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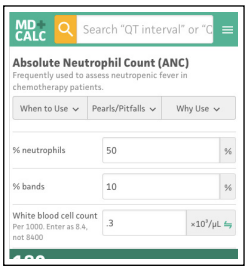

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Absolute Neutrophil Count

Introduction: The Absolute Neutrophil Count is frequently used to assess neutropenic fever in chemotherapy patients.

Points & Pearls

- Absolute Neutrophil Count (ANC) calculation is not a static measurement done only once upon hospital admission. Rather, it is often measured daily in critically ill patients (for example, to assess the bone marrow's response after chemotherapy).
- Recall that the ANC is dynamic; it is an absolute value and is **expected** to drop during the patient's nadir after chemotherapy.

Critical Actions

If the clinical scenario is suggestive of neutropenic fever, appropriate cultures and infectious disease workup should be instituted along with prompt initiation of empiric broad-spectrum antibiotics to cover mostly endogenous flora.

Evidence Appraisal

Al-Gwaiz et al (2007) tested the application of ANC to predict bacterial infections. They examined 105 peripheral blood smears and determined ANC, as well as the sensitivity of predicting bacterial infections. They determined that the ANC and toxic granulations are more sensitive than band count in predicting bacterial infections. Rivera et al (2003) performed a cross-validation study of Silber et al's 1998 findings to test if the first-cycle nadir ANC predicted the risk of febrile neutropenia. An ANC of $\leq 0.5 \times 10^9$/L was associated with a relative odds ratio of 4.8. The goal of this study was to provide a foundation for which dose adjustments in chemotherapy can be made to provide maximal anti-neoplastic therapy while minimizing side effects.

CALCULATOR REVIEW AUTHOR

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Instructions

Use in neutropenic patients with a fever of at least 38°C (100.4°F). Do not use in patients with acute leukemia who are undergoing induction chemotherapy or allogeneic hematopoietic stem cell transplant conditioning, per IDSA guidelines.

Use The Calculator Now

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Calculator Creator

Layla A. Al-Gwaiz, MD, FCAP
Click here to read more about Dr. Al-Gwaiz.

References

Original/Primary Reference

- Al-Gwaiz LA, Babay HH. The diagnostic value of absolute neutrophil count, band count and morphologic changes of neutrophils in predicting bacterial infections. *Med Princ Pract.* 2007;16(5):344-347.

Validation References

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- Rivera E, Haim Erder M, Fridman M, et al. First-cycle absolute neutrophil count can be used to improve chemotherapy-dose delivery and reduce the risk of febrile neutropenia in patients receiving adjuvant therapy: a validation study. *Breast Cancer Res.* 2003;5(5):R114-R120.

Why to Use

The ANC can be calculated with a routine complete blood cell (CBC) count and differential. No additional laboratory work is needed to complete the calculation. It is a tool that provides rapid risk stratification.

When to Use

- The ANC can be critical in assessing an immunocompromised patient's risk for developing opportunistic infections. It is commonly used in the hospital setting, clinic, and emergency department.
- If a patient undergoing active myelosuppressive chemotherapy presents with a sustained fever (with or without localizing symptoms), there is a risk of progression to sepsis. Thus, it is imperative to calculate the ANC to help decide whether empiric antibiotics should be initiated.

Next Steps

- Neutropenic fever (without a source of infection found) is typically the result of direct toxic effects of chemotherapy on mucosal surfaces and the immune system, in addition to the impact of the underlying malignancy. It is defined as a single oral temperature of ≥ 38.3°C (100.9°F), or a sustained temperature of > 38°C (100.4°F) for over 1 hour in a patient with neutropenia. Neutropenic fever is typically seen in those who have received anticancer therapies in the last 6 weeks. Filgrastim (Neupogen®, Zarxio®), also known as G-CSF, can stimulate production of neutrophils, but is rarely indicated in the evaluation and treatment of neutropenic fever.
- Additional tools to risk stratify a neutropenic fever patient and predict complications include the Clinical Index of Stable Febrile Neutropenia (CISNE) score and the Multinational Association for Supportive Care in Cancer (MASCC) score.
- Obtain a complete blood count with differential.
- ANC is calculated as 10 x WBC count in 1000s x (% PMNs + % bands)
- Classify neutropenia as mild, moderate, or severe according to the following:
  Neutropenia: ANC < 1500 cells/mm³
  - Mild neutropenia: 1000-1500 cells/mm³
  - Moderate neutropenia: 500-999 cells/mm³
  - Severe neutropenia: < 500 cells/mm³
- ANC values also can be interpreted by NCI risk categories, as in the table below:

NCI Risk Category	ANC
0	Within normal limits
1	≥ 1500 to < 2000 cells/mm³
2	≥ 1000 to < 1500 cells/mm³
3	≥ 500 to < 1000 cells/mm³
4	< 500 cells/mm³

Other References

- Klastersky J, Paesmans M, Rubenstein EB, et al. The Multinational Association for Supportive Care in Cancer risk index: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients. *J Clin Oncol.* 2000;18(16):3038-3051.
- Carmona-Bayonas A, Jiménez-Fonseca P, Virizuela Echaburu J, et al. Prediction of serious complications in patients with seemingly stable febrile neutropenia: validation of the Clinical Index of Stable Febrile Neutropenia in a prospective cohort of patients from the FINITE study. *J Clin Oncol.* 2015 Feb 10;33(5):465-471.
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Related Calculator

- Click here to access the Clinical Index of Stable Febrile Neutropenia (CISNE).

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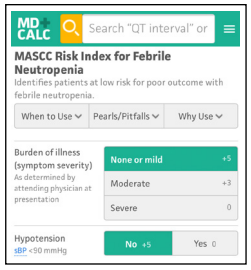

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MASCC Risk Index for Febrile Neutropenia

Introduction: The MASCC risk index for febrile neutropenia identifies patients who are at low risk for poor outcomes with febrile neutropenia.

Points & Pearls

- The Multinational Association for Supportive Care in Cancer (MASCC) risk index applies only to adult patients.
- It is validated as a dichotomous outcome: low-risk versus not-low-risk. Obviously, patients who are "not-low-risk" have varying degrees of risk.

Critical Actions

The Infectious Diseases Society of America (IDSA) recommends admission for empiric antibiotics for high-risk patients who are not already admitted to the hospital.

Evidence Appraisal

The derivation study for the MASCC risk index was performed in the late 1990s (1994-1997) and included 756 patients in the derivation cohort and 383 patients in the validation cohort. While many claim that the MASCC risk index cannot be applied to patients with hematologic malignancies, over 40% of the patients included in the study had a hematologic malignancy. Logistic regression analysis was used to determine a weighted risk score with a positive predictive value (PPV) of 91%, specificity of 68%, and sensitivity of 71%.

Of note, patients were only included in the study for a single episode of febrile neutropenia and were not allowed to re-enter the study for subsequent episodes; thus, it is unclear whether the score should be applied to patients with multiple episodes of febrile neutropenia, although this is routinely done in clinical practice.

There have been at least 8 external validation studies showing a PPV from 83% to 98% with sensitivity from 59% to 95%. Studies that included more patients with hematologic malignancies had lower PPV and sensitivity, suggesting a poorer performance of the score in that population.

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Instructions

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Use The Calculator Now

Click here to access the calculator.

Calculator Creator

Jean Klastersky, MD
Click here to read more about Dr. Klastersky.

References

Original/Primary Reference

- Klastersky J, Paesmans M, Rubenstein EB, et al. The Multinational Association for Supportive Care in Cancer risk index: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients. *J Clin Oncol.* 2000;18(16):3038-3051.

Validation References

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Why to Use

Febrile neutropenia is a potentially life-threatening complication of chemotherapy, but some patients are at low risk for serious complications. The MASCC risk index is an internationally validated scoring system that identifies these low-risk patients who can potentially be treated as outpatients with early antibiotics.

When to Use

- Use at onset of fever, to assess the risk of complications in febrile neutropenia for patients undergoing chemotherapy treatment.
- Use after addressing immediate concerns, to identify patients who may not need to be admitted to the hospital or could be discharged early.

Next Steps

- Higher scores indicate lower risk, with a maximum of 26 points. Using a cutoff value of ≥ 21 points discriminates patients with low risk from those with high risk (< 21 points) for serious complications of febrile neutropenia, eg, death, admission to the intensive care unit, or hypotension.
- The MASCC score has been endorsed by the IDSA since 2002 with Level B (moderate) evidence supporting its use. However, most experts consider high-risk patients to be those with anticipated prolonged neutropenia (> 7 days), profound neutropenia (absolute neutrophil count < 100), and/or comorbid conditions (in addition to chronic obstructive pulmonary disease) – Level A evidence – that are not necessarily accounted for in the MASCC score. Therefore, clinical judgment by specialists (in infectious disease, hematology/oncology, or emergency medicine/internal medicine/critical care) with knowledge of predicted disease-specific chemotherapy effects may override the MASCC score.
- High-risk patients require admission for intravenous antibiotics.
- Carefully selected low-risk patients should receive oral or intravenous empiric antibiotics in a clinic or hospital setting, and may be transitioned to outpatient regimens if they meet certain criteria.

- Carmona-Bayonas A, Gómez J, González-Billalabeitia E, et al. Prognostic evaluation of febrile neutropenia in apparently stable adult cancer patients. *Br J Cancer.* 2011;105(5):612-617.

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