MULTICENTER RETROSPECTIVE DEVELOPMENT AND VALIDATION OF A CLINICAL PREDICTION RULE FOR INVASIVE CANDIDIASIS(IC) IN THE INTENSIVE CARE SETTING.

Ostrosky-Zeichner L[1], Sable C[2], Sobel J[1], Alexander B[1], Donowitz G[1], Kan V[1], Kauffman CA[1], Kett D[1], Larsen R[1], Morrison V[1], Nucci M[1], Pappas PG[1], Bradley ME[1], Major S[3], Wallace D[3], Rex JH[1].
[1] NIAID/BAMSG Candidiasis subgroup, Birmingham, USA
[2] Merck & Co., Inc., Whitehouse Station USA
[3] Rho/BAMBU, Chapel Hill, USA

Introduction: A prediction rule that correctly identifies subjects at high risk for IC in the intensive care setting is essential for prophylactic interventions. Currently, there are no such prediction rules that have been validated in a multicenter fashion.
Methods: Based on a previous study (ICAAC 2002, M-1239), a retrospective chart review was performed at 12 intensive care units (ICU) from 9 hospitals in the United States and Brazil. Demographics, hospital course, and incidence of proven and probable IC (according to EORTC/MSG criteria), along with classically described risk factors were collected for adult patients who stayed in the ICU ≥ 4 days over a period of one year. The population was subsequently split in two sub-populations: a training sample (75%) and a validation sample (25%). Multiple combinations with increasing numbers and conditionals of the most frequent risk factors with specific time frames were systematically evaluated to see which combinations predicted an incidence of invasive candidiasis ~ 10% in the training sample and then were subsequently validated.
Results: The analysis included 2890 patients from 7 medical, 4 surgical, and 1 medical-surgical ICUs. Overall proven and probable IC rates in the different units ranged from 0.6% to 12.5% with a mean of 3%. The best performing clinical prediction rule was: Patients hospitalized in the ICU for at least 48hrs with an estimated stay of an additional 48hr or more with at least one of the following: Any systemic antibiotic on days 1-4 of ICU stay OR presence of a central venous catheter on days 1-4 of ICU stay and still present at time of enrollment, AND at least two of the following: Use of total parenteral nutrition on days 1-4 of ICU stay, any type dialysis on days 1-4 of ICU stay, any major in-patient surgery in the 7 days prior to or on ICU admission, pancreatitis in the 7 days prior to or on ICU admission, use of systemic steroids in the 7 days prior to ICU admission and up to enrollment, and use of other systemic immunosuppressive agents in the 7 days prior to ICU admission. The performance of the prediction rule in the different subpopulations is shown in the table below. While the specific rate of infection in patients meeting the rule varied across centers, the rule consistently identified a group that had a higher rate than the overall rate for that unit.
Conclusion: A clinical prediction rule that identifies subjects with ~ 10% risk of IC in the ICU was developed and validated in the multicenter setting. This rule should be prospectively validated and may be useful in prophylaxis trials.

Population (N)	N (%) of eligible patients who meet the rule	N (%) of IC patients who meet the rule	IC rate among patients who do not meet the rule	IC rate among patients who meet the rule	OR (95% CI)
Training (2175)	218 (10.1%)	20 (30.3%)	2.4%	9.2%	3.86 (2.32, 6.39)
Validation (715)	85 (12.0%)	10 (45.5%)	1.9%	11.8%	6.11 (2.72, 13.70)
All data (2890)	303 (10.6%)	30 (34.1%)	2.3%	9.9%	4.36 (2.85, 6.67)