Clinical risk score for prediction of invasive candidiasis to guide empiric echinocandin therapy

Mary Jane Braham, PharmD[1], Wei Fang, PhD[2], Lauren K. Freeman, PharmD, BCIDP[1]
WVU Hospitals – Department of Pharmaceutical Services, Morgantown, WV[1];
WVU Health Sciences Center – West Virginia Clinical and Translational Science Institute, Morgantown, WV[2]

Accredited

Background

- Recommendations for empiric therapy with an echinocandin for invasive candidiasis (IC) based upon risk factors do not exist[1,2]
- Current treatment guidelines for IC largely recommend an echinocandin as initial therapy[1,2]
- Echinocandins have demonstrated non-inferiority to other antifungals for the treatment of IC with low toxicity, few drug-drug interactions, and activity against azole-resistant *Candida* species[3]
- Bedside-scoring tools are useful in guiding clinical decision-making[4]
- Guidelines recommend risk prediction instruments (e.g., Candida Score) to facilitate earlier recognition and initiation of antifungals[2]
- Application of these apparatuses are limited due to poor positive predictive value, lack of validation, and absence of use in certain patient populations[5]

Objectives

Primary

- Develop a risk score to predict probability of IC and guide empiric antifungal treatment in hospitalized, adult patients

Secondary

- Identify risk factor(s) present in patients treated with empiric echinocandin therapy for proven or suspected IC
- Internally validate an IC prediction score using a multivariable logistic regression model

Methods

Study Design

- Retrospective, multi-center, case-control study
- Study protocol was deemed exempt by the West Virginia University Institutional Review Board

Setting and Population

- Patients ≥ 18 years that received ≥ 1 dose of an echinocandin (i.e., micafungin) for proven or suspected IC between July 1, 2020 and June 30, 2021 were included
- Patients pregnant or incarcerated were excluded

Data Collection

- Randomization tool was utilized to screen patients for inclusion
- Data extracted from Epic electronic medical record (EMR) using a standardized data collection tool

Results

- A total of 318 patients that received ≥ 1 dose of micafungin during the time frame were included

Table 1. Demographic and clinical characteristics of patients with proven or suspected IC

Characteristic	Result (N=318)
Age (years), median [IQR]	61 [48, 70]
Sex (male), n (%)	168 (52.8)
Confirmed IC (Y), n (%)	110 (34.6)
Endovascular, n/N (%)	59/110 (53.6)
Intra-abdominal, n/N (%)	27/110 (24.5)
Bone and joint, n/N (%)	11/110 (10)
Skin and soft tissue, n/N (%)	11/110 (10)
Other, n/N (%)	2/110 (1.8)
Risk factor(s) suspected IC, median [IQR]	2 [2, 3]
Risk factor(s) confirmed IC, median [IQR]	2 [1, 3]
Risk factor(s) overall cohort, median [IQR]	2 [2, 3]
Anti-anaerobic agent(s), n (%)	275 (86.5)
Critically ill, n (%)	175 (55)
Intravascular device(s), n (%)	112 (35.2)
Gastrointestinal (GI)[a], n (%)	115 (36.2)
Renal replacement therapy (RRT), n (%)	65 (20.4)
Parenteral nutrition, n (%)	40 (12.6)

a – GI manipulation, necrotizing pancreatitis, anastomotic leak

Table 2: Micafungin utilization characteristics

Characteristic	Result (N=318)
Dose (mg/day), median [IQR]	100 [100, 100]
Antifungal duration (day), median [IQR]	4 [2, 10]
Infectious diseases (ID) consult (Y), n (%)	163 (51.2)
ID recommended (Y), n/N (%)	134/163 (82.2)

Table 3: Univariable logistic regression for IC risk factors

Risk Factor	Odds Ratio (95% Confidence Interval)
Anti-anaerobic agent(s)	0.5 (0.2 – 0.9)
Critically ill	0.5 (0.3 – 0.8)
Intravascular device(s)	1.4 (0.8 – 2.3)
GI	1.4 (0.8 – 2.4)
RRT	0.8 (0.4 – 1.4)
Parenteral nutrition	2.1 (1 – 4.4)

Figure 1. Estimated probability of IC based on IC risk prediction score (RPS)

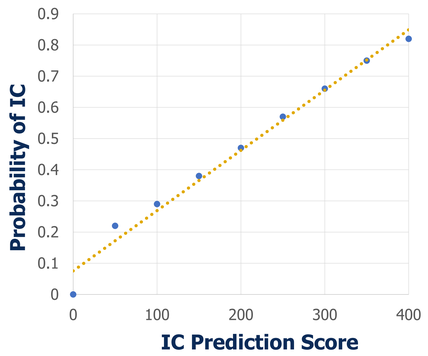
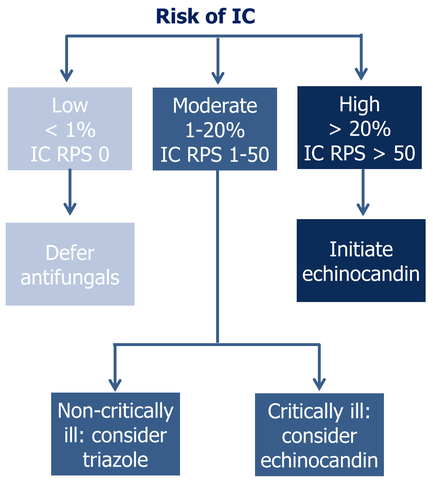


Table 4: Internal validation IC RPS

IC RPS	Sen[a]	Spe[b]	PPV[c]	NPV[d]
> 50	90%	30%	41%	85%

a – sensitivity; b – specificity; c – positive predictive value; d – negative predictive value

Figure 2: Algorithm for application of IC RPS in management of IC



Results continued

- The six selected predictors had an overall significant predictive power on IC (p = 0.0017)
- Critically ill (χ^2 = 7.4, p = 0.0066), anti-anaerobic agent(s) (χ^2 = 4.9, p = 0.0267), and parenteral nutrition (χ^2 = 4, p = 0.0442) had the highest predictive values and were significantly associated with IC
- Using a cutoff score of > 50 to indicate high probability of IC provided the best performance with a sensitivity of 90% and negative predictive value of 85%
- Echinocandin utilization (days of therapy) has been reduced by 19% year-to-date

Discussion

- Implementation of the IC RPS improves empiric antimicrobial therapy and echinocandin utilization
- Effects are increased in combination with other antimicrobial stewardship interventions (e.g., prospective audit and feedback in patients on echinocandin therapy and/or with candidemia, institution specific guidelines for candidemia, dose optimization via order instructions and antimicrobial dosing guidance, clinical education)
- Strengths include the multi-center design which comprised data from patients at five hospitals within the health system
- Limitations include the retrospective design of the evaluation in determining if subjects analyzed had identified risk factors for development of IC

References

1. Pappas PG, *et al. Clin Infect Dis.* 2016; 62(4): 1-50.
2. Martin-Loeches I, *et al. Intensive Care Med.* 2019; 45(6): 789-805.
3. Wiederhold NP, *et al. Infect Drug Resist.* 2008; 1: 63-77.
4. Cortegiani A, *et al. Crit Care.* 2019; 23: 190.
5. Leon C, *et al. Crit Care Med.* 2009; 37: 1624-33.

Contact information Mary Jane Braham, PharmD
mary.braham@wvumedicine.org
(304) 288-7080

Contact information Lauren Freeman, PharmD, BCIDP
lauren.freeman@wvumedicine.org
(843) 532-6826

Disclosure: Authors have no conflicts of interest to disclose.