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MODIFIED NUTRIC SCORE AND SEVERITY OF ACUTE KIDNEY INJURY IN MECHANICALLY VENTILATED ADULT ICU PATIENTS: A PROSPECTIVE SINGLE-CENTRE INDIAN OBSERVATIONAL STUDY.

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Abstract

Background: The modified Nutrition Risk in the Critically Ill (mNUTRIC) score has been associated with adverse outcomes in critical care, but its relationship with acute kidney injury (AKI) severity in mechanically ventilated patients has not been formally characterised in Indian critical care settings. ***Methods:*** Adult patients (n=100) invasively ventilated within 24 h of ICU admission were prospectively enrolled in a tertiary care teaching hospital in India. The mNUTRIC score categorised patients as high-risk (≥5) or low-risk (≤4). Baseline serum creatinine (defined as the first ICU value) and peak ICU creatinine were used to stage AKI according to KDIGO 2012 creatinine criteria. Multivariable logistic regression for ICU mortality included the mNUTRIC score, KDIGO Stage 3 AKI, sepsis, and admission vasopressor use. ***Results:*** Sixty-three patients (63%) were high-risk by mNUTRIC. AKI of any stage was present in 67%; KDIGO Stage 3 in 36%. AKI was more common in high-risk than low-risk patients (77.8% vs. 48.6%; relative risk [RR] 1.60; P=0.004), and Stage 3 AKI was substantially more frequent in high-risk patients (49.2% vs. 13.5%; RR 3.64; P<0.001). High-risk patients had longer ICU stay (10.76 ± 4.13 vs. 8.00 ± 4.23 d; P=0.002) and longer mechanical ventilation (8.59 ± 3.52 vs. 5.86 ± 3.34 d; P<0.001). The unadjusted between-group ICU mortality difference (33.3% vs. 18.9%; RR 1.76) was not statistically significant (P=0.167). In multivariable logistic regression, Stage 3 AKI was the strongest predictor of ICU mortality (adjusted odds ratio [aOR] 4.70, 95% confidence interval [CI] 1.17–18.99; P=0.030); the mNUTRIC score (aOR 1.11 per point; P=0.340), sepsis (aOR 0.26; P=0.054) and vasopressor use (aOR 0.84; P=0.773) were not independently significant. Findings were consistent across pre-specified sensitivity analyses. ***Conclusion:*** In mechanically ventilated adult ICU patients, the mNUTRIC score was associated with severity of AKI, and Stage 3 AKI was the strongest predictor of ICU mortality among the variables examined. Findings are hypothesis-generating and require confirmation in larger multicentre studies.

Keywords: Acute kidney injury; critical care; KDIGO; nutrition assessment; respiration, artificial.

INTRODUCTION

Malnutrition is highly prevalent among critically ill patients and is associated with hospital-acquired infections, ICU-acquired weakness, prolonged mechanical ventilation, prolonged ICU stay, and increased mortality1,2. The modified Nutrition Risk in the Critically Ill (mNUTRIC) score, calculated from age, APACHE II, SOFA, number of comorbidities and pre-ICU hospital stay, has been validated as a bedside risk-stratification tool3–5 and has been associated with adverse ICU outcomes in multiple cohorts6–9.

Acute kidney injury (AKI) is reported in 30–60% of mechanically ventilated patients and is associated with increased ICU mortality10,11. The Kidney Disease: Improving Global Outcomes (KDIGO) classification provides a standardised method for staging AKI severity12. The relationship between admission mNUTRIC status and the severity of AKI in mechanically ventilated patients has not been characterised in Indian critical care settings, where ICU populations differ from Western cohorts in age structure, comorbidity profile, and access to renal replacement therapy.

The present study was undertaken in a population of mechanically ventilated adult Indian ICU patients to: (i) describe the prevalence of AKI by KDIGO stage and its distribution across mNUTRIC risk categories; (ii) describe the association of the mNUTRIC score with ICU mortality, ICU length of stay and duration of mechanical ventilation; and (iii) describe the

association of KDIGO Stage 3 AKI with ICU mortality after adjustment for the mNUTRIC score and other key clinical covariates.

MATERIALS AND METHODS

Study setting and design

This prospective observational study was conducted in the adult ICU of a tertiary care teaching hospital in India over a 12-month period from [Month YYYY] to [Month YYYY]. The study was approved by the Institutional Ethics Committee (Reference [XXX/XXX/XXXX]; date [DD Month YYYY]) and conducted in accordance with the Declaration of Helsinki (revised 2013). Written informed consent was obtained from all participants or their legally authorised representatives. The study is reported in accordance with the STROBE checklist.

Population

Consecutive adult patients (≥18 yr) admitted to the ICU and requiring invasive mechanical ventilation within 24 h of admission were screened for inclusion. Patients declared brain dead at admission, those requiring ICU readmission during the same hospital stay, and those receiving chronic dialysis prior to admission were excluded.

Sample size

This was a prospective convenience sample of 100 consecutively eligible patients. The sample provided adequate power (≥80%) to detect a between-group difference of approximately 2.5 d in ICU length of stay (assuming pooled SD 4 d, two-sided $\alpha = 0.05$). The study was not powered to detect a difference in ICU mortality. The events-per-variable ratio for the four-predictor multivariable mortality model was 7.

Data and variables

Baseline data collected at ICU admission included demographic characteristics, comorbid conditions, primary diagnosis category (sepsis, medical non-sepsis, surgical, or other), use of vasopressors within 24 h of admission, length of hospital stay prior to ICU admission, and severity-of-illness scores (APACHE II and SOFA). The mNUTRIC score was calculated and patients categorised as high-risk (≥5) or low-risk (≤4)[4]. Serum creatinine was recorded at two time points: baseline (the first value obtained within 24 h of ICU admission, used as a proxy for pre-illness baseline; pre-admission creatinine values were not available) and peak (the highest value during the ICU stay).

AKI staging

AKI was staged according to the KDIGO 2012 creatinine criteria using each patient's baseline and peak serum creatinine values[12]. Stage 1 AKI was defined as a peak creatinine 1.5–1.9 times baseline or an absolute increase ≥0.3 mg/dL; Stage 2 as 2.0–2.9 times baseline; and Stage 3 as ≥3.0 times baseline, or peak ≥4.0 mg/dL with an acute increase of ≥0.3 mg/dL. Urine-output criteria were not consistently available and were not used. AKI staging was performed contemporaneously by the clinical team using the MDCalc clinical calculator and was independently re-derived computationally for the present analysis from the recorded baseline and peak creatinine values.

Nutritional therapy

All patients received individualised nutritional therapy with caloric and protein targets calculated according to body weight and clinical requirements, in accordance with institutional ICU nutrition guidelines and international recommendations[13,14]. Enteral nutrition was preferred and initiated within 24–48 h of admission. Daily delivered calorie and protein quantities were not individually charted and are not available for analysis.

Outcomes

Pre-specified primary outcomes were ICU mortality, ICU length of stay (in days, d) and duration of invasive mechanical ventilation (in d). Prolonged mechanical ventilation (>7 d) and prolonged ICU stay (>10 d) were defined a priori.

Statistical analysis

Continuous variables are expressed as mean ± SD and compared by t-test; categorical variables as n (%) and compared by Fisher's exact test. Discriminative performance was assessed by AUC. Multivariable logistic regression for ICU mortality included the mNUTRIC score (continuous), KDIGO Stage 3 AKI (binary), sepsis (binary), and admission vasopressor use (binary). Stage 3 AKI was used as the principal AKI severity term in the model because mortality was not monotonically related to KDIGO stage in this cohort, with the principal severity-related signal concentrated at Stage 3; this analytical choice is acknowledged as post-hoc and is reported alongside sensitivity analyses using KDIGO as a continuous ordinal variable.

Variance inflation factors (VIF) were computed; calibration was assessed by Hosmer–Lemeshow goodness-of-fit. Three pre-specified sensitivity analyses were performed: (i) substituting KDIGO continuous (0–3) for Stage 3 binary; (ii)

excluding the mNUTRIC term to address conceptual overlap with AKI severity; and (iii) excluding the AKI term to estimate the unadjusted contribution of the mNUTRIC score. Adjusted odds ratios (aOR) with 95% CIs are reported. Two-sided P values are reported to three decimal places, with P<0.05 considered statistically significant. Statistical analyses were performed using [insert software].

RESULTS

Baseline characteristics and AKI prevalence

A total of 100 mechanically ventilated adult ICU patients were enrolled and analysed. Sixty-three (63%) were high-risk (mNUTRIC ≥5) and 37 (37%) low-risk; mean age 62.20 ± 12.80 yr, 59 (59%) male. Sepsis was the commonest admission diagnosis (56%); 22 patients (22%) were on vasopressors at admission. High-risk patients were older (P<0.001) and had higher APACHE II (P<0.001), SOFA (P<0.001), baseline creatinine (2.87 ± 1.32 vs. 1.33 ± 0.49 mg/dL; P<0.001) and peak creatinine (5.43 ± 2.86 vs. 1.96 ± 1.07 mg/dL; P<0.001) (Table I).

Tables

Table I. Baseline characteristics by mNUTRIC risk category.

Variable	Total (n=100)	High-risk (n=63)	Low-risk (n=37)	P value
Age (yr), mean ± SD	62.20 ± 12.80	67.44 ± 10.50	53.35 ± 11.38	<0.001
Male sex, n (%)	59 (59)	34 (54)	25 (68)	0.211
APACHE II, mean ± SD	—	29.40 ± 8.44	17.43 ± 5.46	<0.001
SOFA, mean ± SD	—	10.84 ± 3.79	7.46 ± 2.14	<0.001
Comorbidities, mean ± SD	1.11 ± 1.07	1.27 ± 1.12	0.84 ± 0.93	0.051
Baseline creatinine (mg/dL)	2.30 ± 1.32	2.87 ± 1.32	1.33 ± 0.49	<0.001
Peak creatinine (mg/dL)	4.50 ± 2.79	5.43 ± 2.86	1.96 ± 1.07	<0.001
Sepsis as primary diagnosis, n (%)	56 (56)	38 (60)	18 (49)	0.300
Vasopressor at admission, n (%)	22 (22)	16 (25)	6 (16)	0.327

Note: Continuous variables are mean ± SD, compared by t-test; categorical variables are n (%), compared by Fisher's exact test.

AKI of any stage was present in 67% of the cohort (Stage 1, 22%; Stage 2, 9%; Stage 3, 36%). AKI was more common in high-risk than low-risk patients (49/63 [77.8%] vs. 18/37 [48.6%]; RR 1.60, 95% CI 1.13–2.27; P=0.004); Stage 3 AKI was substantially more frequent in high-risk patients (31/63 [49.2%] vs. 5/37 [13.5%]; RR 3.64, 95% CI 1.55–8.55; P<0.001) (Table II).

Clinical outcomes

Overall ICU mortality was 28%. The unadjusted between-group mortality difference was not statistically significant (21/63 [33.3%] high-risk vs. 7/37 [18.9%] low-risk; RR 1.76, 95% CI 0.83–3.74; P=0.167). High-risk patients had longer ICU stay (P=0.002) and longer mechanical ventilation (P<0.001) (Table II).

Table II. AKI prevalence and clinical outcomes by mNUTRIC risk category.

Outcome	High-risk (n=63)	Low-risk (n=37)	P value
Any AKI (KDIGO Stage 1–3), n (%)	49 (77.8)	18 (48.6)	0.004
Severe AKI (KDIGO Stage 3), n (%)	31 (49.2)	5 (13.5)	<0.001
ICU mortality, n (%)	21 (33.3)	7 (18.9)	0.167
ICU length of stay (d)	10.76 ± 4.13	8.00 ± 4.23	0.002
Mechanical ventilation (d)	8.59 ± 3.52	5.86 ± 3.34	<0.001
Prolonged ventilation >7 d, n (%)	36 (57)	8 (22)	<0.001
Prolonged ICU stay >10 d, n (%)	28 (44)	8 (22)	0.026

Note: AKI staged by KDIGO 2012 creatinine criteria. Continuous variables mean ± SD; categorical variables n (%).

Mortality across KDIGO stages

Mortality across KDIGO stages was: Stage 0, 10/33 (30.3%); Stage 1, 3/22 (13.6%); Stage 2, 1/9 (11.1%); Stage 3, 14/36 (38.9%) (Table III). The relationship was not strictly monotonic, with intermediate stages showing lower observed mortality than Stage 0; the small number of events in intermediate strata (1–3 deaths in Stages 1–2 combined) limits inference. Stage 3 AKI mortality (38.9%) was higher than that in Stages 0–2 combined (14/64; 21.9%; RR 1.78, 95% CI 0.97–3.27; P=0.103). The Cochran–Armitage test for trend across stages was not statistically significant (χ^2 = 5.73, P=0.126).

Table III. ICU mortality by KDIGO stage

KDIGO stage	n	Deaths	Mortality (%)	Cumulative %
Stage 0 (no AKI)	33	10	30.3	33
Stage 1	22	3	13.6	22
Stage 2	9	1	11.1	9
Stage 3	36	14	38.9	36
Total	100	28	28.0	100

Note: The relationship between KDIGO stage and mortality is not strictly monotonic in this cohort, with intermediate stages containing small numbers of events. Cochran–Armitage trend test $\chi^2 = 5.73$, P = 0.126.

Multivariable analysis

In the pre-specified multivariable logistic regression for ICU mortality (events-per-variable = 7), KDIGO Stage 3 AKI was the strongest predictor (aOR 4.70, 95% CI 1.17–18.99; P=0.030) (Table IV). The mNUTRIC score (aOR 1.11 per point, 95% CI 0.89–1.38; P=0.340), sepsis (aOR 0.26, 95% CI 0.07–1.02; P=0.054) and admission vasopressor use (aOR 0.84, 95% CI 0.27–2.67; P=0.773) were not independently associated with mortality. Variance inflation factors were all <2 (mNUTRIC 1.15, Stage 3 AKI 1.61, sepsis 1.49, vasopressor 1.06). The Hosmer–Lemeshow goodness-of-fit test was non-significant ($\chi^2 = 4.28$, P=0.831), consistent with acceptable calibration. The wide confidence interval for Stage 3 AKI reflects the limited number of mortality events.

The counter-intuitive direction of the sepsis odds ratio is explained by the underlying univariate distribution: ICU mortality was numerically lower in sepsis patients than in non-sepsis patients in this cohort (25.0% vs. 31.8%; unadjusted RR 0.79; P=0.505), and the strong correlation between sepsis and Stage 3 AKI (89.3% AKI in sepsis vs. 38.6% in non-sepsis) further attenuates the sepsis term once Stage 3 AKI is in the model.

Sensitivity analyses

Three pre-specified sensitivity analyses supported the robustness of the Stage 3 AKI finding (Table IV). When KDIGO was modelled as a continuous ordinal variable (0–3), the directional association with mortality was preserved (aOR 1.42 per stage, 95% CI 0.85–2.35; P=0.178), although attenuated relative to the binary Stage 3 specification, consistent with the non-monotonic relationship between intermediate stages and mortality. When the mNUTRIC term was excluded, the Stage 3 AKI association strengthened (aOR 5.62, 95% CI 1.46–21.69; P=0.012). When the AKI term was excluded, the mNUTRIC score showed a non-significant trend toward an association with mortality (aOR 1.20 per point, 95% CI 0.98–1.46; P=0.082

Table IV. Multivariable logistic regression for ICU mortality with sensitivity analyses)

Predictor	aOR (95% CI)	P value
Primary model: mNUTRIC + Stage 3 AKI + sepsis + vasopressor		
mNUTRIC (per point)	1.11 (0.89–1.38)	0.340
KDIGO Stage 3 AKI	4.70 (1.17–18.99)	0.030
Sepsis (yes vs. no)	0.26 (0.07–1.02)	0.054
Vasopressor at admission	0.84 (0.27–2.67)	0.773
Sensitivity 1: KDIGO continuous (0–3) instead of Stage 3 binary		
mNUTRIC (per point)	1.14 (0.92–1.41)	0.231
KDIGO stage (per stage)	1.42 (0.85–2.35)	0.178
Sensitivity 2: Excluding mNUTRIC		
KDIGO Stage 3 AKI	5.62 (1.46–21.69)	0.012
Sensitivity 3: Excluding AKI term		
mNUTRIC (per point)	1.20 (0.98–1.46)	0.082

Note: aOR, adjusted odds ratio. Primary model events-per-variable = 7. All variance inflation factors <2 (mNUTRIC 1.15, Stage 3 AKI 1.61, sepsis 1.49, vasopressor 1.06). Hosmer–Lemeshow goodness-of-fit $\chi^2 = 4.28$, df = 8, P = 0.831.

Discriminative performance

AUCs for ICU mortality were modest: mNUTRIC 0.61, KDIGO Stage 3 binary 0.60, mNUTRIC + Stage 3 combined 0.64. The mNUTRIC score discriminated prolonged mechanical ventilation more strongly (AUC 0.70) (Table V).

Sepsis subgroup

Among the 56 patients with sepsis, AKI was present in 50 (89.3%) and Stage 3 AKI in 33 (58.9%); subgroup mortality was 25.0%. Sepsis-specific multivariable analyses are not reported because of the limited number of events within the subgroup.

Table V. Discriminative performance of single predictors and combined model.

Predictor	AUC for ICU mortality (95% CI)	AUC for prolonged ventilation
mNUTRIC score	0.61 (0.48–0.74)	0.70 (0.59–0.80)
KDIGO Stage 3 AKI	0.60 (0.48–0.71)	0.65 (0.54–0.76)
APACHE II	0.54 (0.41–0.67)	0.63 (0.52–0.74)
SOFA	0.53 (0.40–0.66)	0.59 (0.48–0.71)
mNUTRIC + KDIGO Stage 3 (combined)	0.64 (0.51–0.76)	—

Note: AUC, area under the receiver-operating-characteristic curve. AUC 95% CIs computed using the Hanley–McNeil method.

DISCUSSION

In this prospective single-centre cohort of 100 mechanically ventilated adult ICU patients, high-mNUTRIC status was associated with a substantially higher rate of severe (KDIGO Stage 3) AKI (49.2% vs. 13.5%). In multivariable logistic regression, Stage 3 AKI was the strongest predictor of ICU mortality among the variables examined (aOR 4.70; P=0.030); the mNUTRIC score, sepsis and admission vasopressor use were not independently significant. The findings were broadly consistent across sensitivity analyses. The unadjusted between-group ICU mortality difference (33.3% vs. 18.9%) did not reach statistical significance (P=0.167), and the wide confidence interval for Stage 3 AKI in the multivariable model reflects limited statistical power. Findings should therefore be interpreted as hypothesis-generating.

Several methodological points warrant explicit acknowledgement. First, the mNUTRIC score includes APACHE II and SOFA, and the SOFA score in turn includes a renal subscore based on serum creatinine. The observed association between mNUTRIC and AKI severity therefore partly reflects this structural overlap rather than a fully independent relationship; the mNUTRIC score in this analysis functions as a composite severity-and-comorbidity index, and our findings should not be interpreted as evidence that nutritional risk per se causes AKI3–5. Second, baseline creatinine was defined as the first ICU value because pre-admission creatinine was not available; some patients may therefore have had pre-existing chronic kidney disease, or AKI already established at admission, which we cannot reliably distinguish from acute in-ICU AKI. Third, although individualised nutritional targets were prescribed, daily delivered calorie and protein quantities were not measured; we cannot examine whether actual nutrient delivery contributed to outcomes. Fourth, the association of mNUTRIC and Stage 3 AKI with mortality should not be interpreted as evidence of mediation in the formal statistical sense; the design of the study, the sample size, and the absence of formal mediation analysis preclude such a claim. Fifth, urine-output KDIGO criteria were not used; AKI staging therefore relied on creatinine alone, consistent with much of the published literature but at the cost of some misclassification12. Sixth, important confounders including nephrotoxin exposure, fluid balance, mean arterial pressure profile and renal replacement therapy details were not extracted; residual confounding cannot be excluded. Seventh, the choice to use Stage 3 AKI as a binary term in the principal model was made post-hoc on the basis of the observed non-monotonic relationship between KDIGO stage and mortality, with intermediate stages containing too few events for stable estimation; the sensitivity analysis using KDIGO as a continuous ordinal variable showed a directionally consistent but weaker association. Finally, the cohort was confined to a single Indian tertiary care setting, and findings may not generalise.

Our findings are broadly concordant with the existing literature on the mNUTRIC score in critical care. The proportion of high-risk patients in our cohort (63%) is comparable to that reported in other ventilated ICU populations6–9, and the higher AKI rates in high-risk patients are consistent with the shared antecedents of nutritional risk and AKI in critical illness — advanced age, comorbidity burden, and acute physiological derangement10,11,15. The longer ICU stay and prolonged ventilation in high-risk patients are concordant with literature linking severity of illness and metabolic stress to delayed recovery and ventilator dependence1,2. Our principal contribution is the description — in a population of adult Indian patients invasively ventilated within 24 h of ICU admission — of a graded relationship between mNUTRIC risk category and the proportion of patients developing severe (KDIGO Stage 3) AKI, and the observation that Stage 3 AKI is the strongest predictor of mortality among the variables examined in our model. Whether severe AKI is itself a causal driver of mortality in this population, or a marker of severity of illness more broadly, cannot be determined from these data11,15.

Clinically, our findings support the use of the mNUTRIC score as one of several bedside risk-stratification tools in mechanically ventilated patients in Indian and other resource-variable ICUs. Whether mNUTRIC-stratified preventive

strategies for AKI — including nephrotoxin avoidance, haemodynamic optimisation and earlier renal replacement consideration — might influence outcomes in high-risk patients is a hypothesis that requires testing in adequately powered prospective studies. In conclusion, in this cohort of mechanically ventilated adult ICU patients, the mNUTRIC score was associated with severity of AKI, and Stage 3 AKI was the strongest predictor of ICU mortality among the variables examined. Findings are hypothesis-generating and require confirmation in larger multicentre studies that include direct measurement of nutrient delivery, urine-output AKI criteria, and formal modelling of intermediate causal pathways.

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