A clinical score identified cancer patients with febrile neutropenia at low risk for complications

Klastersky J, Paesmans M, Rubenstein EB, et al, for the Study Section on Infections of Multinational Association for Supportive Care in Cancer. **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 Aug;18:3038-51.

Question

In cancer patients with febrile neutropenia (FN), can a scoring system be developed to identify patients at low risk for complications?

Design

2 cohorts, 1 for derivation and 1 for validation of the scoring system.

Setting

20 institutions from 15 countries.

Patients

756 patients (median age 52 y, 52% women) were in the derivation cohort (random 67% of participating centers), and 383 patients (median age 52 y, 52% men) were in the validation cohort (33% of centers). Inclusion criteria were granulocyte count < 500/μL, including polymorphonuclear leukocytes and band forms associated with malignancy; temperature > 38° C; age > 16 years; and treatment with appropriate empiric antibiotics. The first febrile episode was analyzed.

Description of prediction guide

After multivariate analysis, the factors and weighted scores (points) in the final model were burden of illness (no or mild symptoms, 5 points; moderate symptoms, 3 points), no hypotension (5 points), no chronic obstructive pulmonary disease (4 points), solid tumor or no previous fungal infection (4 points), no dehydration (3 points), outpatient status (3 points), and age < 60 years (2 points). Factor scores were added, and a score of ≥ 21 points was considered to be low risk.

Main outcome measure

Low risk (high probability of fever resolution without serious complications or death) at fever onset.

Main results

6% of patients in the derivation cohort and 9% in the validation cohort who were determined to be at low risk developed complications (confusion, cardiac problems, respiratory failure, hypotension, renal failure, bleeding, and death). Of those patients predicted to be at high risk, 39% in the derivation and 36% in the validation cohort developed complications. Sensitivity, specificity, and likelihood ratios for 2 scores of low risk are in the Table.

Conclusion

In cancer patients with febrile neutropenia, a validated, international scoring system identified those at low risk for complications.

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Test characteristics of the prediction scores to identify patients with febrile neutropenic cancer treated with empiric antibiotic regimens who are at low risk for developing complications*

Score	Cohort	Sensitivity (95% CI)	Specificity (CI)	+LR	–LR
≥ 21	Derivation	80% (77 to 83)	71% (62 to 79)	2.8	0.27
	Validation	71% (66 to 76)	68% (57 to 79)	2.3	0.42
≥ 22	Derivation	57% (53 to 61)	88% (81 to 94)	4.8	0.49
	Validation	47% (42 to 53)	86% (76 to 93)	3.5	0.61

*LRs and CIs defined in Glossary and calculated from data in article.

Commentary

Klastersky and colleagues studied variables that reflect conventional clinical judgment about which patients with FN are at risk for serious complications. Mortality rates among patients with a high score were 1% in the derivation set and 1.6% in the validation set. None of these patients died immediately, so physicians could presumably still hospitalize them. This scoring system compares favorably with others (1, 2). Nevertheless, I am surprised to see that the type of treatment (e.g., bone marrow transplant [BMT]) does not influence the outcome. Perhaps too few patients with BMT (32 underwent allogeneic BMT) were analyzed. On the other hand, this analysis implies that at least some patients with BMT might be managed as outpatients.

I believe this scoring system can be useful, but I am reluctant to change my own practice for 2 reasons. First, the threshold of 21 recommended by the authors is problematic. It is based on misclassification rates that give false-positive results (low-risk patients who developed serious complications) and false-negative results (high-risk patients with resolution and no serious complications) equal weight. This is not necessarily an appropriate balance. In my practice, false-positive predictions are disastrous, whereas false-negative ones are unpleasant. The optimal threshold for a given rule should take into account the relative seriousness of adverse sequelae associated with false-positive and false-negative errors (3). Second, this scoring system should be verified in the BMT setting (4). If accuracy is confirmed in this setting, this scoring system may dramatically affect the management of FN.

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