



Impact of Revised Infectious Diseases Society of America and Society for Healthcare Epidemiology of America Guideline on the Classification of *Clostridioides difficile* Infection Severity

Contact Information:
Travis J. Carlson, PharmD
High Point University
Phone: (336) 841-2860
Email: tcarlso2@highpoint.edu

Travis J. Carlson¹, Anne J. Gonzales-Luna², Kimberly Nebo², Hannah Y. Chan², Ngoc-Linh T. Tran², Sheena Antony², Kevin W. Garey²

¹Department of Clinical Sciences, High Point University Fred Wilson School of Pharmacy, ²Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

ABSTRACT

Background: The Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) revised their *Clostridioides difficile* infection (CDI) severity classification criteria in 2017 to include a serum creatinine (SCr) value above a threshold (≥ 1.5 mg/dL) rather than a relative increase from baseline (≥ 1.5 times the pre-morbid level). To date, these criteria have not been validated and may overestimate the number of severe CDI cases in patients with underlying renal insufficiency.

Methods: This multicenter, retrospective cohort study included all patients ≥ 18 years of age with CDI diagnosed in two large health systems in the Houston, Texas area between 2016 and 2018. Patients were assessed for presence of acute kidney injury (AKI) and chronic kidney disease (CKD), defined per the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, and IDSA/SHEA CDI severity classification criteria per the 2010 and 2017 CDI guidelines. The primary outcome was all-cause inpatient mortality.

Results: The study cohort consisted of 770 CDI episodes from 12 hospitals. A large proportion of episodes occurred in patients with preexisting CKD (36.5%) and concomitant AKI (29.6%). Eighty-two episodes (10.6%) showed discordant results when applying the 2017 revised severity classification criteria due to the identification of patients with preexisting CKD. However, the 2017 severity classification criteria were better correlated with all-cause mortality (OR, 5.40; 95% CI, 1.84-15.86; $P=0.002$) than were the 2010 severity classification criteria (OR, 3.12; 95% CI, 1.35-7.19; $P=0.008$) as the 2017 SCr criterion was an independent predictor of mortality (OR, 3.66; 95% CI, 1.66-8.05; $P=0.001$) while the 2010 SCr criterion was not (OR, 1.47; 95% CI, 0.71-3.08; $P=0.30$).

Conclusion: Our findings support the inclusion of the 2017 IDSA/SHEA CDI severity classification criteria in future CDI guideline updates.

SPECIFIC AIMS

- 1) Describe the number of patients diagnosed with CDI that have concomitant AKI, CKD, and/or require chronic renal replacement therapy
- 2) Assess the impact of the revised SCr criterion on the number of CDI cases classified as severe
- 3) Assess the ability of both the 2010 and 2017 IDSA/SHEA SCr criteria to predict mortality

This work was supported by the Society of Infectious Diseases Pharmacists and the National Institutes of Health NIAID (U01AI124290-01)

METHODS

Study design / population

- Multicenter, retrospective cohort study
 - 12 hospitals
 - 2016-2018
 - Houston, TX
- Inclusion criteria:
 - Age ≥ 18 years
 - Diagnosed with CDI
 - Documented values for:
 - Baseline SCr within 1 year of CDI diagnosis
 - SCr within 24 hours of CDI diagnosis
 - White blood cell (WBC) count within 24 hours of CDI diagnosis

Definitions and outcomes

- Laboratory analytes measured at the time of CDI diagnosis (± 24 hours)
 - WBC count
 - SCr
 - Serum eosinophil count
 - Serum albumin level
- AKI and CKD were defined per the KDIGO guidelines
 - Glomerular filtration rate (GFR) was estimated using the 2009 CKD-EPI equation
 - Patients receiving chronic renal replacement therapy (hemodialysis or peritoneal dialysis) were classified as having KDIGO CKD category G5 regardless of their GFR
- Primary outcome: all-cause inpatient mortality

Statistical analysis

- Multivariable logistic regression
 - Selection using univariate analysis ($P < 0.20$)
 - Backwards elimination ($P > 0.05$) using partial likelihood ratio test

RESULTS

Table 1. Cohort characteristics

Covariate	Cohort (n = 770)
Age, mean (\pm SD), y	65.3 (16.7)
Female, no. (%)	418 (54.3)
Race/ethnicity, no. (%)	
White, non-Hispanic	453 (58.8)
Black, non-Hispanic	158 (20.5)
Hispanic	116 (15.1)
Asian	18 (2.3)
Other	25 (3.3)
Admitted from home, no. (%)	593 (77.0)
Charlson Comorbidity Index, median (IQR)	2 (1-4)
History of solid organ transplantation, no. (%)	66 (8.6)
History of stem cell transplantation, no. (%)	2 (0.3)
History of CDI ever, no. (%)	217 (28.2)
CDI diagnostic testing method, no. (%)	
NAAT	747 (97.0)
EIA	23 (3.0)
Healthcare facility-onset CDI, no. (%)	331 (43.0)
Recurrent CDI, no. (%)	94 (12.2)
Temperature, mean (\pm SD), °F	98.8 (1.4)
SCr (baseline), median (IQR), mg/dL	0.90 (0.66-1.32)
Collected within 30 days, no. (%)	417 (54.2)
Collected within 31-90 days, no. (%)	110 (14.3)
Collected within 91-365 days, no. (%)	243 (31.5)
SCr (within 24 hrs of diagnosis), median (IQR), mg/dL	1.10 (0.74-2.20)
WBC, median (IQR), cells/ μ L	10,900 (7,200-16,400)
Eosinophils, median (IQR), cells/ μ L	80 (10-190)
Albumin, mean (\pm SD), g/dL	3.0 (0.7)

Figure 1. Cohort stratified by type of kidney injury



Table 2. Severity classification based on 2010 vs. 2017 severity classification criteria

	2010 Severity Criteria		2017 Severity Criteria	
	SCr ≥ 1.5 x baseline	SCr < 1.5 x baseline	SCr ≥ 1.5 mg/dL	SCr < 1.5 mg/dL
WBC $\geq 15,000$ cells/ μ L	Severe (n = 94)	Severe (n = 147)	Severe (n = 113)	Severe (n = 128)
WBC $< 15,000$ cells/ μ L	Severe (n = 134)	Mild-to-moderate (n = 395)	Severe (n = 178)	Non-severe (n = 351)

Figure 2. Multivariable analyses for predictors of mortality

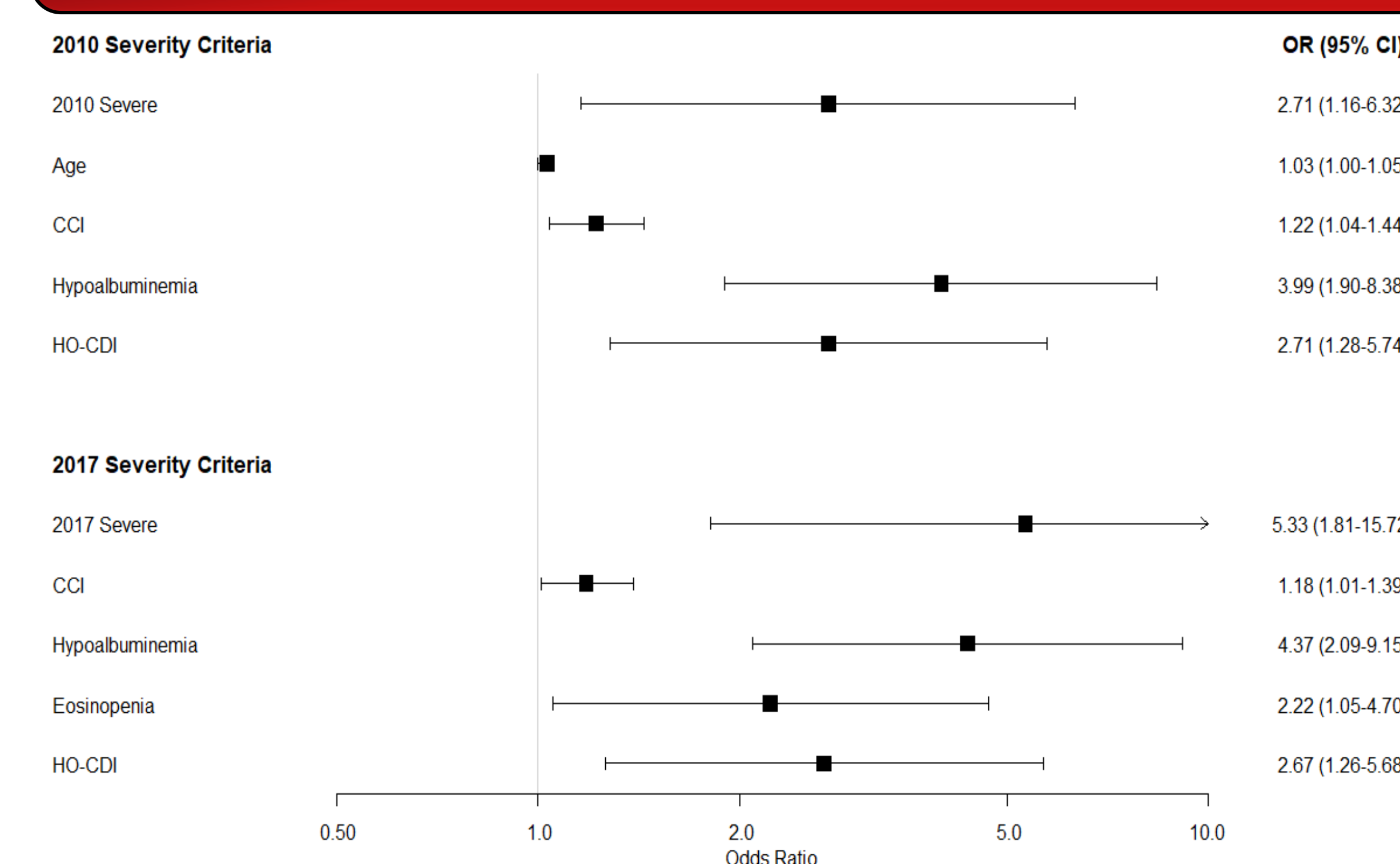
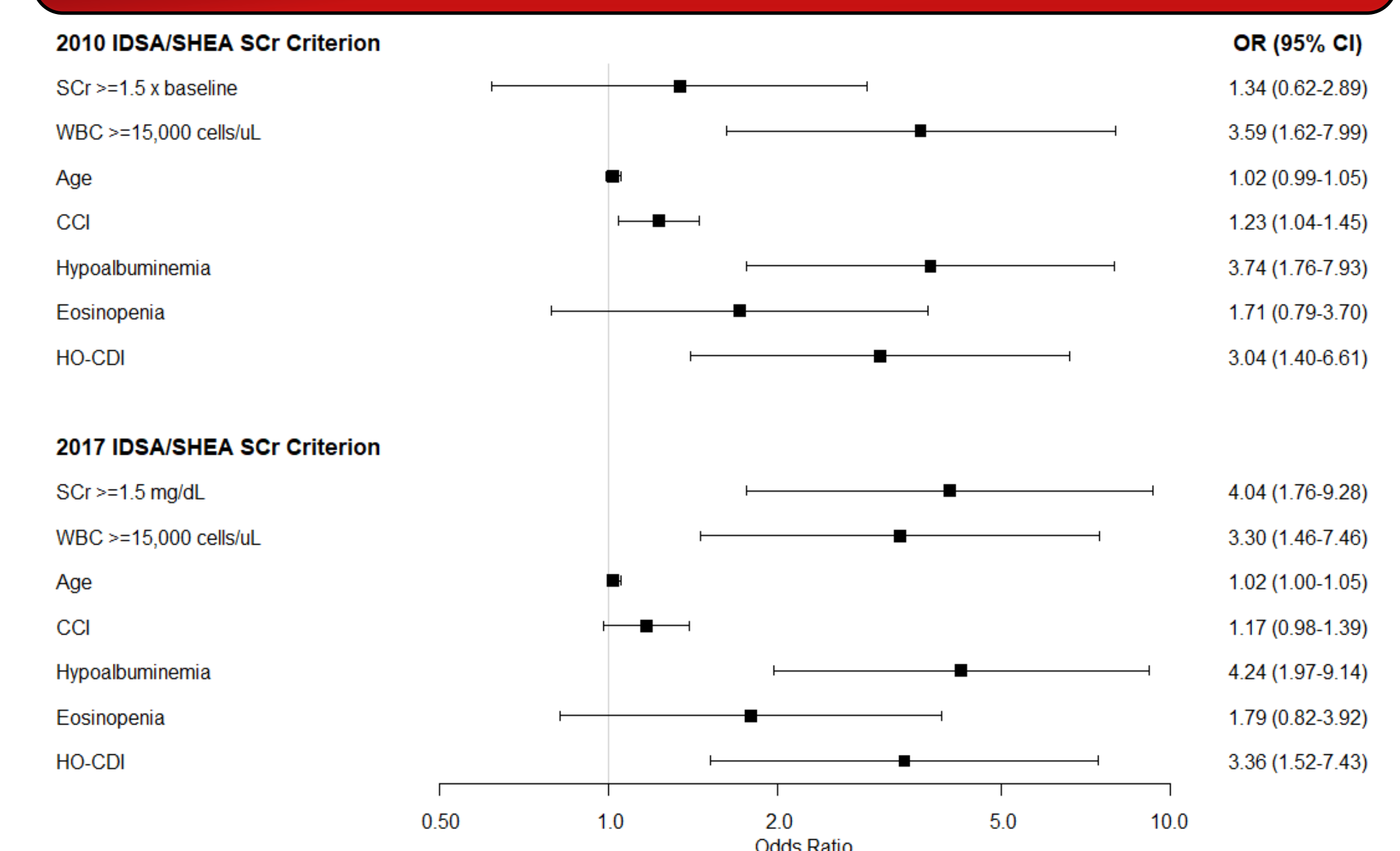


Figure 3. Multivariable analyses of SCr criterion for association with mortality



CONCLUSIONS

- The changing criteria for kidney injury from a relative change to an absolute serum creatinine threshold changed the CDI severity classification for 82 of 770 patients (10.7%).
- The change in criteria better predicted all-cause inpatient mortality both as a single criterion and together with WBC assessment.