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LETTER TO THE EDITOR

The prognostic value of circulating myeloblasts in patients with myelodysplastic syndromes treated with azacitidine

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Dear Editor,

The myelodysplastic syndromes (MDS) is a representative of myeloid clonal blood diseases with relatively heterogeneous spectrums of symptoms. The major clinical problem in MDS are morbidities caused by cytopenia or transition to acute myeloid leukemia (AML). The current clinical management of MDS focuses on assessing disease risk at diagnosis by assaying clinical and patient characteristics and using established prognostic scoring systems to estimate survival and risk of evolution to AML. Several prognostic scoring systems have been developed and validated, but the most widely used systems include the International Prognostic Scoring System (IPSS) and the Revised International Prognostic Scoring System (IPSS-R). Because the IPSS is limited in its ability to identify poor prognosis lower-risk patients, a prognostic scoring system specifically for lower-risk MDS patients (LR-PSS) was also developed at MD Anderson cancer center [1]. Recently, several studies demonstrated that the presence of peripheral blasts has a negative impact on overall survival (OS) independent of available prognostic risk models including the IPSS-R [2, 3]. However, the prognostic value of peripheral blasts (PBs) is not well-studied in patients with MDS treated with azacitidine. We, therefore, retrospectively evaluated the prognostic value of PBs in patients with MDS treated with azacitidine.

We enrolled 56 MDS patients treated with azacitidine as the first-line treatment. The definition of MDS with PBs was based on WHO-2016 criteria. From 2011 to 2018, 19 patients had PBs and 37 had no PBs at the time of starting azacitidine. The baseline characteristics of both groups are summarized in Table 1. There were no significant differences between the groups except for those in the IPSS-R score and World Health Organization (WHO) classification (Table 1). Patients with PBs (PB-MDS) had a significantly shorter median OS than those without PBs

Table 1 Baseline patient characteristics

	BM-MDS (n = 19)	PB-MDS (n = 37)	*p* value
Age > 75	8 (42.1%)	19 (51.4%)	0.580
Gender—male	11 (57.9%)	28 (75.7%)	0.223
Blood counts, median [range]			
White blood cell count (K/mcl)	3.0 [0.6–10.9]	2.9 [0.9–27.3]	0.261
Absolute neutrophil count (K/mcl)	0.8 [0.2–4.0]	1.2 [0.1–18.2]	0.350
Hemoglobrin (g/dL)	7.4 [6.3–13.3]	7.4 [5.1–9.3]	0.762
Platelets (K/mcl)	62 [7–273]	53 [8–194]	0.809
Blast percentage, median [range]			
Bone marrow	4 [0–20]	6 [1–16]	0.188
Peripheral blood	0 [0–0]	2 [1–11]	< 0.001
WHO classification			0.004
RA	1 (5%)	0 (0%)	
RARS	0 (0%)	0 (0%)	
RCMD	8 (42%)	5 (14%)	
Del 5q	0 (0%)	0 (0%)	
RAEB-I	4 (21%)	16 (43%)	
RAEB-II	4 (21%)	16 (43%)	
MDS-U	1 (5%)	0 (0%)	
CMML	1 (5%)	0 (0%)	
IPSS-R			0.029
Very low	0 (0%)	0 (0%)	
Low	2 (11%)	0 (0%)	
Int	7 (37%)	5 (14%)	
High	2 (11%)	8 (22%)	
Very high	8 (42%)	24 (65%)	
Karyotype complex	6 (31.6%)	17 (45.9%)	0.394

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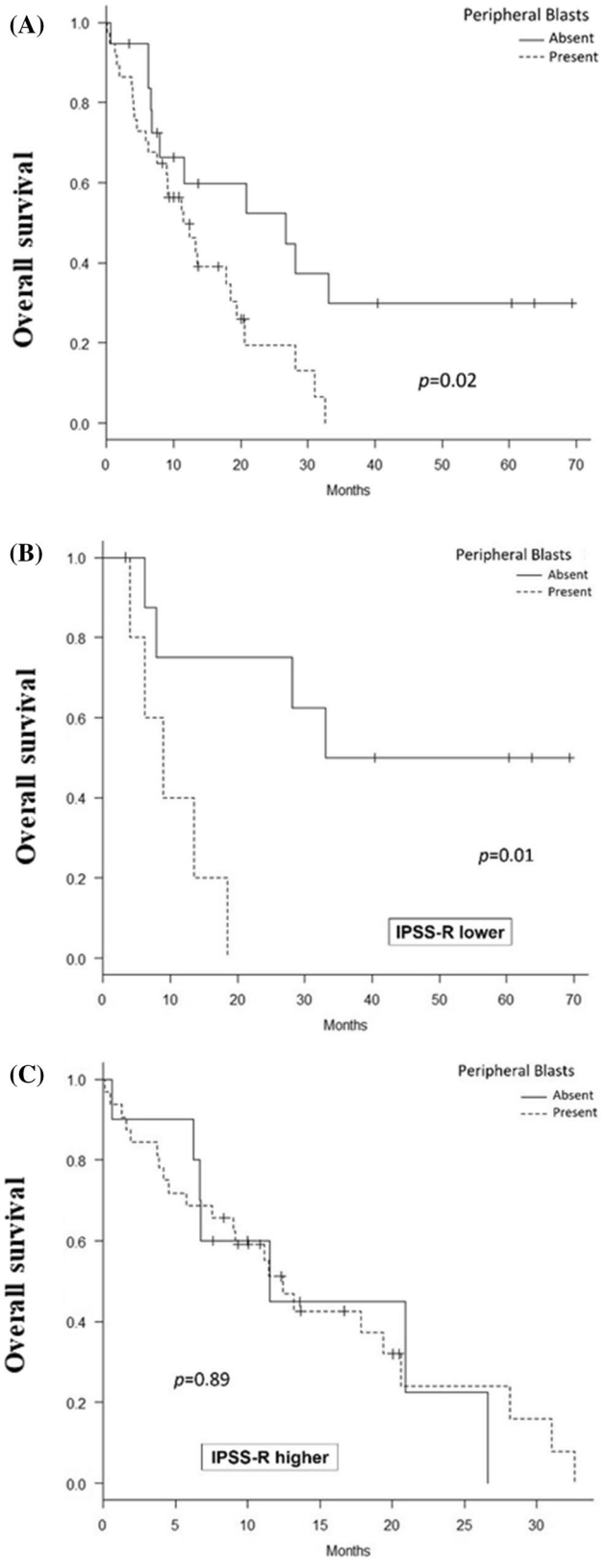

Fig. 1 Overall survival for: **a** the entire cohort. **b** IPSS-R lower-risk patients. **c** IPSS-R higher-risk patients

(BM-MDS) (11.0 vs. 28.0 months, $p < 0.02$, Fig. 1a). A Cox regression analysis showed that the presence of PBs was a negative independent prognostic variable for the OS (HR 2.4; 95% CI 1.1–5.1, $p = 0.02$). We then examined the impact of PBs among IPSS-R categories. As a result, differences in the survival were evident in patients with low or intermediate risk scores (8.9 vs. 33.1 months, $p = 0.01$, Fig. 1b). In contrast, the impact of PBs on the OS was relatively low in the high- and very-high-risk groups (12.4 vs. 11.5 months, $p = 0.89$, Fig. 1c). Among the five patients with PBs whose IPSS-R scores were low or intermediate, four died of disease progression and the other died of severe infection. In addition, their karyotype risk on IPSS-R was not complex type (one patient was very good, three patients were good, and one patient was intermediate).

It is well known that a subset of patients with lower-risk MDS as predicted by the available prognostic models fares poorly and has a median survival similar to patients with higher-risk disease [1]. Our results show that the presence of PBs is a predictor of poor outcome in patients with MDS treated with azacitidine, particularly in lower-risk cases of IPSS-R. This coincides with the findings of a previous study [2]. We confirmed there was no association between bone marrow blasts and peripheral blood blasts by Mann–Whitney U test (Table 1) or Correlation analysis ($r = 0.219$, $p = 0.104$). In addition, the median OS of the patients with lower-risk PB-MDS were shortest among all groups (8.9 months). Therefore, it is very meaningful to promote segmentation of prognostic predictions in order to detect subsets of high-risk patients with lower-risk MDS as predicted by available prognostic models. Since our results were obtained in a small-sized retrospective analysis, further large-scale prospective studies are warranted to verify these findings.

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Compliance with ethical standards

Conflict of interest All authors have no potential conflicts of interest to report.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patients. The study was approved by the Ethics Committee of Yokohama Municipal Citizen's Hospital.

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