Letter to the Editor

Flagging performance of two automated hematology analyzers in blast cell screening

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With the rapid development of automated hematology analyzers, hematology analyzers have gradually become routinely adopted in hematology laboratories, with improved efficiency and accuracy. To enable the laboratory to review specific blood specimens selectively and to significantly improve the efficiency and quality of clinical laboratories, the capability of hematology analyzers to identify and flag abnormal cells has become one of the most critical links (1). Whether there are blast cells in peripheral blood (PB) is of great value for clinical screening and monitoring of the occurrence and progression of hematological malignancies (2,3). For hematological malignancies, early diagnosis and treatment are beneficial to patients' long-term survival (4,5). Therefore, the sensitivity of hematology analyzers for the detection of blast cells has become a focus of hematology laboratories. We carried out comparative adding experiments of blast cells with 2 automated hematology analyzers (Mindray BC-7500CRP, Sysmex XN-1000) in our laboratory to compare their flags for blast cells and evaluated the blast flagging capability of the 2 hematology analyzers, with the microscopic results of blast cells as the quantitative gold standard.

In this study, 16 cases of EDTA-K2-anticoagulated venous whole blood specimens from the clinical laboratory of Fujian Medical University Union Hospital were collected from June 2020 to August 2020, including 11 cases of acute myeloid leukemia (AML) and 5 cases of acute lymphoblastic leukemia (ALL). Specimens from 10 healthy controls with the same blood grouping were collected as the base pool. The volume of each anticoagulated whole blood specimen was not less than 1.5 mL, and the experiment was completed within 8 h after collection.

The instruments and supporting reagents used in this study were the Mindray BC-7500CRP automated hematology analyzer and supporting calibrators, quality controls, and reagents (Mindray, Shenzhen, China); the Mindray SC-120 automated blood smear preparation instrument and supporting reagents (Shenzhen Mindray, China); and the Sysmex XN-1000 automated hematology analyzer and supporting reagents (Sysmex, Kobe, Japan). When the blast cell is detected, the instrument will generated by the instrument. The microscopic results of blast cells is performed by two clinical pathologists with ample experience in morphology, who observed and recorded the morphological features of various blood cells.

Blood specimens containing a series of concentration gradients of blast cells were prepared in this study and detected in parallel on 2 hematology analyzers. The concentration points of blast cells that were flagged by the instruments were summarized and the detection thresholds were calculated. The specific operating procedures were described in Appendix 1.

The minimum Blast% and Blast# results of the 2 instruments from their "blast" flags were expressed as median (P25–P75) and were statistically analyzed with Prism v8.2.1 (GraphPad). The quantitative data of the 2 groups were compared using the Wilcoxon signed rank test for paired samples. $P<0.05$ indicated statistical significance.

In the 16 groups of experimental data (*Figure 1*), the sensitivities of the 2 instruments in blast cell screening had their own advantages and disadvantages. Paired statistical analysis showed that the results of Blast# and Blast% at the minimum threshold of the Mindray BC-7500CRP were 0.09×10^9/L (0.04×10^9/L–0.16×10^9/L) and 1.4%

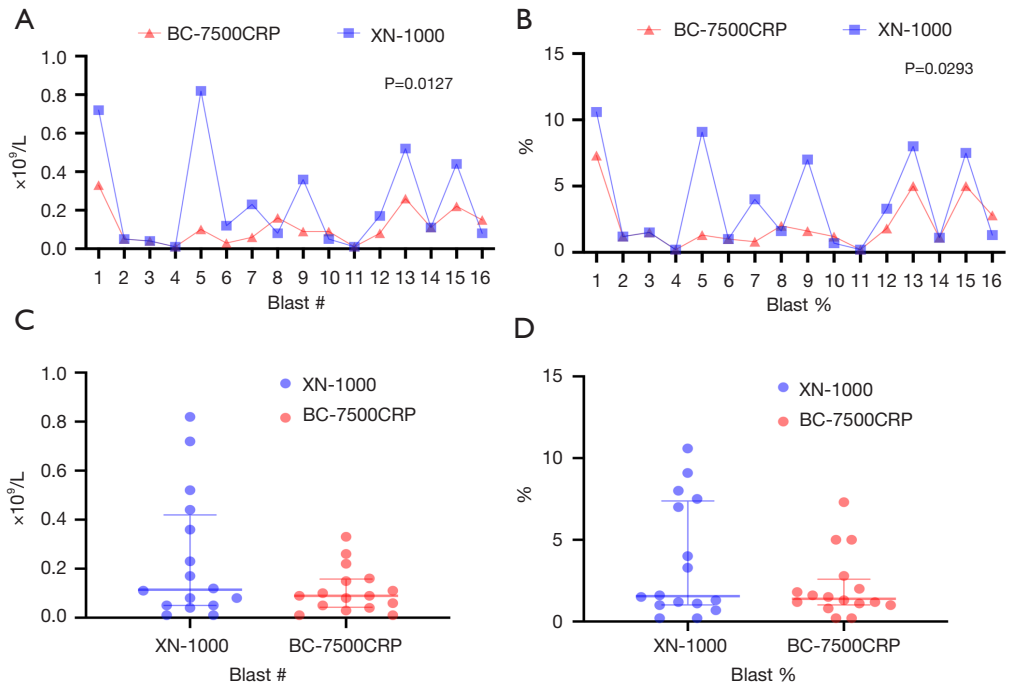

Figure 1 Comparison of blast flagging capability between the Mindray BC-7500CRP and the Sysmex XN-1000. (A) Minimum Blast# of the 2 instruments for the 16 groups of specimens; (B) minimum Blast% of the 2 instruments for the 16 groups of specimens; (C) median of the minimum Blast# of the 2 instruments; (D) median of the minimum Blast% of the 2 instruments.

(0.2–2.6%), respectively, which were significantly lower than those of the Sysmex XN-1000 at the minimum threshold [0.12×10^9/L (0.05×10^9/L–0.42×10^9/L) and 1.6% (1.0–7.4%), respectively] (P<0.05).

According to the above experiments, the minimum thresholds of the Mindray BC-7500CRP and the Sysmex XN-1000 for Blast# were both 0.01×10^9/L, and the 2 hematology analyzers could detect all blasts larger than 0.33×10^9/L and blasts larger than 0.82×10^9/L, respectively. Some studies have shown that if the number of PB blasts is higher than 2,000/μL (i.e., 2×10^9/L) at the time of initial diagnosis, PB examination can replace bone marrow (BM) examination as a means to evaluate the diagnosis and treatment of AML (6). In addition, the National Comprehensive Cancer Network (NCCN) guidelines for the diagnosis and treatment of ALL in 2020 state that the results of PB examination can be used to diagnose ALL if the blast cells in PB are higher than 1,000/μL (i.e., 1×10^9/L) (7). The blast flagging thresholds of the 2 instruments met the detection requirements of PB blast cells for the clinical initial diagnosis of acute leukemia (AL), and the high sensitivity of their blast flagging can provide reliable and effective auxiliary information during initial diagnosis of AL.

Studies on AML have found that there are residual blast cells in the PB at the early stage (3–7 days) after chemotherapy, with little interference from background cells and with a high sensitivity and specificity for minimal residual disease (MRD) detection (8). By calculating the decline rate of the tumor load, the existing prognostic stratification system of molecular biology/cytogenetics can be further supplemented, which can be used as the clinical basis for the adjustment of individualized treatment (9).

At present, clinical guidelines still regard BM examination as the main method of monitoring MRD in AL patients in the remission stage. Compared with BM examination, PB examination is simpler and more convenient, and patients have a higher acceptance of it and tolerate relatively frequent sampling. One AML study found a significant correlation between the PB-based MRD rate and the BM-based MRD rate, so PB-MRD, given its high specificity, can be used as an independent predictor of efficacy duration (8). In addition, ALL-MRD related studies have demonstrated that PB-MRD detection can be used to monitor the disease changes of T-cell ALL and can also provide prognostic information for patients with

B-cell ALL (9,10). The blast flags of hematology analyzers indicate the appearance of blast cells in PB which is helpful in the clinical warning of the early recurrence of AL and for starting timely treatment of the disease (8-10). Accurate and timely detection of blast cells in PB is helpful for the screening and diagnosis of AL, timely observation of hematological reactions to chemotherapy, and continuous monitoring of disease changes as well as significantly bolstering clinical monitoring from diagnosis to treatment to recurrence detection (4,8).

Manual microscopy usually is the last step of the laboratory process for the screening of abnormal cells in patient PB. However, routine manual microscopy examination often causes some troubles, such as affecting laboratory work flow, efficiency and requiring a high labor cost. We suggest that the proper reference interval and high sensitivity and acceptable specificity of blast flagging capability by automated hematology analyzer can reduce unnecessary labor-intensive visual differential counts. The 2 automated hematology analyzers above meet the clinical needs of detecting PB blast cells. However, this study was mainly based on adding specimens in the laboratory, and we will continue to evaluate the detection of real-world PB blast cells.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-5238). The authors reported funding support from the Joint Funds for the Innovation of Science and Technology, Fujian Province (No. 2017Y9051), and Fujian Provincial Health Technology Project, promote appropriate technology projects for the grass-roots (No. 2019014). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All the specimens enrolled in this study were specimens left over after the laboratory issued its test reports. We had no contact with the patients, and the privacy and interests of patients were not infringed, so the signing of informed consent forms was not required.

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Supplementary

Appendix 1

The specific operating procedures of blood specimens containing a series of concentration gradients of blast cells

(I) Whole blood samples containing a high concentration of blasts were centrifuged to obtain white blood cells as the 100% concentration point.
(II) Mix it with the DS diluent to obtain a 50% concentration point, and follow the above steps to prepare the white blood cell suspension with 10 concentration gradients;
(III) Ten leukocyte suspensions (50 μL) with different concentration gradients was added to 10 healthy controls (950 μL) of the same blood grouping to obtain 10 specimens with different blast cell concentration gradients (test pool #1–10, 1 mL/specimen);
(IV) Ten test pools were tested twice in the full channel mode of the Mindray BC-7500CRP and Sysmex XN-1000;
(V) The "Blast" flags (including Blast? and Abn Lympho/Blast?) of the 2 instruments were compared and recorded. Mindray SC-120 micro mode was used to prepare a blood smear (Wright-Giemsa staining) with 100% concentration point specimens. Two senior experimenters reviewed the blood smears above and calculated the absolute value of blast cells in a series of concentrations of the specimens (halved in succession) according to the microscopic examination results of the Blast% and leukocyte counts of the test pool #1 specimens;
(VI) Another 15 specimens with high concentrations of blast cells were selected to repeat steps (I–VI) to obtain a total of 16 groups of experimental data;
(VII) The minimum blast cell percentage (Blast%) and the minimum blast cell count (Blast#) corresponding to the "blast" flags of the 2 instruments were counted.

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