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Prognostic impact of splenomegaly on survival of Chinese with primary myelofibrosis

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ABSTRACT

Predicting survival in persons with primary myelofibrosis (PMF) is typically based on the International Prognostic Scoring System (IPSS), the Dynamic IPSS (DIPSS) or the DIPSS-Plus. These scoring systems use clinical and laboratory data developed predominately in persons of European descent. Splenomegaly is not a prognostic variable in any of these scoring systems. Recently, we reported differences in clinical and laboratory features between Chinese *vs.* persons of European descent with PMF. Based on this we developed a modified prognostic model to predict survival of Chinese subjects in which splenomegaly is an independent favorable prognostic factor. In the current study, we analyzed data from 874 Chinese with PMF including 495 with splenomegaly. Subjects with splenomegaly had significantly higher hemoglobin concentrations ($P < 0.001$), higher levels of WBCs ($P < 0.001$), platelets ($P < 0.001$), excess blood blasts ($\geq 1\%$; $P = 0.012$), less RBC-transfusion-dependence ($P < 0.001$) and lower DIPSS risk distribution ($P = 0.024$). Frequency of $JAK2^{V617F}$ (62% *vs.* 50%; $P = 0.003$) was also different. In univariate analyses subjects without splenomegaly had briefer survival (median, 64 mo [95% CI, 43–85] *vs.* 110 mo [95% CI, 67–153]; $P < 0.001$). In multivariate analyses, splenomegaly was a favorable prognostic correlate of survival independent of DIPSS risk-cohort (hazard ratio [HR] = 1.445; [95% CI, 1.101–1.895]; $P = 0.008$). Our data suggest including splenomegaly improves the predictive accuracy of the prognostic model to estimate survival of Chinese with PMF.

1. Introduction

Median survival of persons with primary myelofibrosis (PMF) is about 7 years but ranges from <2 to >10 years [1]. Different scoring systems were developed to predict survival of persons with PMF including the International Prognostic Scoring System (IPSS) [2], the Dynamic IPSS (DIPSS) [3], and the DIPSS-Plus [4].

These scoring systems were developed predominately in persons of European descent and include few Asians. Recently, we analyzed a large dataset of Chinese with PMF to test validity of these scoring systems and determine if additional clinical or laboratory variables improved the prognostic accuracy of these scoring systems in Chinese with PMF who constitute a substantial proportion of people with PMF worldwide [5]. We found frequencies of splenomegaly and anemia were significantly different between Chinese and persons of European descent with PMF and that splenomegaly, not included in the European-derived scoring systems, was an important independent predictor of survival in Chinese, and only 1% of Chinese are classified as high-risk in the DIPSS [5]. Based on these data we developed a modified prognostic scoring system for Chinese subjects which included splenomegaly. The aim of our current study is to validate the prognostic value of

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Table 1
Clinical characteristics ($N = 874$).

Characteristics	All subjects, *n* (%)	Splenomagaly, *n* (%)	No splenomegaly, *n* (%)	*P*
No.	874	495	379	
Gender				0.888
Male	445 (51)	251 (51)	194 (51)	
Age, years				0.395
Median (range)	55 (7–89)	55 (7–87)	56 (14–89)	
>65	175 (20)	83 (17)	92 (24)	0.006
Hemoglobin, g/L				<0.001
Median (range)	93 (28–211)	100 (29–200)	81 (28–211)	
WBC, ×10E9/L				<0.001
Median (range)	7.56 (0–170)	9.60 (0–170)	5.19 (1–160)	
Platelets, ×10E9/L				0.001
Median (range)	169.5 (2–2022)	198 (5–2022)	111(2–1800)	
Blood blasts ≥1%	187 (21)	121 (24)	66 (17)	0.012
Constitutional symptoms	180 (21)	108 (22)	72 (19)	0.307
RBC-transfusion-dependence	212 (24)	94 (19)	118 (31)	<0.001
$JAK2^{V617F}$ (582)	332 (57)	217 (62)	115 (50)	0.003
Cytogenetics				
Normal	316 (72)	194 (72)	122 (72)	0.939
Abnormal	123 (28)	76 (28)	47 (28)	
CK	24 (6)	16 (6)	8 (5)	0.593
MK	15 (3)	11 (4)	4 (2)	0.338
DIPSS				0.024
Low-risk	182 (21)	114 (23)	68 (18)	
Intermediate-1-risk	398 (46)	234 (47)	164 (43)	
Intermediate-2-risk	281 (32)	139 (28)	142 (38)	
High-risk	13 (2)	8 (2)	5 (1)	

CK, complex karyotype; MK, monosomal karyotype; DIPSS, Dynamic International Prognostic Scoring System (percents may not add to 100 because of rounding).

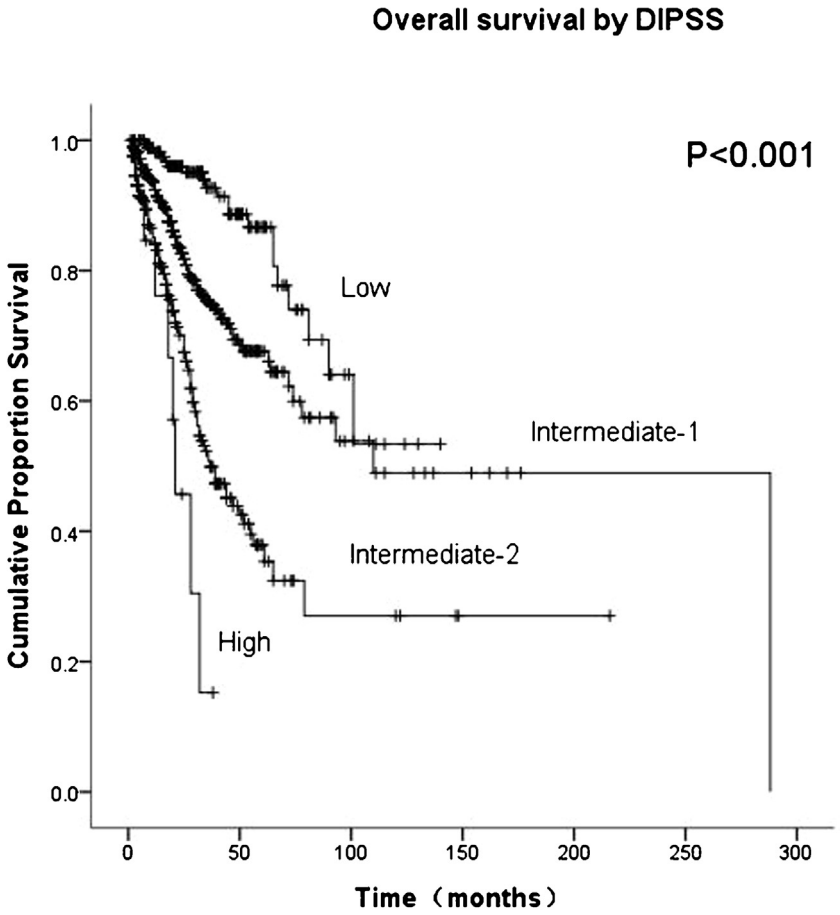

Fig. 1. Survival of subjects ($N = 874$) by Dynamic International Prognostic Scoring System (DIPSS) risk score.