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Original Article

Comparison of Initial Absolute Monocyte Counts in 7-Day Recovery vs Nonrecovery Neutrophil Counts After Chemotherapy in Patients With Solid Organ Malignancy

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Abstract

Background: Neutropenia following chemotherapy is a common side effect that often delays treatment cycles, potentially affecting therapeutic outcomes in patients with cancer. Studies suggest that baseline monocyte count may predict neutrophil recovery after chemotherapy, aiding in better treatment planning.

Objective: To investigate the association between the initial monocyte count on the day of neutropenia and neutrophil recovery on day 7. Patients were categorized into 2 groups: recovery (absolute neutrophil count [ANC] ≥ 1500 cells/μL) and nonrecovery (ANC < 1500 cells/μL).

Methods: A retrospective cohort study was conducted at Chonburi Hospital, and the records of patients with solid organ malignancy who received chemotherapy from 1 January 2022 to 31 August 2023, were analyzed. Patients with neutropenia on chemotherapy day were included in the study. The initial monocyte count was compared between patients who recovered on day 7 and those who did not. Predictive power was assessed using the area under the receiver operating characteristic curve (AUROC).

Results: Of 42 patients, 29 (69.04%) achieved neutrophil recovery. The initial monocyte count was significantly higher in the recovery group than in the nonrecovery group (mean [SD], 422.97 [144.66] vs 272.00 [82.13] cells/μL; *P* = .001). An initial monocyte count of ≥ 375 cells/μL was identified as a predictive threshold for recovery, with an AUROC of 0.803, sensitivity of 58.6%, and specificity of 100%.

Conclusions: The initial monocyte count significantly differs between patients who recover and those who do not. A threshold of ≥ 375 cells/μL accurately predicts neutrophil recovery on day 7, potentially optimizing chemotherapy scheduling.

Keywords: Chemotherapy-induced neutropenia, Neutrophil, Absolute neutrophil count, Monocyte, Absolute monocyte count, Recovery from neutropenia

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Introduction

Chemotherapy remains a cornerstone in cancer treatment, contributing to survival improvements across various malignancies. However, its myelosuppressive effects, particularly chemotherapy-induced neutropenia (CIN), represent a significant clinical challenge. CIN often requires dose reductions or delays, compromising the efficacy of chemotherapy regimens. Moreover, neutropenia is associated with an increased risk of

infections, febrile neutropenia, and, in severe cases, mortality.[1-6] Monitoring hematologic parameters is crucial for timely intervention; however, neutrophil recovery prediction after CIN remains complex and inconsistent.[7, 8]

Current clinical practice at Chonburi Hospital has highlighted a recurrent issue where patients undergoing chemotherapy for solid organ malignancies experience neutropenia, resulting in treatment delays. Although complete blood count (CBC) is routinely checked before each chemotherapy cycle, identifying patients at risk of prolonged neutropenia remains challenging. Recent evidence suggests that monocyte levels may serve as an early predictor of neutrophil recovery, with changes in monocyte counts preceding alterations in neutrophil levels. Nevertheless, prospective studies specifically investigating the predictive value of baseline monocyte counts for 7-day neutrophil recovery in patients with CIN, particularly in the context of clinical management at Chonburi Hospital, are lacking.

Early prediction of neutrophil recovery could considerably improve clinical decision-making, reduce unnecessary treatment delays, and optimize chemotherapy scheduling. If baseline monocyte counts can reliably predict neutrophil recovery, clinicians may better identify patients who are likely to recover within 1 week, thereby minimizing additional hospital visits, patient inconvenience, and healthcare costs. Furthermore, such predictive capability could improve patient safety by informing the appropriate timing of myeloid growth factor administration and infection surveillance.

This study aimed to evaluate the predictive value of baseline monocyte counts for 7-day neutrophil recovery in patients with CIN undergoing treatment for solid organ malignancies at Chonburi Hospital. By establishing a reliable predictive marker, we hope to facilitate better treatment planning and reduce the clinical burden associated with chemotherapy delays.

Methods

Study Design

This retrospective, cross-sectional observational study aimed to evaluate the predictive value of baseline monocyte counts for 7-day neutrophil recovery in patients with CIN undergoing chemotherapy for solid organ malignancies.

Study Population

Inclusion criteria were as follows: 1) patients aged 18 years or older diagnosed with solid organ malignancies receiving chemotherapy and attending follow-up at the outpatient Medical Oncology Department (OPD Med and OPD Onco Med) of Chonburi Hospital, 2) absolute neutrophil count (ANC) < 1500 cells/μL on the scheduled chemotherapy date or within 1 day prior, 3) documented delay of chemotherapy due to neutropenia, 4) CBC evaluation performed on day 7 following the detection of neutropenia, and 5) Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2.

Exclusion criteria were as follows: 1) radiotherapy within 30 days before enrollment, 2) bone marrow metastasis, 3) receipt of granulocyte colony-stimulating factor (G-CSF) postchemotherapy, 4) chronic use of immunosuppressive agents (except corticosteroids administered during chemotherapy), and 5) active febrile illness or infection at the time of assessment.

Data Collection

Data were collected retrospectively from the electronic medical record system (CBH-EPHIS) using the *International Statistical Classification of Diseases and Related Health*

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Problems, Tenth Revision (*ICD-10*) coding for solid organ malignancies (C11, C15, C16, C18, C19, C22, C23, C24, C25, C34, C37, C40, C50, C61, C64, and C67) and neutropenia (D60). The study variables included demographic data (age, gender, body mass index [BMI], and comorbidities), cancer type and staging, chemotherapy regimens, number of chemotherapy cycles, laboratory findings, and neutrophil/monocyte counts.

Patient data were recorded from 1 January 2022 to 31 August 2023. For each patient, only the first occurrence of neutropenia (< 1500 cells/μL) during the study period was included to prevent confounding factors.

Follow-Up and Grouping

Neutrophil counts were assessed on day 7 after the initial detection of neutropenia. Patients were categorized into 2 groups: recovery (ANC ≥ 1500 cells/μL on day 7) and nonrecovery (ANC < 1500 cells/μL on day 7).

The initial absolute monocyte counts (AMCs) of both groups were recorded and analyzed to determine the predictive value of neutrophil recovery.

Sample Size Calculation

This study aimed to compare the initial monocyte counts between the recovery and nonrecovery groups. A preliminary analysis of 25 patients at Chonburi Hospital showed average initial monocyte counts of 377.67 cells/μL (SD 132.64) and 277.6 cells/μL (SD 88.62) in the recovery and nonrecovery groups, respectively. Stata version 15 (StataCorp LLC) was used for 2 independent means with a significance level of 0.05 and power of 0.8. A total of 42 patients were required (29 and 13 in the recovery and nonrecovery groups, respectively).

Statistical Analysis

Descriptive statistics were applied to summarize baseline characteristics and hematological parameters, with categorical variables presented as frequencies and percentages, and continuous variables as mean (SD) or median (IQR), depending on data distribution. The Shapiro-Wilk test was used to assess normality.

Comparative analysis between the recovery (ANC ≥ 1500 cells/μL on day 7) and nonrecovery (ANC < 1500 cells/μL on day 7) groups was performed using chi-square tests for categorical variables, and independent *t* tests or Mann-Whitney *U* tests for continuous variables based on distribution normality.

Predictive accuracy of baseline monocyte counts was assessed using receiver operating characteristic curve analysis. The optimal cutoff point was identified by the area under the curve. All analyses were conducted using Stata version 15, with statistical significance set at $P < .05$.

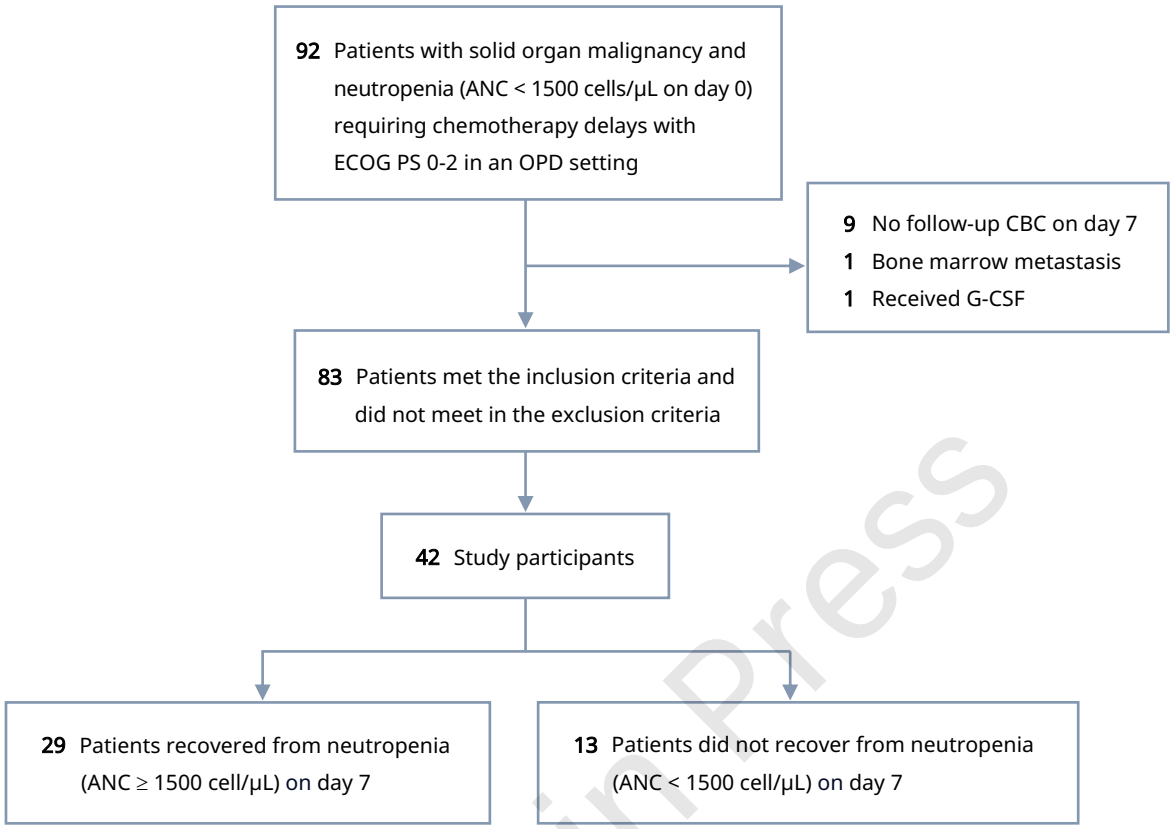
Results

Study Population

A total of 92 patients with solid organ malignancies who developed CIN were identified at Chonburi Hospital between 1 January 2022 and 31 August 2023. After applying the inclusion and exclusion criteria, 83 patients remained eligible. Of these, 42 patients were randomly selected for analysis: 29 (ANC ≥ 1500 cells/μL on day 7) and 13 (ANC < 1500 cells/μL on day 7) in the recovery and nonrecovery groups, respectively (Figure 1).

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Figure 1. Flow Diagram of Patient Selection



Abbreviations: ANC, absolute neutrophil count; CBC, complete blood count; ECOG PS, Eastern Cooperative Oncology Group performance status; G-CSF, granulocyte colony-stimulating factor; OPD, outpatient department.

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Baseline Characteristics

In this study population, the mean age of the patients was 61 years, with 27 females (64.29%). The average BMI was 22.28 kg/m^2. Smoking history was found in 11 patients (26.19%). Comorbidities included 4 patients (9.52%) with diabetes, 13 (30.95%) with hypertension, 8 (19.05%) with dyslipidemia, 1 (2.38%) with cardiovascular disease, 2 (4.67%) with liver cirrhosis, and 6 (14.29%) with other conditions, including 1 with emphysema, 1 with allergic rhinitis, 1 with HIV infection (CD4 = 546 cell/μL), 1 with hyperthyroidism, 1 with benign prostatic hyperplasia, and 1 with epilepsy. The ECOG performance status was 0, 1, and 2 in 19 (45.24%), 18 (42.86%), and 5 (11.90%) patients, respectively.

The recovery group (ANC ≥ 1500 cells/μL on day 7) included 29 patients (69.04%) with a mean age of 60 years, with 20 females (68.97%). The average BMI was 22.34 kg/m^2. Smoking history was found in 9 patients (31.03%). Comorbidities included 1 patient (3.45%) with diabetes, 9 (31.03%) with hypertension, 6 (20.69%) with dyslipidemia, 1 (7.69%) with cardiovascular disease, 2 (6.97%) with liver cirrhosis, and 4 (13.79%) with other conditions, including 1 with HIV infection (CD4 = 546 cell/μL), 1 with hyperthyroidism, 1 with benign prostatic hyperplasia, and 1 with epilepsy. The ECOG performance status was 0, 1, and 2 for 13 (44.83%), 12 (41.38%), and 4 (13.79%) patients, respectively.

Regarding cancer types in the recovery group, the majority had colorectal cancer (18 patients, 62.07%), followed by breast cancer (4 patients, 13.79%). Most patients had stage 4 cancer (15 patients, 51.72%). Among patients with stage 4 cancer, 8 (53.33%) received first-line chemotherapy. The most common chemotherapy regimen was 5-fluorouracil and oxaliplatin (9 patients, 31.03%), followed by 5-fluorouracil and irinotecan (6 patients, 20.69%). The median number of chemotherapy cycles was 2, and the mean initial ANC was 877.06 cells/μL.

In the nonrecovery group (ANC < 1500 cells/μL on day 7), which included 13 patients (30.95%), the mean age was 65.46 years, with 7 females (53.85%). The average BMI was 22.15 kg/m^2. Smoking history was noted in 2 patients (15.38%). Comorbidities included 3 patients (23.08%) with diabetes, 4 (30.77%) with hypertension, 2 (15.38%) with dyslipidemia, and 2 (15.38%) with other conditions, including 1 with emphysema and 1 with allergic rhinitis. The ECOG performance status was 0, 1, and 2 for 6 (44.83%), 6 (44.83%), and 1 (7.69%) patients, respectively.

Regarding cancer types in the nonrecovery group, colorectal cancer (9 patients, 69.23%) was the most common type, followed by breast cancer (2 patients, 15.38%). Most patients had stage 3 cancer (7 patients, 53.85%). Among patients with stage 4 cancer, 4 (80.00%) received first-line chemotherapy. The most common chemotherapy regimen was capecitabine and oxaliplatin (5 patients, 38.46%), followed by 5-fluorouracil and oxaliplatin (3 patients, 23.08%). The median number of chemotherapy cycles was 4, and the mean initial ANC was 889.38 cells/μL.

The comparison of the baseline characteristics between the 2 groups (Table 1) revealed no statistically significant differences in terms of general baseline characteristics, cancer types, or CIN parameters.

Table 1. Baseline Characteristics of Patients With Solid Organ Malignancies Who Developed Chemotherapy-Induced Neutropenia

Characteristic	No. (%)			*P* Value
	Total (N = 42)	Recovery From Neutropenia (ANC ≥ 1500 cells/μL) at Day 7 (n = 29)	No Recovery From Neutropenia (ANC < 1500 cells/μL) at Day 7 (n = 13)	
Age, mean (SD), y	61.71 (9.08)	60.03 (8.13)	65.46 (10.25)	.072
Sex				
Female	27 (64.29)	20 (68.97)	7 (53.85)	.488
Male	15 (35.71)	9 (31.03)	6 (46.15)	
BMI, mean (SD), kg/m^2	22.28 (4.24)	22.34 (4.18)	22.15 (4.53)	.893
Smoking history				
Smoker	11 (26.19)	9 (31.03)	2 (15.38)	.453
Nonsmoker	31 (73.81)	20 (68.97)	11 (84.62)	
Comorbidity				
Diabetes	4 (9.52)	1 (3.45)	3 (23.08)	.080
Hypertension	13 (30.95)	9 (31.03)	4 (30.77)	> .999
Dyslipidemia	8 (19.05)	6 (20.69)	2 (15.38)	> .999
Cardiovascular disease	1 (2.38)	1 (7.69)	0	.310
Liver cirrhosis	2 (4.67)	2 (6.90)	0	> .99
Other	6 (14.29)	4 (13.79)	2 (15.38)	> .99

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Table 1. Baseline Characteristics of Patients With Solid Organ Malignancies Who Developed Chemotherapy-Induced Neutropenia (Continued)

Characteristic	No. (%)			*P* Value
	Total (N = 42)	Recovery From Neutropenia (ANC ≥ 1500 cells/μL) at Day 7 (n = 29)	No Recovery From Neutropenia (ANC < 1500 cells/μL) at Day 7 (n = 13)	
ECOG performance status				
0	19 (45.24)	13 (44.83)	6 (46.15)	> .99
1	18 (42.86)	12 (41.38)	6 (46.15)	
2	5 (11.90)	4 (13.79)	1 (7.69)	
Cancer type				
Colorectal	27 (64.29)	18 (62.07)	9 (69.23)	.607
Breast	6 (14.29)	4 (13.79)	2 (15.38)	
Lung	3 (7.14)	3 (10.34)	0	
Cholangiocarcinoma	3 (7.14)	2 (6.90)	1 (7.69)	
Gastric	2 (4.76)	2 (6.90)	0	
Pancreatic	1 (2.38)	1 (7.69)	0	
Stage				
2	3 (7.14)	2 (6.90)	1 (7.69)	.770
3	19 (45.24)	12 (41.38)	7 (53.85)	
4	20 (47.62)	15 (51.72)	5 (38.46)	
Line of chemotherapy treatment in patients with stage 4 cancer				
1st	12 (60.00)	8 (53.33)	4 (80.00)	.603
2nd	8 (40.00)	7 (46.67)	1 (20.00)	
Chemotherapy regimen				
5-fluorouracil + oxaliplatin	12 (28.57)	9 (31.03)	3 (23.08)	.259
capecitabine + oxaliplatin	8 (19.05)	3 (10.34)	5 (38.46)	
5-fluorouracil + irinotecan	7 (16.67)	6 (20.69)	1 (7.69)	
AC (doxorubicin + cyclophosphamide)	5 (11.90)	4 (13.79)	1 (7.69)	
Platinum (cisplatin or carboplatin) + 5-fluorouracil	2 (4.76)	2 (6.90)	0	
Platinum (cisplatin or carboplatin) + paclitaxel	2 (4.76)	2 (6.90)	0	
Platinum (cisplatin or carboplatin) + gemcitabine	1 (2.38)	0	1 (7.69)	
Paclitaxel	1 (2.38)	0	1 (7.69)	
Platinum (cisplatin or carboplatin) + vinorelbine	1 (2.38)	1 (3.45)	0	
Others	3 (7.14)	2 (6.90)	1 (7.69)	
Cycles of chemotherapy, median (IQR)	2.00 (1.00-5.00)	2.00 (1.00-4.00)	4.00 (1.00-9.00)	.158
Initial ANC, mean (SD), cell/μL	880.88 (317.21)	877.06 (65.32)	889.38 (65.00)	.909

Abbreviations: AC, adriamycin (also called doxorubicin) and cyclophosphamide; ANC, absolute neutrophil count; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

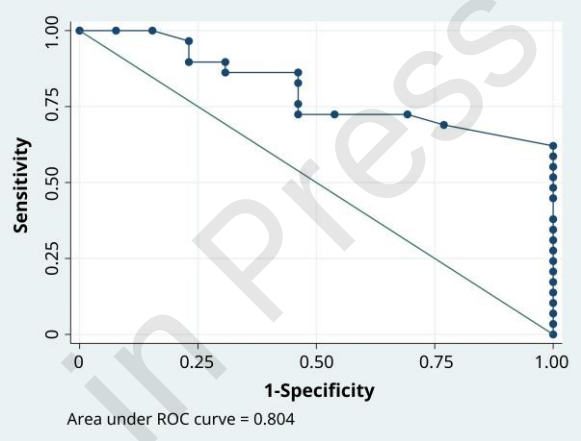
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Monocyte Count and Neutrophil Recovery

The mean (SD) initial AMC for the entire cohort was 376.23 (145.79) cells/μL. The mean (SD) initial AMC in the recovery group was 422.97 (144.66) cells/μL, whereas in the nonrecovery group, it was 272.00 (82.13) cells/μL (P = .001).

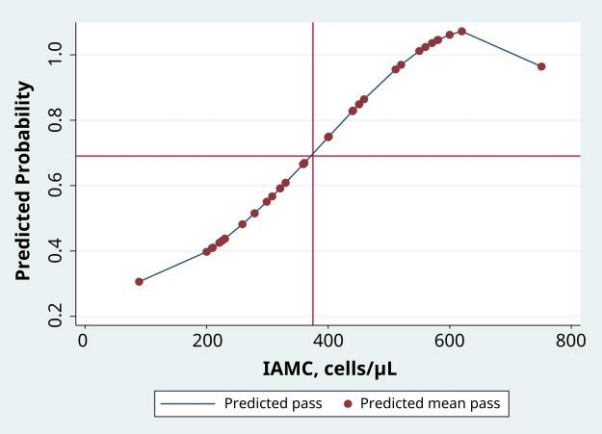
To evaluate the predictive value of initial AMC for neutrophil recovery, the area under the receiver operating characteristic curve (AUROC) was calculated. The AUROC was 0.804 (Figure 2). The optimal cutoff value of 375 cells/μL for the initial AMC predicted neutrophil recovery (ANC ≥ 1500 cells/μL) on day 7 with a sensitivity of 58.6%, specificity of 100%, positive predictive value (PPV) of 100%, and negative predictive value (NPV) of 52% (Figure 3).

Figure 2. Area Under the Receiver Operating Characteristic Curve of the Initial Absolute Monocyte Count for Predicting Neutrophil Recovery on Day 7



Abbreviation: ROC, receiver operating characteristic.

Figure 3. Relationship Between the Initial Absolute Monocyte Count and of Neutrophil Recovery Prediction on Day 7, Including the Optimal Cutoff Point



Abbreviation: IAMC, initial absolute monocyte count.

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Discussion

This study evaluated patients with solid organ malignancies who developed CIN while receiving chemotherapy at Chonburi Hospital between 1 January 2022 and 31 August 2023. Among the 42 patients enrolled, 29 (69.04%) showed neutrophil recovery (ANC ≥ 1500 cells/μL) on day 7, whereas 13 (30.95%) did not recover (ANC < 1500 cells/μL). The initial AMC was significantly higher in the recovery group (mean [SD], 422.97 [144.66] cells/μL) than in the nonrecovery group (mean [SD], 272 [82.13] cells/μL), with a statistically significant difference (*P* = .001). Furthermore, the optimal AMC threshold of 375 cells/μL was determined to predict neutrophil recovery with an AUROC of 0.804, sensitivity of 58.6%, specificity of 100%, PPV of 100%, and NPV of 52%.

The findings of this study indicate that a higher initial AMC is associated with better neutrophil recovery after CIN.[9-11] This relationship aligns with previous studies, such as the work of Sugimoto et al,[12] which found that colony-forming unit granulocyte-monocyte transitions to monocytes earlier than neutrophils in murine bone marrow.

The predictive role of monocytes is further supported by clinical evidence. Ouyang et al,[13] demonstrated in a study of 103 patients with solid organ malignancies that peripheral blood monocyte counts consistently change before neutrophil levels; specifically, monocytes began to decrease 1.39 days earlier, reached their nadir 3.81 days before neutrophils, and recovered 2.36 days earlier. Similarly, Moriyama et al[14] conducted a retrospective study of 75 small cell lung cancer (SCLC) patients receiving platinum-based chemotherapy and found that monocyte nadir could significantly predict neutrophil nadir. In their study, the median time to monocyte nadir was 6 days, whereas the median time to neutrophil nadir was 12 days, indicating that the monocyte nadir preceded the neutrophil nadir by mean (SD) of 6 (4) days.

Consistent with these findings, a study at Chulalongkorn Hospital, Thailand,[15] highlighted the predictive capacity of baseline AMC, showing that patients with higher counts (≥ 15% or ≥ 400 cells/μL) had a significantly higher incidence of neutrophil recovery by day 3, highlighting the predictive capacity of AMC.

At the oncology outpatient department of Chonburi Hospital, chemotherapy administration is delayed when neutropenia is detected on the scheduled chemotherapy day, and patients are scheduled for follow-up CBC evaluation on day 7. Currently, no local or international studies have investigated monocyte count as a predictor of neutrophil recovery at a 7-day interval after CIN. Therefore, this study aimed to identify the optimal initial AMC threshold to predict neutrophil recovery after 7 days of follow-up. The cutoff value of 375 cells/μL, determined through AUROC analysis, showed high specificity (100%) and PPV (100%), indicating that this threshold could be clinically useful in predicting neutrophil recovery.

The findings of this study are comparable with those of a previous study,[15] which determined an optimal AMC threshold of 340 cells/μL for predicting neutrophil recovery on day 3 with 65.9% sensitivity and 70.5% specificity. The results suggest that at day 3, the initial AMC value may not yet be a sufficiently strong predictor for recovery from neutropenia (ANC < 1500 cells/μL). However, this study, which evaluated AMC levels on day 7, demonstrated that an initial AMC of ≥ 375 cells/μL could serve as a practical predictive marker for neutrophil recovery with high specificity and PPV.

The practical application of this finding holds important value in clinical oncology, particularly in managing chemotherapy scheduling. When a patient presents for a subsequent treatment cycle and the ANC is < 1500 cells/μL, standard practice dictates a treatment delay.

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The clinician can immediately check the initial AMC in this scenario. The demonstration that an AMC of ≥ 375 cells/μL provides 100% specificity and 100% PPV in this trial offers a high degree of certainty for a critical clinical decision. In particular, this threshold strongly predicts that if the chemotherapy is delayed by exactly 7 days, the patient's ANC will reliably recover to > 1500 cells/μL, allowing the planned treatment to be administered safely. This allows the clinical team to manage the delay confidently, minimizing unnecessary uncertainty and resource utilization while ensuring timely treatment resumption for patients who meet this favorable predictive criterion. Future studies with larger populations and multicenter designs are warranted to validate this cutoff and explore its applicability across different malignancies and chemotherapy regimens.

Strengths and Limitations

To the best of our knowledge, this study is the first to explore the optimal initial AMC threshold for predicting neutrophil recovery on day 7 following CIN. AUROC analysis enabled the identification of a clinically relevant cutoff value. However, as this was a retrospective study, it is prone to biases associated with data retrieval and documentation errors. Additionally, the sample size was limited, and the chemotherapy regimens were varied, which may limit the generalizability of the findings to other cancer types and treatment protocols. Prospective, larger-scale studies are recommended to confirm these findings and potentially refine the AMC threshold for clinical use.

Conclusions

This retrospective cohort study demonstrated that the initial AMC is significantly associated with neutrophil recovery in patients with CIN. An initial AMC of ≥ 375 cells/μL was found to predict neutrophil recovery (ANC ≥ 1500 cells/μL) on day 7 with high specificity (100%) and a PPV of 100%, indicating its potential utility in clinical practice for guiding treatment planning. Integrating initial AMC measurement during routine chemotherapy visits may enhance neutrophil recovery prediction and improve patient management strategies.

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Additional Information

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Ethics Approval: This study was conducted at the outpatient Medical Oncology Department (OPD Med and OPD Onco Med) of Chonburi Hospital, Thailand, from 1 January 2022 to 31 August 2023. Ethical approval for this study was obtained from the Ethics Committee, Chonburi Hospital (No. 15/67/R/h3 on 26 July 2024). This study strictly adhered to the principles of the Declaration of Helsinki and Good Clinical Practice guidelines.

Clinical Trial Consideration: This study does not report on a clinical trial.

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Conflict of Interest: The authors declare no conflicts of interest associated with this study.

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