Correspondence

Choosing wisely during the COVID-19 pandemic: optimising outpatient cancer care while conserving resources with a new algorithm to report automated ANC results

In the face of the COVID-19 pandemic, efficient outpatient management is paramount to minimise wait times and reduce exposure to respiratory illnesses, particularly in patients with cancer receiving chemotherapy. The complete blood cell count (CBC) with white cell count (WCC) differential (CBC-D) is an essential laboratory test used to screen cancer patients prior to chemotherapy. Patients receiving cytotoxic chemotherapy are at risk for developing neutropenia; the absolute neutrophil count (ANC) can be used to determine if a patient is neutropenic.[1] Neutropenia is generally defined as an ANC $<1.5\times10^9$/L–2.0×10^9/L, with severe neutropenia defined as $<0.5\times10^9$/L.[2]

WCC differential analysis is performed by automated haematology platforms in the clinical laboratory. These platforms have been found to provide accurate and precise ANC results.[3] However, automated results often require manual review if the analysis is associated with instrument flags that indicate the potential for inaccurate results. Review and confirmation of flagged results by laboratory technologists is time consuming and increases test result turnaround time (TAT), thereby prolongs onset of chemotherapy.[4–7] Given that chemotherapy administration requires an adequate ANC, we examined the reliability of the automated ANC in the presence of instrument flags in outpatients with solid tumour and haematological malignancies. We aimed to confirm if discrete ordering of a 'CBC with ANC only' test could be used to replace the traditional CBC with full WCC differential (CBC-D) and shorten patient wait times.

We performed a retrospective analysis of 1648 sequential CBC with WCC differential results flagged for manual peripheral blood smear review performed for patients with cancer. Results across five outpatient locations were analysed during October 2018. The cases were separated based on malignancy type, solid tumour (n=1078) or haematological malignancies (n=570). The accuracy of automated ANC results (Sysmex XN) was assessed by comparison to the manual differential using Rumke statistics.[8] Manual review of automated differential results was performed by experienced clinical laboratory technologists and consisted of either a peripheral blood smear review with confirmation of automated differential results or a full 100 cell manual differential.

Differential review flags associated with automated CBC-D results are summarised in table 1. Multiple flags were frequently observed in the same sample. As shown in figure 1, the automated differential was confirmed by peripheral blood smear review in 327 of 1078 (30%) samples from patients with solid tumour malignancies. A full manual differential was performed in the remaining 751 of 1078 cases (70%). In contrast, the automated differential was confirmed by peripheral blood smear review in 108 of 570 (19%) samples from

Table 1 Distribution of differential flags requiring manual peripheral blood smear review

	No of flagged instances	
Instrument flags	Solid tumour malignancies, %	Haematological malignancies, %
Nucleated red blood cells (NRBC)	512 (33)	256 (20)
Blasts/abnormal lymphoid	386 (25)	297 (23)
Monocytosis (≥1.5×10^3/µL or ≥30%)	106 (7)	167 (13)
Immature granulocytes	189 (12)	137 (11)
WCC abnormal scattergram	123 (8)	112 (9)
Atypical lymphoid	127 (8)	51 (4)
Previous sample with blasts	65 (4)	167 (13)
Eosinophilia (≥20%)	35 (2)	10 (0.8)
Absolute lymphocytosis (≥5×10^3/µL)	25 (2)	93 (7)
Basophilia (≥1×10^3/µL or ≥5%)	4 (0.3)	9 (0.7)
New patient with WCC >11×10^9/L	1 (0.1)	1 (0.1)
Total flags	1573	1300

WCC, white cell count.

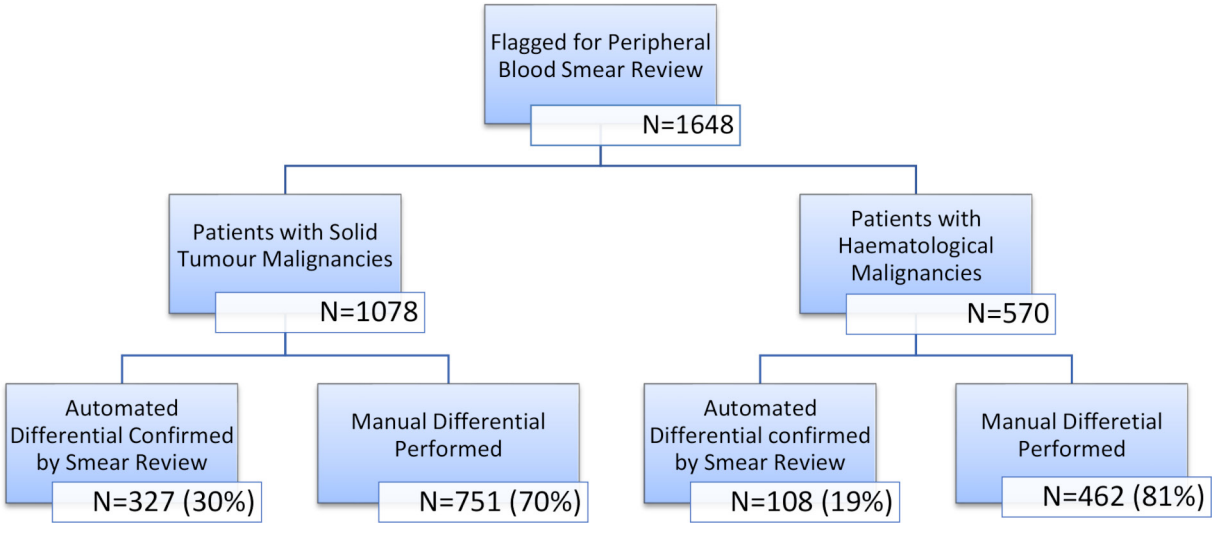

Figure 1 Study design to evaluate automated ANC performance in flagged CBC-D samples. ANC, absolute neutrophil count; CBC-D, complete blood cell count differential.

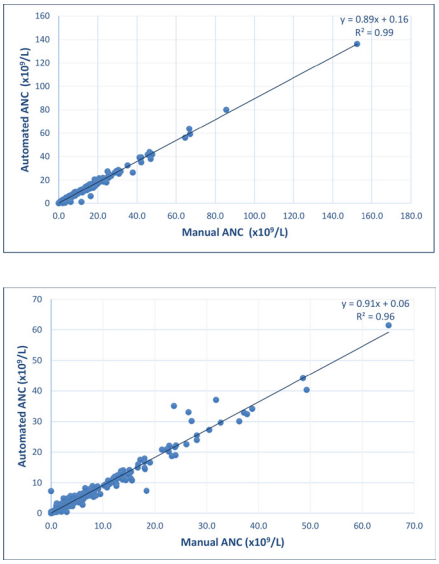

Figure 2 Correlation between manual and flagged automated ANC results in patients with solid tumour malignancies (top) and in patients with haematological malignancies (bottom). ANC, absolute neutrophil count.

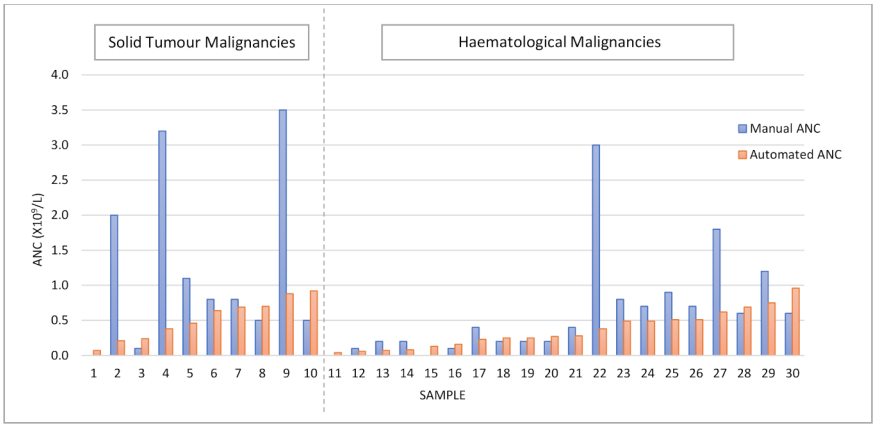

Figure 3 Differences between flagged automated and manual ANC results for samples with an automated ANC ≤1000/µL in patients with solid tumour (n=10) and in haematological (n=20) malignancies. ANC, absolute neutrophil count.

patients with haematological malignancies, and a full manual differential was performed in the remaining 462 of 570 cases (81%). The correlation between manual and automated ANC results was strong for patients with solid tumour and those with haematological malignancies with a R^2 of 0.99 (slope=0.89) and a R^2 of 0.96 (slope=0.91), respectively, despite instrument flags (figure 2). Subset analysis of haematological malignancies showed a similarly strong correlation between automated and manual ANC results for samples from patients with leukaemia, lymphoma, plasma cell dyscrasia, bone marrow transplant (BMT), myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN) and non-malignant haematological disorders (table 2).

Discordant automated and manual neutrophil results were identified in a total of 247 cases; 102 from patients with solid tumour malignancies and the remaining 145 from patients with haematological malignancies. The majority of these cases (n=217), had an automated ANC $>1.0\times10^9$/L, and the difference in ANC results was not clinically significant. In general, automated ANC results were slightly lower than manual results. Thirty samples, 10 from patients with solid tumours and 20 from patients with haematological malignancies, were found to have discordant ANC results with an automated ANC of $\leq1.0\times10^9$/L (figure 3).

This study investigated the feasibility of reporting a CBC with ANC only in cancer patients with solid tumour or haematological malignancies. The data support creating a distinct test order for 'CBC with ANC only,' when the ANC is required for the initiation of chemotherapy, discharge or other intervention. Our results confirm previous reports describing the validity of the automated ANC in a general patient population[3 5–7] and that the automated ANC results are consistently marginally lower than the manual count.[9] Additionally, this study provides new data on patients with haematological malignancies, subclassifying haematological malignancy by type (leukaemia, lymphoma, MDS, MPN and plasma cell dyscrasias), as well as including patients with recent BMT. Based on our review of discordant manual and automated ANC results, as well as the clinical definition of neutropenia, we suggest manual review of samples with flagged automated differential results, when the ANC is $<1.0\times10^9$/L.

A 'CBC with ANC only' order has the potential to decrease the manual review of CBC with differentials in patients with solid tumour and haematological malignancies by 91% and 75%, respectively (table 3). If clinicians transition from ordering a conventional CBC with differential to the 'CBC with ANC only' test option patient wait times can be reduced and laboratory and clinical resources conserved. In our institution, the TAT for a CBC with automated ANC is 10–15 min compared with 30–60 min for a manual ANC. A reduction in manual peripheral blood smear reviews from 1648 to 247 would represent substantial laboratory labour savings. Additional institutional savings are expected based on more efficient management of patient appointments and discharge.

The need for more efficient patient management is highlighted during the COVID-19 pandemic. Reduction in staffing

Table 2 ANC correlation in samples from patients with haematological malignancies

Haematological malignancy type	Total cases, %	ANC confirmed by smear review, %	Manual differential performed, %	Automated and manual differential correlation characteristics	
				R^2	Slope
Lymphoma	196 (34)	35 (6)	161 (28)	0.97	0.85
Leukaemia	189 (33)	18 (3)	171 (30)	0.95	0.99
Plasma cell dyscrasia*	59 (10)	21 (3)	38 (6)	0.97	0.84
BMT	56 (10)	15 (3)	41 (7)	0.97	0.85
MDS	38 (6)	13 (2)	25 (4)	0.99	0.89
MPN	25 (4)	6 (1)	19 (3)	0.99	0.94
Non-malignant haematological disorders	7 (1)	0 (0)	7 (100)	0.98	0.88

*Plasma cell dyscrasias include multiple myeloma and plasmacytoma.
ANC, absolute neutrophil count; BMT, bone marrow transplant; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm.

Table 3 Proposed reduction in automated ANC review of flagged CBC-D samples

	Solid tumour malignancies (N)	Haematological malignancies (N)
Current state: manual review of all flagged samples	1078	570
Proposed manual review for flagged samples with automated ANC ≤1000/µL	102	145
Anticipated reduction in manual review for automated ANC in flagged samples	91%	75%

ANC, absolute neutrophil count; CBC-D, complete blood cell count differential.

and the necessity for social distancing in the clinical laboratory as well as patient care areas has led healthcare institutions to reconsider established workflows. A 'CBC with ANC only' test offers an opportunity to preserve resources without adversely impacting patient care.

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