

RESEARCH ARTICLE

Establishment of improved review criteria for hematology analyzers in cancer hospitals

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Abstract

Background: Although hematologic review criteria for general hospitals have been established, they may be insufficient for cancer hospitals. This study aimed to establish the appropriate review criteria for hematology analyzers in cancer hospitals.

Methods: A total of 1003 samples from our hospital were randomly selected for blood smear preparation and microscopic review. The review criteria of the International Consensus Group for Hematology Review (ICGH) and Chinese consensus group were used to obtain the review, true-negative (TN), true-positive (TP), false-negative (FN), and false-positive (FP) rates, as well as the triggered rules. Our review criteria were established by comparing flag or numeric value information of TP and FP samples, adjusting rules to obtain better efficiency, a low slide review rate, and an acceptable FN rate.

Results: Overall, 197 (19.64%) samples showed positive smear findings. Compared to the ICGH criteria, the slide review rate of the newly established criteria declined from 51.25% to 39.28%, and the TP and TN rates increased from 17.85% and 46.06% to 23.13% and 55.83%, respectively. The FN rate of the newly established criteria was 3.69%. Another set of samples used to validate the newly established criteria yielded the review, FN, and FP rates as 33.49%, 1.86%, and 25.58%, respectively.

Conclusion: The newly established review criteria for hematology analyzers enabled the prompt identification, smear, and further verification of doubtful specimens, without a significant increase in the workload, thus improving the efficiency of the review process. This study provided data support for other cancer hospitals to establish review criteria.

KEYWORDS

alarm flag, cancer hospital, hematology analyzer, morphology, review criteria

Xiaoyan Wang and Xu Wang These authors have contributed equally to this study.

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1 | INTRODUCTION

Although automated hematologic analyzers are widely used for a complete blood cell count, a peripheral blood smear review is still required when abnormal blood cells appear.^{1,2} Improvements in hematologic analysis technology have enabled rapid and highly accurate results for clinicians. The emergence of automatic blood smear preparations and microscopy examination units has also simplified the manual slide review.^{3,4} Artificial intelligence is projected to be widely used in medical laboratories.^{5,6} As such, review criteria for hematologic analysis systems that can shorten the working time, while covering all morphologic abnormality information, are becoming increasingly important.⁷

The International Consensus Group for Hematology Review (ICGH) has developed the guidelines for action after the introduction of the automated hematology analysis in 2005.⁷ Accordingly, medical laboratories in China have achieved a consensus that each laboratory should have a manual slide review criteria for hematology analyzers.^{8,9} In 2008, the Chinese consensus group developed 23 guidelines for the Sysmex XE-2100 hematology analyzer (SYSMEX).¹⁰ However, the detection principle and performance of XN-9000 are considerably different from those of XE-2100. Hence, new review criteria for the XN-9000 automated hematology analysis system for clinical operation need to be established.

Moreover, the samples obtained from patients in cancer hospitals are different from those in general hospitals, and thus, the available review criteria might be inapplicable for the laboratories in cancer hospitals. The number and morphology of blood cells in cancer patients are often altered due to treatment (eg, radio/chemotherapy) or other cancer-related conditions (eg, anemia, neutropenia, and myelosuppression).^{11,12} Thus, specimens in cancer hospitals have higher positive and review rates than those in general hospitals.

This study aimed to establish the appropriate review criteria for hematology analyzers specific for cancer hospitals.

2 | MATERIALS AND METHODS

2.1 | Instruments and reagents

XN-9000 automatic hematology analysis system (analysis modules: A1 × 2, A2 × 1, slide marker/stainer modules: SP-10 × 1, slide review modules: DI-60 × 1; Sysmex, Kobe, Japan) and OLYMPUS BX53 optical microscope (Olympus) were used. Several channels have been newly introduced in the XN series: WDF channel, WNR channel, WPC channel, and fluorescent platelet (PLT-F) channel. Fluorescent labeling of cells occurs after the cell membrane is perforated by specific lysing reagents. Thereafter, a polymethine dye enters the cell and binds to nucleic acid and bioreactive proteins in the cytoplasmic organelles. Three signals are produced: forward scattered light, providing information on cell size; side scattered light, providing information on internal cell structure; and side fluorescence, providing information on DNA/RNA content.¹³

The hematology analyzers were calibrated using XN CAL (Lot #: 62842101) and XN CALPF (Lot #: 62842102) prior to use and were included in the Sysmex global network of external quality control system every day. The accepted coefficient of variations (CVs) of the parameters in the internal quality control was 1/3 total CV% given by Clinical Laboratory Improvement Amendment 88 (CLIA'88). The CV% of white blood cells (WBCs), red blood cells (RBCs), hemoglobin, mean corpuscular volume, and platelets (PLT) were 2.15%, 0.96%, 0.87%, 1.15%, and 3.73% for lower-level quality control samples and were 1.64%, 0.92%, 0.6%, 0.91%, and 2.55% for higher-level quality control samples in our laboratory, respectively. Each instrument has passed the performance verification standard recommended by the National Committee for Clinical Laboratory Standard H26 (NCCLS-H26).

2.2 | Patients

This study comprised a total of 1003 blood samples from the daily laboratory workload of the Tianjin Medical University Cancer Institute and Hospital. The samples were collected in K₂-EDTA tubes (Becton Dickinson) and were tested using the XN-9000 system within 30 minutes to 2 hours after collection. The automated results obtained by analysis modules were inputted to Laboman 6.0 software. For preparing the smear, the speed and angle of the slide were adjusted automatically using SP-10, according to the hematocrit (HCT) value of each sample, and then, two smears were pushed and stained. Each smear was pre-examined using DI60. The samples were collected from more than 20 clinical in-patient departments, including hematology, breast, colorectal, lymphoma, pediatrics, and lung oncology from February 2017 to November 2017. Among the included patients, 458 were males and 545 females, aged 1-90 years, including first-time and re-visiting patients. Another 215 samples from the daily laboratory workload were used for validation.

This study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of Tianjin Medical University Cancer Institute and Hospital. Written informed consent was obtained from the participants.

2.3 | Manual slide review

Each sample was examined independently by two experienced technicians blinded to the automated DI-60 and microscope results. Discrepant smear results between the two technicians were reviewed by one laboratory physician to achieve consensus. A positive smear result was defined according to the ICGH criteria and entered to Laboman software manually. If a rule was triggered, and the smear contained a positive finding, the sample was graded as true positive (TP). If a rule was triggered, but the smear did not contain any positive findings, the sample was graded as false positive (FP). True negative (TN) indicated that a sample did not trigger any rule, and the smear did not contain any positive finding. False negative (FN) indicated that

the sample did not trigger any rule, but the smear contained a positive finding.⁷ The review rate represented the percentage of review samples that triggered the smear rules without “3R” function.

2.4 | Study design

This study used 1003 samples to compare the review rate, FP, and FN rates between ICGH criteria and Chinese criteria. We accepted a FN rate <5%, as recommended by ICGH. We adjusted rules to obtain better efficiency, a low slide review rate.

2.5 | Statistical analysis

All statistical analyses were performed using SPSS 13.0 (SPSS Inc) and GraphPad Prism 5.0 (Graph Pad Software Inc). The receiver

operating characteristic (ROC) curve was used to evaluate the sensitivity and specificity of the cutoff values. The Kappa value was used to evaluate the agreement between the two technicians, with a Kappa value below 0.4 indicating poor agreement; 0.40-0.75, fair to good agreement; and >0.75, high agreement.¹⁴ The review, FN, and FP rates of the different criteria were obtained using Laboman software.

3 | RESULTS

3.1 | Analysis of smear review findings

In total, 197 (19.64%) of the 1003 samples showed positive smear results, including 285 occurrences, according to the ICGH definition. The proportion of morphology abnormality is shown in Figure 1. Among the positive samples, the three most common findings of

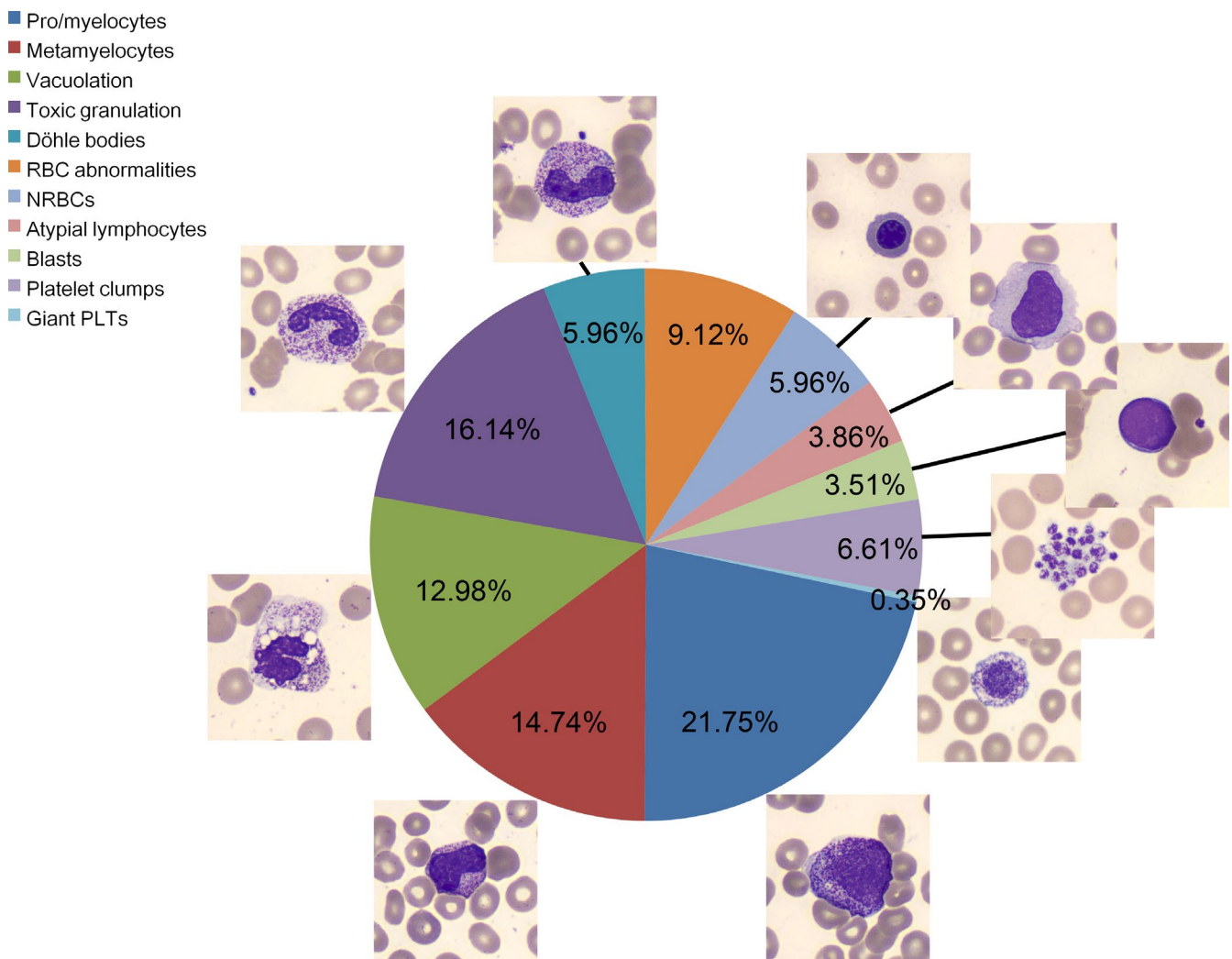


FIGURE 1 Proportion of morphology abnormality. Among the 285 positive occurrences, the proportion of neutrophil abnormalities was 71.57%, including pro/myelocyte, metamyelocyte, toxic granulation, vacuolation, and Döhle bodies. The proportion of RBC abnormalities was only 9.12%, which were not shown with images, and those of NRBCs were only 5.96%. Abnormal WBCs included atypical lymphocytes (3.86%) and blasts (3.51%). Platelet clumps (5.61%) were more common than giant PLTs (0.35%). All images were collected from the DI-60

abnormal morphology were pro/myelocytes (21.75%), toxic granulation (16.14%), and metamyelocyte (14.74%). Other abnormal WBCs were vacuolation (12.98%), Döhle bodies (5.96%), atypical lymphocytes (3.86%), and blasts (3.51%). There were 26 (9.12%) and 17 (5.96%) RBC abnormalities and nucleated RBCs (NRBCs), respectively. Platelet clumps (5.61%) were more common than giant PLTs (0.35%). Excellent agreement was obtained between the two technicians, with a kappa value of 0.758 ($P < .001$).

3.2 | False-negative sample analysis

The FN rate of the Chinese criteria was 4.99%, which was close to the upper limit of the recommended level. The ICGH criteria had a lower FN rate of 1.79% than did the Chinese criteria. Therefore, we established new criteria based on the ICGH criteria. We conducted an FN analysis of the ICGH criteria, and the most frequent FN findings were abnormalities of WBC morphology and pro/myelocyte/metamyelocyte, followed by abnormalities of RBC morphology and by atypical lymphocyte and blast cell (Table 1).

3.3 | False-positive and true-positive analyses

The FP and TP rates are shown in Table 2. In total, 95 FP cases triggered the WBC count rule (rule 5), with 47 cases triggering the single rule. The TP cases that only triggered rule 5 included PLT clump

TABLE 1 False-negative analysis of the ICGH criteria

Microscopic review	n (%)
Metamyelocyte, myelocyte, promyelocyte	8 (34.78)
Atypical lymphocyte	1 (4.35)
NRBCs	0 (0.00)
Blast	1 (4.35)
RBC morphology	5 (21.74)
Platelet morphology	0 (0.00)
WBC morphology	8 (34.78)
Total number of FN occurrences	23 (100.00)
Total FN cases	18

Abbreviations: FN, False negative; NRBCs, Nucleated red blood cells; RBC, Red blood cell; WBC, White blood cell.

(four cases), immature granulocytes (three cases), toxic granulation (one case), and abnormal RBC morphology (one case). There were 74 FP cases that triggered the NRBC# rule (rule 22), with 29 cases triggering a single rule. The TP cases, which only triggered rule 22, included abnormal RBC morphology (one case), metamyelocyte (one case), NRBC (one case), and toxic granulation (one case). Meanwhile, 37 FP cases triggered the reticulocyte# rule (rule 23), with 14 cases triggering a single rule. Only one case that triggered rule 23 was TP, which was discovered to have a metamyelocyte on blood smear.

A total of 81 FP cases triggered the platelet clumping flag rule (rule 30), with 23 cases triggering a single rule. The TP cases that only triggered rule 30 included one case of blast (no lineage

Rule no.	Parameters	Rules	FP rate % (n)	TP rate % (n)
5	WBC count	$<4.0 \times 10^9/L$ or $>30.0 \times 10^9/L$, first test	12.42% (95)	4.61% (25)
30	Platelet clumping flag	Flag	10.59% (81)	9.59% (52)
24	Suspect flags (except IG/ band)	Flag (adult), first test	10.20% (78)	5.72% (31)
22	NRBC#	>0 , first time	9.67% (74)	5.90% (32)
31	Platelet flags	PLT and MPV flags except PLT clumps	6.41% (49)	8.30% (45)
35	Atypical lymphocyte flag	Flag, first test	5.49% (42)	3.14% (17)
23	Reticulocytes#	$>100 \times 10^9/L$, first test	4.84% (37)	1.48% (8)
32	Immature granulocyte flag	Flag, first test	4.58% (35)	5.90% (32)
33	Immature granulocyte flag	Flag and previously confirmed data with positive delta that failed for WBC count	4.58% (35)	6.83% (37)
34	Left shift flag	Flag	4.18% (32)	12.73% (69)

TABLE 2 False- and true-positive analyses of the ICGH criteria

Abbreviations: FP, false positive; IG, immature granulocyte; MPV, mean platelet volume; NRBC, nucleated red blood cells; PLT, platelet; TP, true positive; WBC, white blood cell.

specificity), one case of abnormal RBC morphology, and one case of toxic granulation and vacuoles. There were 35 FP cases that triggered the immature granulocyte flag rule (rule 32), of which only 13 cases triggered a single rule. Some immature granulocytes were observed in the slide review of the 13 cases, but the percentage of immature granulocytes did not meet the microscopic review criteria for a positive smear.

Patients with cancer generally have high automated results of IG%. Thus, we determined the cutoff value using the ROC curve. The IG% results from the analyzers were between 0% and 39.5%, and 96 cases of immature granulocytes were positive on microscopic review. The ROC curve showed that the optimal cut-off value was 1.85% (AUC: 0.832, $P < .001$), with a sensitivity of 90.69% and specificity of 73.0%.

No sample triggered the single rules' suspect flags (except ImmG/band flag, rule 24) and platelet flags (rule 31).

3.4 | Established criteria

The criteria were established according to the analysis of the FN, FP, and the characteristics of WPC and PLT-F channel. The adjustments are shown in Table 3. The FN sample of the missing blast cell was

found in a patient with lymphoma. The automated results showed that the white blood cell count was $4 \times 10^9/L$, the monocyte percentage was 15%, and the absolute monocyte value was $0.60 \times 10^9/L$, which did not trigger the mono# rule (rule 19). Therefore, to avoid the leak in abnormal blood cells, we changed rule 19 as follows: first-time result, monocyte $>1.5 \times 10^9/L$ (adult) or $>3.0 \times 10^9/L$ (child, <12 years), or mono% $\geq 15\%$.

According to FP and TP analyses, we adjusted rules 5, 22, 23, 30, and 32. We identified the cutoff value of IG% as 1.85% according to the detection results of immature granulocyte and the positive occurrences in the smear slide. Rule 32 was adjusted to smear review when the IG% was $>1.85\%$ and other WBC-associated flags. Given that no sample triggered rules 24 and 31, these rules were not adjusted. We also did not adjust rules 33 and 34 according to clinical treatment because the granulocyte colony-stimulating factor was often used to increase the total number of white blood cell in our hospital.

We added a specific channel (WPC or PLT-F) retest to rules 35, 10, and 27. The comparison of the performance between the ICGH and newly established criteria is shown in Table 4. The review, FN, FP, TP, and TN rates were compared. The newly established criteria obtained review, FN, and FP rates of 39.28%, 3.69%, and 17.35%, respectively. Compared with the ICGH criteria, the newly established

TABLE 3 Newly established criteria

Rule no.	Parameters	Newly established criteria
5	WBC count	<ul style="list-style-type: none"> $<2.0 \times 10^9/L$, or $>30.0 \times 10^9/L$ First test Slide review
10	MCV	<ul style="list-style-type: none"> <80 fl (IP) Abn histogram of platelets Reflex: PLT-F channel
19	Monocyte#	<ul style="list-style-type: none"> $>1.5 \times 10^9/L$ (adult) or $>3.0 \times 10^9/L$ (child [age <12 y]) or mono% $\geq 15\%$ Slide review
22	NRBC#	<ul style="list-style-type: none"> >0 (IP) flags associated with WBC or PLT (left shift/WBC abn scattergram/IG present/blast/abn lymphocyte/PLT clumps/PLT abn distribution and scattergram) Slide review
23	Reticulocytes#	<ul style="list-style-type: none"> $>100 \times 10^9/L$ (IP) flags associated with RBC (fragment/iron deficiency/ret abn scattergram/PRBC?) Slide review
27	RBC fragment flag	<ul style="list-style-type: none"> Flag (IP) abnormal histogram of platelets Reflex: PLT-F channel
30	Platelet clumping flag	<ul style="list-style-type: none"> Flag Platelet $\leq 75 \times 10^9/L$ Slide review
32	IG flag	<ul style="list-style-type: none"> IG $> 1.85\%$ (IP) flag (left shift/WBC abn scattergram/blast/abn lymphocyte/atypical lymphocyte) Slide review
35	Blast/abn lympho?flag	<ul style="list-style-type: none"> Flag First time Reflex: WPC channel

Abbreviations: Abn, abnormal; IG, immature granulocyte; MCV, mean corpuscular volume; NRBC, nucleated red blood cells; PLT, platelet; PRBC, red blood cell infected by plasmodium; RBC, red blood cell; WBC, white blood cell.

TABLE 4 Comparison between the ICGH and newly established criteria (n = 1003 samples)

	ICGH criteria, n (%)	Newly established criteria, n (%)	P value*
TP	179 (17.85)	232 (23.13)	.003
TN	462 (46.06)	560 (55.83)	<.001
FP	344 (34.30)	174 (17.35)	<.001
FN	18 (1.79)	37 (3.69)	.009
Review	514 (51.25)	394 (39.28)	<.001

Abbreviations: FN, false negative; FP, false positive; TN, true negative; TP, true positive.

*The *p* value was calculated using the *chi-square* test.

criteria had a significantly lower review (39.28% vs 51.25%, $P < .001$) and FP rates (17.35% vs 34.30%, $P < .001$) and higher TN rate (55.83% vs 46.06%, $P < .001$). FN sample analysis of the newly established criteria showed that the most frequent FN findings were pro/myelocyte/metamyelocyte, RBC morphology abnormalities, and WBC morphology, including toxic granulation and vacuolation.

We repeated the validation of the established criteria by using another separate set of samples (n = 215). In the validation set, the FN rate was only 1.86%, and the review, FP, TP, and TN rates were 33.49%, 25.58%, 7.91%, and 64.65%, respectively.

4 | DISCUSSION

Hematology reviews are composed of three parts, namely, (1) smear (morphology) review, (2) counting repeat, and (3) sample review character.⁷ Although hematologic review criteria for general hospitals have been established, they may be insufficient for cancer hospitals. In this study, 1003 samples were evaluated using the ICGH criteria. The FN rate was as low as 1.79%, but the smear review rate was extremely high at 51.25%, which considerably restricted the work efficiency of routine hematologic tests.

According to the detection results and alarm information of FN and FP samples, as well as the new functional characteristics of the XN hematology analyzer, we established our criteria specific for a cancer hospital.

The WBC of patients with cancer who underwent radiotherapy or chemotherapy is always less than the lower limit of the reference range ($4.0 \times 10^9/L$).^{11,15,16} Thus, we decreased the low WBC threshold of rule 5 to $2.0 \times 10^9/L$, and the FP rate decreased by 4.69%. The FP rates of rules 22 and 23 were high, and there were TP cases that did not contain blast cells. We added associated flags in the rules, and the FP rate decreased by 2.89% and 1.1%. Rule 30 was extremely sensitive, and most of the smear slides that triggered the rule were negative. Patients with cancer are susceptible to bone marrow suppression after chemotherapy. $PLT \leq 50 \times 10^9/L$ is considered a critical indicator of grade III bone marrow suppression, which in turn indicates a possibility of complications and the

need for clinical intervention. Clinicians need to closely monitor chemotherapy patients when their PLT is less than $75 \times 10^9/L$,¹⁷ and thus, an accurate PLT count is crucial. Therefore, we adjusted rule 30 because the sample needs to be smeared when the PLT count is $\leq 75 \times 10^9/L$ and a PLT clump is found. Such adjustment decreased the FP rate by 2.0%.

As shown above, 81.73% of the TP cases triggered more than one rule, and positive samples can be captured by the other rules after adjustment. In total, 18.27% of the positive samples that triggered a single rule of the ICGH criteria changed as false negative, such as immature granulocytes, abnormal RBC morphology, toxic granulation, and vacuoles. This can be acceptable because these parameters are not important influencing factors of clinical treatment. Only one case of blast cell was missed, which was from a patient of the hematology department. The patient was on follow-up visit and already had previously confirmed positive results. This indicates that patients in the hematology department need a smear review.

Another sample of missing blast cell was found in a patient with lymphoma. Given that hematology analyzers generally count the original cells that appear in the peripheral blood as monocytes, the absolute value of monocytes did not trigger rule 19 (mono#) when the WBC count was low ($<4.0 \times 10^9/L$). Hence, we added mono% $\geq 15\%$ to rule 19.

The XN hematology analyzer has three extra automatic counting functions, that is, rerun, repeat, and reflex. Rerun indicates that the samples are analyzed again while retaining the initial results. Repeat indicates performing the initial analysis again, and reflex indicates the analysis of the sample with another testing channel. The WDF channel of the XN hematology analyzer has high sensitivity but low specificity for blast/abnormal lymphocyte flag. The WPC channel added in the XN A1 and A2 series analyzers can improve the specificity. Therefore, when a sample has blast/abnormal lymphocyte flag, the analyzer automatically adds WPC channel analysis.¹⁸ Therefore, we changed rule 35 to add reflex WPC channel analysis when a blast/abnormal lymphocyte flag emerged.

The most common interference in PLT detection by impedance assay is the presence of RBC fragments and small RBCs in the sample with abnormal platelet histogram.¹⁹ The PLT-F channel in the XN A1 series can exclude the interference of small RBCs and RBC fragment and avoid missed detection of giant platelet and microplatelets.²⁰ PLT-F involves staining the nucleic acid substances in the mitochondria and ribosome in the platelet. It improves the repeatability of PLT counting by analyzing the particles five times. Hence, we also added reflex PLT-F to rules 10 and 27 of the ICGH criteria.

Our newly established criteria were established after the above adjustments. Compared with the ICGH criteria, the FP rate of our newly established criteria significantly decreased, while the FN rate slightly increased, which was acceptable in the range of international requirements.⁷ The smear review rate was $>30\%$ in our hospital, which was higher than those in other reports.^{21,22} Large changes in blood concentration and morphology after frequent radiochemotherapy treatment cause a high smear slide rate. The hematology

analysis system can slide blood films according to the review criteria, and smear images can be captured using DI-60 in the system, thereby considerably improving the efficiency of the analysis.

We acknowledge some limitations to this study. First, only 1003 samples were used to establishing the criteria, which is lower than that in previous studies.^{21,22} However, single disease species and similar treatment methods exist in our hospital. The 1003 samples were adequate to cover all patients with different conditions. Further, specimens in cancer hospitals have higher positive and review rates than those in general hospitals. The samples in our study were from 584 first-time patients (58.23%) and 419 follow-up patients (41.77%), and the positive smear result rate of the follow-up patients ($n = 116$, 27.68%) was significantly higher than that of first-time patients ($n = 81$, 13.87%; $P < .001$). This indicated that despite the small number of samples, our study had sufficient positive samples, and the results are credible. The second limitation is that the samples used in the validation set were consecutively collected in 1 month. Therefore, some uncommon positive findings were not observed in the set. Thus, the FN and TP rates of the validation set were both lower than those of the established set. We will further validate the newly established criteria in the daily clinical setup.

In conclusion, this study established criteria for XN hematology analyzer systems in cancer hospitals. The newly established criteria enabled identification, smear, and further verification of doubtful specimens in a timely manner without a significant increase in the workload. This study also provided data support to other clinical laboratories of cancer hospitals or cancer centers to establish review criteria.

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REFERENCES

- Adewoyin AS, Nwogoh B. Peripheral blood film - a review. *Ann Ib Postgrad Med*. 2014;12:71-79.
- Gulati G, Song J, Florea AD, Gong J. Purpose and criteria for blood smear scan, blood smear examination, and blood smear review. *Ann Lab Med*. 2013;33:1-7.
- Eilertsen H, Saether PC, Henriksson CE, Petersen AS, Hagve TA. Evaluation of the detection of blasts by Sysmex hematology instruments, CellaVision DM96, and manual microscopy using flow cytometry as the confirmatory method. *Int J Lab Hematol*. 2019;41:338-344.
- Marionneaux S, Maslak P, Keohane EM. Morphologic identification of atypical chronic lymphocytic leukemia by digital microscopy. *Int J Lab Hematol*. 2014;36:459-464.
- Ye JJ. Artificial intelligence for pathologists is not near-It is here: description of a prototype that can transform how we practice pathology tomorrow. *Arch Pathol Lab Med*. 2015;139:929-935.
- Zomnir MG, Lipkin L, Pacula M, et al. Artificial intelligence approach for variant reporting. *JCO Clin Cancer Inform*. 2018;2(2):1-13.
- Barnes PW, McFadden SL, Machin SJ, Simson E. The international consensus group for hematology review: suggested criteria for action following automated CBC and WBC differential analysis. *Lab Hematol*. 2005;11:83-90.
- Pipitone S, Germagnoli L, Da Rin G, et al. Comparing the performance of three panels rules of blood smear review criteria on an Italian multicenter evaluation. *Int J Lab Hematol*. 2017;39:645-652.
- Kim SJ, Kim Y, Shin S, Song J, Choi JR. Comparison study of the rates of manual peripheral blood smear review from 3 automated hematology analyzers, Unicel DxH 800, ADVIA 2120i, and XE 2100, using international consensus group guidelines. *Arch Pathol Lab Med*. 2012;136:1408-1413.
- Cooperation Group of Formulation. Review criteria for automated complete blood count and WBC differential analysis by Sysmex XE-2100 hematology analyzer. *Chin J Lab Med*. 2008;31:674-679.
- Lalami Y, Klastersky J. Impact of chemotherapy-induced neutropenia (CIN) and febrile neutropenia (FN) on cancer treatment outcomes: an overview about well-established and recently emerging clinical data. *Crit Rev Oncol Hematol*. 2017;120:163-179.
- Sah SK, Karn A, Shah A, et al. Incidence and attributes of chemotherapy induced myelotoxicity, anemia and neutropenia in adults with cancer in Nepal: a cross-sectional observational study. *J Oncol Pharm Pract*. 2019;25:1823-1830.
- Briggs C, Longair I, Kumar P, Singh D, Machin SJ. Performance evaluation of the Sysmex haematology XN modular system. *J Clin Pathol*. 2012;65:1024-1030.
- Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33:159-174.
- Marjanovic D, Plesinac Karapandzic V, Stojanovic Rundic S, et al. Acute toxicity of postoperative intensity-modulated radiotherapy and three-dimensional conformal radiotherapy for cervical cancer: The role of concomitant chemotherapy. *J BUON*. 2019;24:2347-2354.
- Common Terminology Criteria for Adverse Events (CTCAE) v5.0 [Cited 2017 Nov 27]. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc. Accessed November 27, 2017.
- Consensus Committee of Chemotherapy Induced Thrombocytopenia, Chinese Society of Clinical Oncology. Consensus on clinical diagnosis, treatment and prevention management of chemotherapy induced thrombocytopenia in China. *Zhonghua Zhong Liu Za Zhi*. 2018;40:714-720.
- Jones AS, Taylor H, Liesner R, Machin SJ, Briggs CJ. The value of the white precursor cell channel (WPC) on the Sysmex XN-1000 analyzer in a specialist paediatric hospital. *J Clin Pathol*. 2015;68:161-165.
- Huang Y, Huang C, Li J, et al. Establishment of review criteria for low PLT count in XN-2000 hematology analyzer. *Chin J Chin Lab Sci*. 2014;32:48-51.
- Wada A, Takagi Y, Kono M, Morikawa T. Accuracy of a new platelet count system (PLT-F) depends on the staining property of its reagents. *PLoS ONE*. 2015;10:e0141311.
- Pratumvinit B, Wongkrajang P, Reesukumal K, Klinbua C, Niamjoy P. Validation and optimization of criteria for manual smear review following automated blood cell analysis in a large university hospital. *Arch Pathol Lab Med*. 2013;137:408-414.
- Wu W, Huang Y, Pei YQ, et al. Establishment of review criteria for a hematology analyzer with an automated review function. *Int J Lab Hematol*. 2016;38:e60-e64.

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