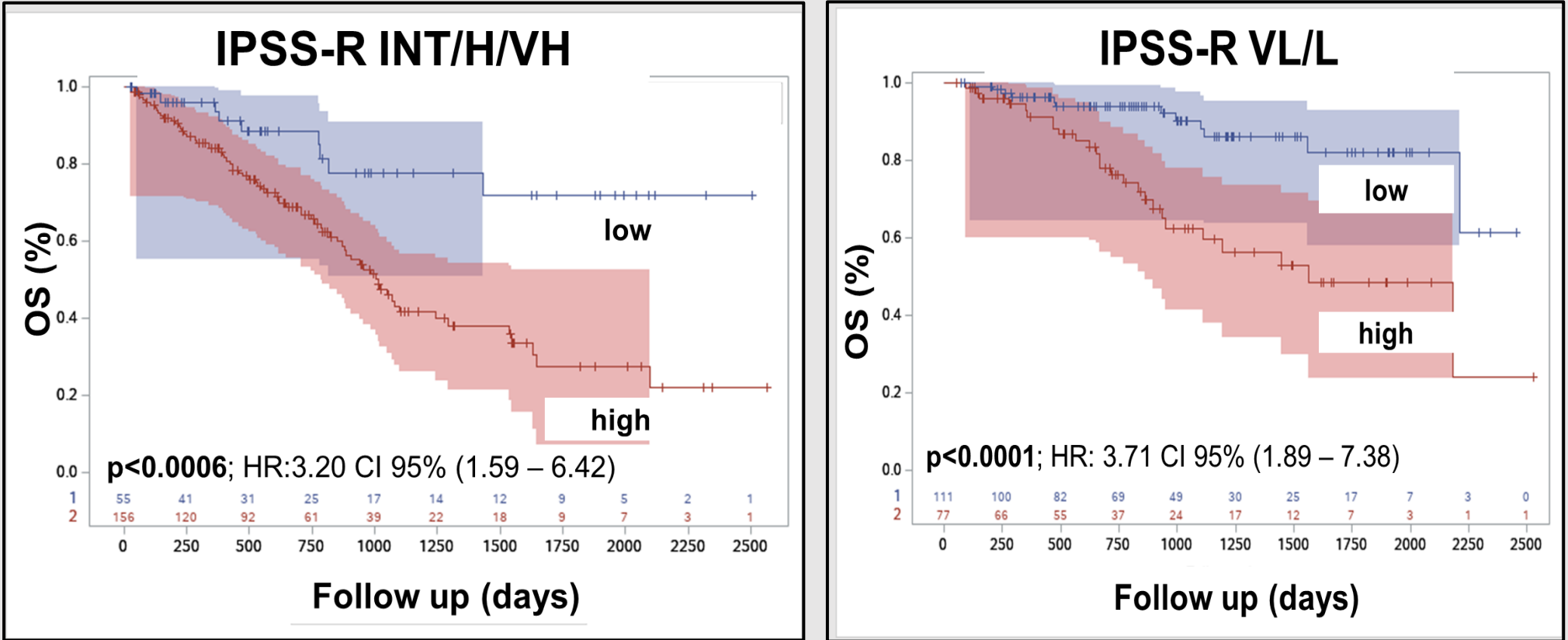
RESULTS

Overall survival Score B



* Low score <2 High score >=2.

Overall survival Score B in IPSS groups



* Low score <2 High score >=2.

* Low score <2 High score >=2.

Validation Prognostic FCM- score A & Score B

Training set
399 patients with MDS with Flow panel

Validation set
110 patients with MDS with Flow panel

Variable	P-value	HR	95% CI	
Prognostic FCM-score A	<0.001	2.077	1.726	2.5
Prognostic FCM-score A high vs low	<0.001	3.195	2.149	4.75
Prognostic FCM-score B	<0.001	1.905	1.598	2.271
Prognostic FCM-score B high vs low	<0.001	4.079	2.54	6.548

Variable	P-value	HR	95% CI	
Prognostic FCM-score A	<.0001	1.696	1.318	2.181
Prognostic FCM-score A high vs low	<.0001	2.914	1.74	4.88
Prognostic FCM-score B	0.0001	1.525	1.231	1.889
Prognostic FCM-score B high vs low	0.0024	2.672	1.416	5.041

Prediction capability (ROC-analysis)

ROC Association Statistics				
ROC Model	Area	Mann-Whitney		
		Standard Error	95% Wald Confidence Limits	
Model	0.724	0.0276	0.6742	0.7925
age	0.4592	0.0296	0.4012	0.5171
sex	0.4699	0.0263	0.4183	0.5814
Score A	0.6913	0.0283	0.6358	0.7469
Score B	0.6999	0.0271	0.6466	0.7529
IPSSR	0.619	0.0309	0.5574	0.6796

ROC Association Statistics				
ROC Model	Area	Mann-Whitney		
		Standard Error	95% Wald Confidence Limits	
Model	0.817	0.0422	0.7343	0.8998
age	0.7272	0.0489	0.6312	0.8231
sex	0.4923	0.0462	0.4017	0.5828
Score A	0.6843	0.0495	0.5873	0.7813
Score B	0.7035	0.0486	0.6082	0.7987
IPSSR	0.5694	0.052	0.4674	0.6714

Overall survival

