



# Digital Morphology Analyzer Sysmex DI-60 vs. Manual Counting for White Blood Cell Differentials in Leukopenic Samples: A Comparative Assessment of Risk and Turnaround Time

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**Background:** Digital morphology (DM) analyzers are increasingly being used for white blood cell (WBC) differentials. We assessed the laboratory efficiency of the Sysmex DI-60 system (DI-60; Sysmex, Kobe, Japan) in comparison with manual counting in leukopenic samples.

**Methods:** In total, 40 peripheral blood smear samples were divided into normal, mild leukopenia, moderate leukopenia, and severe leukopenia groups based on WBC count. In each group, the risk and turnaround time (TAT) were compared between DI-60 and manual counting. Risk was determined by failure mode and effect analysis using the risk priority number (RPN) score, and TAT was recorded for the analytical phase.

**Results:** Overall, DI-60 showed a five-fold lower risk (70 vs. 350 RPN) and longer TAT than manual counting. In severe leukopenic samples, DI-60 showed a shorter TAT/slide and a remarkably lower cell count/slide than manual counting. In all samples, the TAT/cell for DI-60 was substantially longer than that for manual counting (DI-60 vs. manual: total, 1.8 vs. 1.0 sec; normal, 1.5 vs. 0.7 sec; mild leukopenia, 1.9 vs. 0.9 sec; moderate leukopenia, 1.8 vs. 1.0 sec; severe leukopenia, 28.8 vs. 19.0 sec).

**Conclusions:** This is the first comparative assessment of risk and TAT between DI-60 and manual counting in leukopenic samples. DI-60 decreases the laboratory risk and improves patient safety, but requires more time to count fewer cells, especially in severe leukopenic samples. DM analyzers should be applied selectively depending on the WBC count to optimize laboratory efficiency.

**Key Words:** Leukopenia, DI-60, WBC differential, Risk, Turnaround time, Laboratory efficiency

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## INTRODUCTION

White blood cell (WBC) differential is the second most commonly used hematological test to provide crucial clinical information [1]. The gold standard for WBC differential is manual

counting of 200 cells each by two experts on a Romanowsky-stained peripheral blood smear (PBS) [2, 3]. However, the manual method is labor-intensive, time-consuming, and vulnerable to inter- and intra-individual variability and variation in distributed cells among slides [2-5].

Several digital morphology (DM) analyzers are used in clinical practice to replace manual counting, and numerous studies have comprehensively evaluated their performance [3, 5-12]. Sysmex DI-60 (DI-60; Sysmex, Kobe, Japan) is the first fully integrated system comprising an XN hematology analyzer, slide maker, staining device, and DM analyzer [10, 11].

In view of laboratory efficiency, risk management, i.e., identifying risk levels and determining priorities for actions to reduce risks, is essential [13]. Reduced risk ensures cost-effectiveness, patient safety and satisfaction, and high-quality laboratory results [14]. For risk management, the Clinical Laboratory Standards Institute (CLSI) guidelines EP23-A theoretically suggest how to assess and manage risks, and the International Organization for Standardization (ISO) 22367:2020 document practically recommends failure mode and effect analysis (FMEA) [15, 16]. Turnaround time (TAT) is another important metric to monitor laboratory efficiency. A short TAT is essential for early diagnosis and treatment, shortened hospital stay, and increased patient satisfaction [17, 18]. DM analyzers were expected to provide undoubtful advantages over manual counting regarding laboratory efficiency in preventing risks, reducing the workload, simplifying the workflow, and shortening the TAT [19].

Digital images should be validated using different pathological samples in programs for proficiency testing such as the College of American Pathology (CAP) and United Kingdom National External Quality Assurance (UKNEQAS) programs [20, 21]. Thus, most studies have evaluated the performance of DM analyzers using normal and abnormal samples, including different cell types [9-12]. Due to the widespread use of intensive therapies and frequent hematological monitoring, the number of patients with leukopenia has increased [22]. In view of laboratory efficiency, examining slides with leukopenia is more labor-intensive and time-consuming [3, 5, 19]. To the best of our knowledge, no study has evaluated the laboratory efficiency of DM analyzers or focused on leukopenic samples. We hypothesized that the laboratory efficiency of DM analyzers would differ for leukopenic samples. We compared risk and TAT between DI-60 analysis and manual counting using leukopenic samples to assess the laboratory efficiency of both methods.

## MATERIALS AND METHODS

### Sample collection

This *in vitro* comparative study was conducted between January 2021 and April 2021 at Konkuk University Medical Center (KUMC), Seoul, Korea. The Institutional Review Board of KUMC

exempted approval of the study protocol (KUMC 2021-01-041) and waived informed consent. We included 40 samples that were collected for complete blood count (CBC) and PBS. Venous blood samples were collected in K<sub>3</sub>-EDTA-containing Vacuette™ tubes (Greiner Bio-One International GmbH, Frickenhausen, Germany), and CBCs were measured using a Sysmex XN-9000 instrument (XN-9000, Sysmex) within four hours of blood collection. Slides were automatically prepared and stained using RAL Wright-Giemsa (RAL Diagnostics, Bordeaux, France) in a Sysmex SP-10 instrument. According to the WBC counts on XN-9000, all samples were divided into four groups: normal, 4.0-10.0×10<sup>9</sup>/L; mild leukopenia, 2.0-4.0×10<sup>9</sup>/L; moderate leukopenia, 1.0-2.0×10<sup>9</sup>/L; and severe leukopenia, <1.0×10<sup>9</sup>/L. In total, 6,921 cells were evaluated using DI-60 analysis and 6,346 cells using manual counting. The sample characteristics (diagnosis and cellular composition) are summarized in Table 1.

### WBC differentials using DI-60 analysis and manual counting

DI-60 comprises an automated microscope, a high-quality digital camera, and a computer system that collects pre-classified cell images from the slide. Slides prepared using SP-10 were loaded into DI-60. After DI-60 had determined start and end points on the slides for scanning, it scanned them at 10× magnification in a battlement track pattern. DI-60 acquired cell images at 100× magnification. For each slide, the instrument was set up with 210 cells as the acquisition cell number, considering acquisition of non-WBCs along with WBCs. Pre-classified cell images were displayed on a computer screen and were verified by the expert. DI-60 provides 18 pre-classified WBC differentials: WBCs, including segmented and band neutrophils, monocytes, lymphocytes, eosinophils, basophils, blast cells, promyelocytes, myelocytes, metamyelocytes, atypical lymphocytes, and plasma cells, and non-WBCs, including smudged cells, artifacts, giant platelets, platelet clumps, erythroblasts, and unidentified cells [10, 11]. We included only WBCs for the analysis of cell count/slide and TAT/cell.

Manual counting was performed according to the CLSI guidelines H20-A2 [2]. After slide scanning at low power, two qualified experts counted 200 cells per slide under a light microscope at high power and recorded the results. For leukopenic samples, additional slides should be prepared and cells should be counted according to the CLSI guidelines H20-A2 [2]. As the purpose of this study was to evaluate risk and TAT in leukopenic samples, not to evaluate the imprecision of WBC counts, we did not evaluate multiple slides per sample.

**Table 1.** Sample characteristics

	Total (N=40)	Normal (N=10)	Mild leukopenia (N=10)	Moderate leukopenia (N=10)	Severe leukopenia (N=10)
Age, median (IQR)	64 (33-76)	47 (33-71)	77 (64-78)	62 (62-73)	33 (33-65)
Male, N (%)	21 (52.5)	6 (60)	6 (60)	2 (20)	7 (70)
Diagnosis, N (%)					
AML	18 (45)	3 (30)	1 (10)	7 (70)	7 (70)
Lymphoma*	5 (12.5)	-	3 (30)	2 (20)	-
PCM	4 (10)	1 (10)	1 (10)	-	2 (20)
MDS	3 (7.5)	-	3 (30)	-	-
ALL	1 (2.5)	-	-	1 (10)	-
CML	1 (2.5)	1 (10)	-	-	-
AA	1 (2.5)	-	-	-	1 (10)
No hematologic diseases <sup>†</sup>	7 (17.5)	5 (50)	2 (20)	-	-
WBC counts, median (IQR)	2,215 (610-4,863)	7,010 (5,708-7,798)	2,840 (2,615-3,400)	1,710 (1,125-1,930)	60 (50-190)
WBC differentials <sup>‡</sup> , N (%)					
Five differentials	26 (65)	10 (100)	2 (20)	4 (40)	10 (100)
Blasts	3 (7.5)	-	3 (30)	-	-
Immature granulocytes <sup>§</sup>	8 (20)	-	5 (50)	3 (30)	-
nRBCs	1 (2.5)	-	1 (10)	-	-
Lymphocytes, variant form	9 (22.5)	-	6 (60)	3 (30)	-

\*Lymphoma included follicular lymphoma (N=3) and diffuse large B cell lymphoma (N=2); <sup>†</sup>No hematologic diseases included bone marrow donors (N=2), liver disease (N=2), cardiac disease (N=2), and breast cancer (N=1); <sup>‡</sup>The number of WBC differentials included all numbers of five overlapping differentials, blasts, immature granulocytes, nRBC, and variant lymphocytes; <sup>§</sup>Immature granulocytes included promyelocytes, myelocytes, and metamyelocytes.

Abbreviations: N, number; IQR, interquartile range; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; PCM, plasma cell myeloma; MDS, myelodysplastic syndrome; CML, chronic myeloid leukemia; AA, aplastic anemia; WBC, white blood cell; nRBCs, nucleated red blood cells.

### Assessment of risk and TAT

For risk assessment, FMEA was conducted using the following six steps: (1) determination of the analytical test, (2) assembly of a team, (3) risk identification, (4) risk analysis, (5) risk evaluation, and (6) taking action for risk improvement [13, 23]. In FMEA, DI-60 analysis and manual counting were assessed from placing a slide on the microscope stage to recording of the results. The team consisted of a director, a medical doctor, two qualified medical technicians, and two analyzer specialists. The director, who had experience with FMEA, trained the other team members in identifying potential defects and suggesting potential interventions and preventive actions. All members reviewed each step of DI-60 analysis and manual counting and identified risks, causes, and consequences based on their experience and information in the literature. Before the actual risk assessment, all team members conducted the FMEA independently and then, differences were analyzed and discussed until consensus was reached for objectivity. For each potential risk, scores of severity, occurrence, and detectability were assigned

according to the FMEA rating scale (Supplemental Data Table 1). Each score was determined as the median of the scores assigned by the team members. The overall risk priority number (RPN) was calculated by multiplying the three scores. After assessing the risk for each process, all team members suggested preventive actions to reduce the occurrence of risks with high RPN scores.

The TAT was determined for the analytical phases of DI-60 analysis and manual counting, from placing a slide on the microscope stage to recording of the results. For DI-60 analysis, the process of transferring data to a laboratory information system was not instrumentally ready; therefore, we excluded this process from the analytical phases of DI-60 analysis and manual counting. A digital camera recorded the TAT of each process in DI-60 analysis and manual counting. The TAT of DI-60 was additionally checked using a log file of the computer system. Total TAT was calculated as the sum of TATs for all cell counting steps and was represented as the median value (in mins) in each group. The total TAT was transformed into secs for calculating

**Table 2.** Comparison of FMEA between DI-60 and manual counting for WBC differentials (N=40)

	Process step	Potential defect	Potential intervention	Consequence	FMEA			
					S	O	D	RPN
DI-60 analysis	1. Insert a slide in the instrument	Wrong slide or mechanical error	Repeat	Delay	4	3	1	12
	2. Scan ideal zone under low power (10×)	Mechanical error or poor image	Repeat	Delay	3	2	1	6
	3. Acquire images under high power (100×) (pre-classification)	Mechanical error	Repeat	Delay	4	1	1	4
	4. Verify results	Incorrect verification	Correct	WR	6	2	4	48
	Total				-	-	-	70
Manual counting	1. Place a slide on the microscope stage	Wrong slide or incorrectly labeled slide	Repeat	Delay, WR	9	1	6	54
	2. Scan ideal zone under low power (100×)	Low quality of slide or broken slide	Re-prepare	Delay	6	2	1	12
	3. Count cells under high power (1,000×)	Incorrect counting	Repeat	Delay, WR	9	2	8	144
	4. Record results	Clerical error	Correct	WR	10	2	7	140
	Total				-	-	-	350*

The RPN scores based on four groups were not calculated due to no difference in the process step.

\*According to the CLSI guidelines H20-A2, the manual count was calculated as the mean of the results of two experts. The definite RPN of manual counting was 700 (350×2); we compared only the analytical process between DI-60 and manual counting.

Abbreviations: FMEA, failure mode and effect analysis; WBC, white blood cell; N, number; S, severity; O, occurrence; D, detectability; RPN, risk priority number; WR, wrong result.

**Table 3.** Comparison of turnaround time between DI-60 and manual counting for WBC differentials

	Process step	TAT (min:sec) (median, IQR)				
		Total (N=40)	Normal (N=10)	Mild leukopenia (N=10)	Moderate leukopenia (N=10)	Severe leukopenia (N=10)
DI-60 analysis	1. Insert a slide in the instrument	0:33 (0:32-0:34)	0:33 (0:33-0:34)	0:33 (0:32-0:33)	0:33 (0:32-0:33)	0:33 (0:33-0:34)
	2. Scan ideal zone under low power (10×)	0:18 (0:17-0:19)	0:18 (0:17-0:19)	0:18 (0:18-0:20)	0:18 (0:17-0:18)	0:19 (0:17-0:19)
	3. Acquire images under high power (100×) (pre-classification)	2:09 (1:58-2:21)	2:05 (1:58-2:19)	2:27 (2:08-2:43)	2:18 (2:08-2:25)	1:48 (1:37-1:57)
	4. Verification	1:53 (0:45-2:45)	2:03 (1:45-2:27)	3:09 (2:15-4:02)	2:11 (1:21-3:00)	0:20 (0:15-0:27)
	Total*	5:00 (2:36-6:06)	5:05 (4:38-5:23)	6:29 (5:36-7:28)	5:13 (4:35-6:36)	3:02 (2:46-3:14)
Manual counting <sup>†</sup>	1. Place a slide on the microscope stage	0:03 (0:03-0:04)	0:03 (0:03-0:04)	0:03 (0:03-0:04)	0:04 (0:03-0:04)	0:03 (0:03-0:04)
	2. Scan ideal zone under low power (100×)	0:09 (0:05-0:10)	0:05 (0:04-0:09)	0:07 (0:05-0:08)	0:09 (0:06-0:10)	0:12 (0:10-0:13)
	3. Count cells under high power (1,000×)	2:42 (1:54-3:52)	1:47 (1:21-2:01)	2:36 (2:01-3:30)	3:02 (2:32-3:59)	4:30 (3:32-5:21)
	4. Record results	0:18 (0:14-0:20)	0:17 (0:15-0:20)	0:19 (0:17-0:23)	0:18 (0:14-0:21)	0:11 (0:09-0:21)
	Total*	3:11 (2:18-4:21)	2:11 (1:46-2:35)	3:02 (2:30-4:04)	3:27 (3:03-4:28)	5:00 (4:01-5:46)

The last process step of data transfer to the laboratory information system was excluded for both DI-60 analysis and manual counting.

\*Total value indicates median and IQR of total TAT for counting total cells in each slide in total group and each group; <sup>†</sup>We only compared TAT for one analytical process of one expert in manual counting; if the result of manual counting would have been determined as the mean of the results obtained by the two experts, the TAT of manual counting would have been significantly longer.

Abbreviations: WBC, white blood cell; TAT, turnaround time; IQR, interquartile range; N, number.

the overall TAT. TAT/slide represents the overall TAT for cell counting per slide, and TAT/cell represents the overall TAT divided by the total number of counted cells.

All data were analyzed using Microsoft Excel 2016 (Microsoft, Seattle, WA, USA) and MedCalc Statistical Software (v19.4.0, MedCalc Software Bvba, Ostend, Belgium). Normal distribution was checked using the Kolmogorov–Smirnov test, and non-nor-

mally distributed data are presented as median and interquartile range.

## RESULTS

DI-60 analysis showed a five-fold lower risk than manual counting (70 vs. 350 RPN) (Table 2). All DI-60 processes showed

lower severity and detectability than those of manual counting. The RPN for DI-60 pre-classification was remarkably lower than that for manual counting. RPN did not differ among the four WBC count groups (data not shown).

In DI-60 analysis, the TAT for pre-classification and verification showed an inverted-U shape; it increased in mild leukopenia samples, but decreased in severe leukopenia samples. In manual counting, the TAT for cell counting, which was the most time-consuming process, increased as the number of WBCs decreased. The overall TAT of DI-60 analysis in all groups was longer than that of manual counting, except in severe leukopenia samples (DI-60 vs. manual: total, 5:00 [min:sec] vs. 3:11; normal, 5:05 vs. 2:11; mild leukopenia, 6:29 vs. 3:02; moderate leukopenia, 5:13 vs. 3:27; and severe leukopenia, 3:02 vs. 5:00) (Table 3).

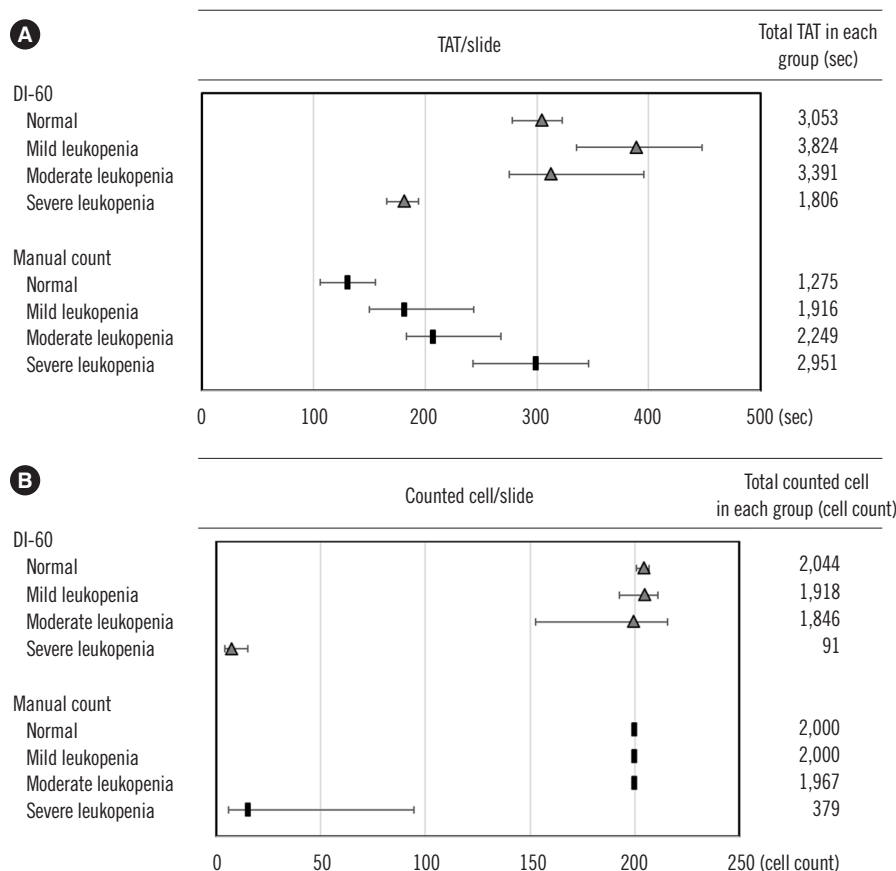
In manual counting, the median TAT/slide increased with decreasing number of WBC, whereas in DI-60 analysis, it increased in mild leukopenia samples and decreased in severe leukopenia samples. In severe leukopenia samples, the TAT/slide and total

TAT of DI-60 analysis were both 0.6-fold those for manual counting (DI-60 vs. manual: 182 vs. 300 seconds; 1,806 vs. 2,951 seconds, respectively) (Fig. 1A). The median cell count/slide in the normal, mild leukopenia, and moderate leukopenia groups was nearly 200 for both DI-60 analysis and manual counting. In severe leukopenia samples, cell count/slide and total cells counted were two-fold and four-fold, respectively, lower for DI-

**Table 4.** Comparison of TAT/cell between DI-60 analysis and manual counting

	TAT/cell (sec), (median, IQR)	
	DI-60 analysis	Manual counting
Total (N=40)	1.8 (1.5-8.3)	1.0 (0.7-2.8)
Normal (N=10)	1.5 (1.4-1.6)	0.7 (0.5-0.8)
Mild leukopenia (N=10)	1.9 (1.6-2.3)	0.9 (0.8-1.2)
Moderate leukopenia (N=10)	1.8 (1.4-2.3)	1.0 (0.9-1.4)
Severe leukopenia (N=10)	28.8 (11.8-48.3)	19.0 (4.6-40.7)

Abbreviations: TAT, turnaround time; IQR, interquartile range.



**Fig. 1.** Comparison of TAT/slide (A) and cell count/slide (B) between DI-60 analysis and manual counting for the four WBC count groups. Triangles and quadrangles indicate median values of DI-60 and manual counting, respectively, and lines indicate interquartile ranges. Total cells counted were summated by each TAT/slide or cell count/slide in each group. Abbreviations: TAT, turnaround time; WBC, white blood cell.

60 analysis than for manual counting (DI-60 vs. manual: 8 vs. 16 cells; 91 vs. 379 cells) (Fig. 1B). The median TATs/cell of DI-60 analysis for all groups, including severe leukopenia, were longer than those of manual counting (DI-60 vs. manual [seconds]: total, 1.8 vs. 1.0; normal, 1.5 vs. 0.7; mild leukopenia, 1.9 vs. 0.9; moderate leukopenia, 1.8 vs. 1.0; severe leukopenia, 28.8 vs. 19.0) (Table 4).

## DISCUSSION

We compared the risk and TAT between DI-60 analysis and manual counting in leukopenic samples to evaluate the laboratory efficiency of both methods. DI-60 analysis showed a five-fold lower risk than manual counting (70 vs. 350 RPN) (Table 2). All DI-60 processes showed lower severity, detectability, and RPN than the corresponding processes of manual counting. In particular, the RPN of DI-60 pre-classification was remarkably different from that of manual counting. These results indicate that DI-60 can contribute to improved laboratory efficiency and patient safety.

Automated analyzers have been introduced in hematology laboratories and blood bank laboratories; however, few studies have focused on laboratory efficiency in these laboratories with high manual workload [24-26]. These studies demonstrated the usefulness and applicability of FMEA in clinical laboratories and showed that automated methods are associated with lower RPNs than manual methods, which is in line with the present results. The substantially lower RPN of DI-60 analysis reflects that automation reduces or eliminates risk associated with human errors in manual steps. Through regular training and examination, medical technicians can be familiarized with manual steps, which would decrease the occurrence of risks. However, uncertain measurement and the possibility of human error in manual counting remain. Considering the last step of FMEA (taking action for risk improvement), hematology laboratories could use DI-60 analysis rather than manual counting for WBC differentials in leukopenic samples. Alternatively, reducing the RPN in manual counting is possible by decreasing the occurrence or increasing the detectability of prioritized risks with high RPN when the severity cannot be altered [23].

DM analyzers have completely revolutionized hematology laboratories by improving their analytical performance and efficiency, with lower risk and manual workload and shorter TAT [3, 19]. However, our results demonstrated that DI-60 analysis showed a longer TAT than manual counting in leukopenic samples (Table 3). Regardless of the WBC count, the TAT of slide insertion

and ideal zone scanning in DI-60 analysis and that of slide insertion, ideal zone scanning, and result recording in manual counting were not considerably different and were relatively short. However, mild leukopenic samples showed the longest TAT for pre-classification and verification in DI-60 analysis, whereas severe leukopenic samples showed the shortest. The cellular composition of mild leukopenic samples included five differentials, blasts, immature granulocytes, nucleated red blood cells (nRBCs), and variant lymphocytes, and that of severe leukopenic samples simply included five differentials. Thus, for mild leukopenic samples with diverse cell types, the TAT was relatively long, whereas severe leukopenic samples with a simple cellular composition required less time for pre-classification and verification in DI-60 analysis. In manual counting, as the number of WBC decreased, the TAT of cell counting remarkably increased, likely because it requires substantially more time to search for cells to count on slides of severe leukopenic samples than on those of samples with a normal WBC count.

Although the CLSI guidelines H20-A2 recommend counting at least 200 cells, this is not always feasible, especially in case of severe leukopenia [2]. The median cell count/slide in normal, mild leukopenia, and moderate leukopenia groups was nearly 200 for both DI-60 analysis and manual counting, but this number was not achievable in cases of severe leukopenia. The short TAT of DI-60 analysis for severe leukopenia samples implies that DI-60 does not actually spend less time on cell counting, but counts fewer cells than are counted in the manual method. Moreover, in manual counting, the experts discriminated between WBCs and non-WBCs, and the latter were not counted. However, DI-60 acquired images before starting the analysis and pre-classified the cells into WBCs and non-WBCs (e.g., a total of 6,921 cells=5,899 WBCs+1,022 non-WBCs). Non-WBCs, including smudge cells, artifacts, and unidentified cells, should have been eliminated during verification. Thus, in severe leukopenia samples, DI-60 spends substantially more time on cell counting (Table 4).

This study had some limitations. TAT can be defined in various ways based on test, priority (emergency or routine), patient (inpatient, outpatient, or emergency department patient), and activity (time of ordering or sample receipt in the laboratory), and a standard protocol to measure TAT is lacking [27]. Although laboratory testing includes pre-analytical, analytical, and post-analytical phases, we only assessed the TAT of the analytical phase [28]. The pre-analytical and post-analytical phases were difficult to control for TAT measurement due to diverse external factors. If the definition of TAT or protocol to measure TAT was

different, TAT comparison between DI-60 analysis and manual counting might have led to a different conclusion. In addition, although the samples with mild and moderate leukopenia contained various pathologic cell types, we compared the risk and TAT rather specifically in leukopenic samples, not in broad pathologic samples. A further comparison of risk and TAT between DI-60 analysis and manual counting would require using more pathologic samples with mixed cellular composition. For efficient utilization of DI-60, further comparative studies to verify the accuracy and precision of WBC count in leukopenic samples are also warranted [29]. Finally, our sample number was rather small; however, we counted 6,921 cells using DI-60 and 6,346 cells by manual counting, which is sufficient to fulfill our study purpose of comparing risk and TAT between DI-60 and manual counting.

In conclusion, this was the first study comparing risk and TAT between DI-60 analysis and manual counting in leukopenic samples. We demonstrated that DI-60 substantially reduces risks in the analytical phase, but spends more time on counting fewer cells in severe leukopenic samples than manual counting. Based on the current need for improved laboratory efficiency, the implementation of DM analyzers is considered inevitable, especially in high-volume laboratories with a large burden of pathologic or leukopenic samples. However, our results underscore that DM analyzers do not necessarily ensure high laboratory efficiency and may even prolong TAT. To optimize laboratory efficiency, DM analyzers should be applied selectively depending on the sample type and each laboratory's situation and only after risk and TAT assessment.

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## AUTHOR CONTRIBUTIONS

Nam M analyzed the data and wrote the draft; Hur M designed the study and finalized the draft; Yoon S, Park M, and Kim HN participated in data collection; Lee GH and Kim H reviewed the draft. All authors have accepted responsibility for the entire content of this manuscript and approved the final version.

## CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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**Supplemental Data Table S1.** Rating scale of severity, occurrence, and detectability of risk to calculate the risk priority number in failure mode and effect analysis

Score	Severity	Occurrence	Detectability
1	No effect	Remote	100% instrumental detection with preventive maintenance
2	Very minor interference		100% instrumental detection with preventive maintenance
3	Minor interference	Low/relatively few	100% instrumental detection with preventive maintenance
4	Creates some rework/very low interference		Partial detection by medical technicians
5	Creates moderate rework/low interference	Once a week	Periodic detection by medical technicians
6	Creates considerable rework/moderate interference		100% manual detection and provides visual cues
7	Causes considerable instrument downtime rework/high interference		100% manual detection
8	Could be reportable error and possible instrument downtime/very high interference	Once a day	Low chance to detect with random manual inspection
9	Could harm patient but not death and/or possible instrument failure/serious interference		Remote chance to detect with random manual inspection
10	Could injure a patient or cause death and/or cause possible instrument failure/hazardous interference	More than once a day	No detection or inspection

This table was created referring to ISO 22367:2020 [15], Han, *et al.* [24], and Chung, *et al.* [25].