Nutritional status plays a crucial role in the mortality of critically ill patients with acute renal failure

Haiyan Zhang, Xiaodong Zhang, Lei Dong

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Department of Emergency, The Hospital of Shunyi District Beijing, Shunyi 101300, China

Correspondence to
Dr Haiyan Zhang, Department of Emergency, The Hospital of Shunyi District Beijing, No.3, Guangming Nanlu, Shunyi 101300, China; 18610366049@163.com

HZ and XZ contributed equally.

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ABSTRACT

We aimed to clarify associations between nutritional status and mortality in patients with acute renal failure. De-identified data were obtained from the Medical Information Mart for Intensive Care III database comprising more than 40,000 critical care patients treated at Beth Israel Deaconess Medical Centerbetween 2001 and 2012. Weight loss and body mass index criteria were used to define malnutrition. Data of 193 critically ill patients with acute renal failure were analyzed, including demographics, nutrition intervention, laboratory results, and disease severity. Main outcomes were in-hospital and 1-year mortality. The 1-year mortality was significantly higher in those with malnutrition than in those without malnutrition (50.0% vs 29.3%, p=0.010), but differences in in-hospital survival were not significant (p=0.255). Significant differences in mortality were found between those with malnutrition and without starting at the 52nd day after intensive care unit (ICU) discharge (p=0.036). No significant differences were found between men and women with malnutrition in in-hospital mortality (p=0.949) and 1-year mortality (p=0.051). Male patients requiring intervention with blood products/colloid supplements had greater risk of 1-year mortality, but without statistical significance. Nutritional status is a predictive factor for mortality among critically ill patients with acute renal failure, particularly 1-year mortality after ICU discharge.

Significance of this study

What is already known about this subject?

- Malnutrition is one of the most important risk factors for mortality and intensive care unit (ICU) admission.
- Malnutrition is known to result in serious consequences for critically ill patients, increasing their risk of infection, decreasing renal and liver function, and impeding wound healing and immune system function.
- Nutritional support has been shown to limit the negative impact of malnutrition.
- A standardized definition of malnutrition in critically ill adults is lacking.

What are the new findings?

- In-hospital mortality was significantly more prevalent in critically ill female patients with malnutrition and acute renal failure than in non-malnutrition female patients.
- The 1-year mortality was significantly higher in critically ill patients with acute renal failure with malnutrition than in non-malnutrition patients.
- Significant differences in mortality were found between those with malnutrition and without starting at the 52nd day after ICU discharge.

How might these results change the focus of research or clinical practice?

- Patients with malnutrition were receiving nutrition intervention after admission to ICU because healthcare professionals will do everything possible to improve patients' health status. This may help to explain why no significant differences were found in *in-hospital* mortality.
- Beginning at 52 days after ICU discharge, significant differences were found in mortality, suggesting that patients' dietary behavior did not likely change after discharge and malnutrition was still present. Nutrition education is necessary to prevent malnutrition.
- Nutritional status is a predictive factor for mortality among critically ill patients with acute renal failure. Early identification of malnutrition and nutritional intervention would likely reduce the risk of mortality. Developing a standardized malnutrition assessment protocol for critically ill adults is crucial.

INTRODUCTION

Malnutrition is defined by the WHO as 'the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions'.[1] Among hospital patients, malnutrition manifesting as muscle mass depletion and excess body fat is associated with increased length of stay,[2] disease severity, complications, and mortality.[3] Although discrepancies exist in reports of the prevalence of poor nutrition,[4] evidence of malnutrition is found in up to 60% of hospitalized patients when assessed by anthropometric and biochemical measures or screening tools.[2]

Undernutrition is common in critically ill patients in whom acute conditions such as

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inflammatory process and fever may lead to a hypercatabolic state and protein-calorie malnutrition.[5] Disease-associated malnutrition is known to result in serious consequences for critically ill patients whose health status is already compromised, increasing their risk of infection, decreasing renal and liver function, and impeding wound healing and immune system function.[3 6] Among critically ill older adults with various admitting diagnoses, malnutrition was one of the three most important risk factors for mortality, along with Apache II scores for prognostic evaluation of mortality and intensive care unit (ICU) admission.[7] In addition, malnutrition limits the effectiveness of medical treatment or nutritional intervention by the presence of inflammation[6] and the underlying acute and chronic illness in the critical care population.[8] Since critically ill patients are typically in an inflammatory prone state,[9] it is understandable why the consequences of malnutrition are more pronounced in ICU patients, including increased mortality. However, studies that link malnutrition to clinical outcomes in ICU patients have often had conflicting results because nutritional status has not been assessed thoroughly and malnutrition has not been diagnosed appropriately.[8] A lack of standardized documentation of nutritional information may be responsible for undocumented malnutrition, and recommendations have been made to standardize the definition of malnutrition so that it accounts for the role of inflammation in critically ill adults.[9]

Consensus-based criteria recommended for use in Europe and internationally to identify risk or diagnosis of malnutrition is based on a low body mass index (BMI) (<18.5 kg/m^2) with or without combined weight loss.[10] In elderly patients (>65 years) malnutrition is defined as unintentional weight loss of more than 10% in the past 6 months and/or a BMI less than 20 kg/m^2.[11] Meanwhile, in the absence of standard protocols to address malnutrition in critically ill patients, even in cases when nutrition intervention is recommended, only about half of critical care patients receive the enteral requirements they need.[12] Thus, although malnutrition is reported to be independently associated with greater risk for mortality[3] and longer length of hospital stay,[2] associations between malnutrition and mortality in critical care patients are not clearly defined. Specifically, while nutritional support has been shown to limit the negative impact of malnutrition, only limited information is available regarding the contribution of nutritional support to patients with acute renal failure. Therefore, the present study aimed to clarify associations between nutritional status and mortality in critically ill patients with acute renal failure.

MATERIALS AND METHODS

Data source

The data source for the present study is the Medical Information Mart for Intensive Care III (MIMIC-III),[13] which is a large, freely available database comprising de-identified health-related data collected from over 40,000 patients admitted to critical care units of the Beth Israel Deaconess Medical Center (BIDMC, Boston, Massachusetts, USA) between 2001 and 2012. The MIMIC research database, a joint venture managed by researchers from the Laboratory for Computational Physiology at Massachusetts Institute of Technology (MIT, Cambridge, Massachusetts, USA) and the Department of Medicine at BIDMC, is supported by grants from the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health under award numbers R01-EB001659 (2003–2013) and R01-EB017205 (2014–2018). Use of the MIMIC database for research purposes has been approved by the institutional review boards of BIDMC and MIT.

Study population

For the present study, the data of patients admitted to the ICU of BIDMC between 2001 and 2012, aged 20–88 years and diagnosed with acute renal failure, were included. A total of 584 ICU patients were identified initially, from whom 391 patients with incomplete malnutrition data or lacking data of other study variables were excluded. Finally, the data of 193 critically ill patients with acute renal failure were included for analysis in the present study.

Main outcome measures and variables

Primary outcome measures were in-hospital mortality and death within 1 year of ICU discharge. In-hospital mortality data were derived from the date of death as recorded in the hospital database. One-year mortality was identified by the date of death recorded in the US Social Security database.

Malnutrition was defined as having a BMI <18.5 kg/m^2 or unintentional weight loss >10 lbs for adults, and BMI <20 kg/m^2 or unintentional weight loss >10 lbs for older adults (age 65 and older).

Demographics included subjects' age, gender, race (categorized by MIMIC as white, black, and others), and marital status (categorized as married/life partner, single, and divorced/separated/widowed), and were obtained from the MIMIC-III database.

Nutritional interventions, including blood products/colloid supplements, were dichotomized and obtained from the MIMIC-III input database. Subjects who received blood products (eg, packed red blood cells, albumin, fresh frozen plasma, and so on) during ICU admission were designated as 'Yes'. Other nutritional supplements (eg, peripheral parenteral nutrition, total parenteral nutrition) during ICU admission were also identified by the MIMIC-III input database.

Laboratory data included blood urea nitrogen (mg/dL), creatinine (mg/dL), serum albumin (g/dL), glucose (mg/dL), sodium (mEq/L), hemoglobin (g/dL), potassium (mEq/L), calcium (mg/dL), and phosphate (mg/dL). All results were obtained from the LabEvent database, which contains all laboratory measurements for a given patient. In the present study, values of first record in ICU for each subject represented baseline laboratory measurements.

DRG severity was provided in the MIMIC database as All Payers Registry Diagnosis Related Groups (APR-DRGs) codes to a distinct set of patient attributes, including severity of illness, risk of dying, prognosis, treatment difficulty, need for intervention, and resource intensity. The present study used 'DRG_SEVERITY' to imply severity of disease, with subsets of minor, moderate, major, and extreme severity.

Statistical analysis

Continuous variables are expressed as median (IQR) and tested by non-parametric Mann-Whitney U test. Categorical

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variables are expressed as counts (percentage), and χ^2 test or Fisher's exact tests were conducted to determine differences in categorical variables. Kaplan-Meier analysis was used to calculate in-hospital mortality and 1-year mortality in malnutrition and non-malnutrition patients with acute renal failure. Univariate and multivariate Cox proportional hazards regression analyses were performed to examine the impact of malnutrition on in-hospital mortality and 1-year mortality. Multivariate Cox proportional hazards regression model was adjusted for significant factors identified in univariate analysis. Analyses were also performed stratifying patients by gender to determine differences between malnutrition and mortality when modified by associated factors. All statistical assessments were two-sided and evaluated at the 0.05 level of significance. Statistical analyses were performed by IBM SPSS V.22 statistical software for Windows.

RESULTS

Subjects' demographic and clinical characteristics

Data of a total of 193 critically ill ICU patients with acute renal failure were analyzed in the present study. Subjects included 46 patients with malnutrition and 147 non-malnutrition patients. Median age was 66.7 years, 59.1% were men, and 67.4% were of white race. Patients' demographic and clinical characteristics are shown in table 1. The prevalence of low serum sodium (less than 135 mEq/L) was significantly higher in malnutrition patients than in non-malnutrition patients (65.2% vs 40.1%, p=0.003). Prevalence of anemia (hemoglobin less than 12 g/dL) was significantly higher in non-malnutrition patients than in malnutrition patients (72.1% vs 56.5%, p=0.047). One-year mortality was significantly more prevalent in malnutrition patients than in non-malnutrition patients (50.0% vs 29.3%, p=0.010).

Malnutrition and mortality

Calculations of in-hospital mortality and 1-year mortality are shown in figures 1A and 2A, respectively. For in-hospital mortality (figure 1A), mean survival time was 89.8 days in non-malnutrition patients and 34.3 days in malnutrition patients, with no significant differences in survival time between the two groups (log-rank test, p=0.255). For 1-year mortality (figure 2A), mean survival time was 281.1 days in non-malnutrition patients and 217.3 days in malnutrition patients, with significant differences in survival time between the two groups (log-rank test, p=0.007). Further analysis revealed significant differences in survival time at 52 days after ICU discharge between non-malnutrition and malnutrition patients (log-rank test, p=0.036).

Malnutrition and mortality stratified by gender

When stratified by gender, significant differences were shown in in-hospital mortality between female non-malnutrition and malnutrition patients (log-rank test, p=0.017), with a mean survival time of 95.8 days for female non-malnutrition patients and 31.1 days for female malnutrition patients (figure 1B). Among male patients (figure 1C), the mean survival time was 35.9 days for non-malnutrition patients and 29.2 days for malnutrition patients; no significant differences were found in in-hospital mortality between male non-malnutrition and malnutrition patients (log-rank test, p=0.759).

For 1-year mortality among female patients (figure 2B), significant differences were shown in survival time between non-malnutrition and malnutrition patients (log-rank test, p=0.027). Mean survival time was 299.0 days for female non-malnutrition patients and 212.5 days for female malnutrition patients. Among men (figure 2C), mean survival time was 268.0 days in non-malnutrition patients and 220.1 days in malnutrition inpatients, with no significant differences in survival time between non-malnutrition and malnutrition groups (log-rank test, p=0.108).

Factors associated with mortality

Table 2 shows the results of univariate and multivariate Cox proportional regression analyses in all study subjects. No significant factors were found associated with in-hospital mortality. Results revealed that malnutrition, blood products/colloid supplements, and DRG (disease) severity were significant factors for 1-year mortality (all p<0.05). After multivariate regression analysis was simultaneously adjusted for significant factors from univariate analysis, results showed that malnutrition patients had a significantly higher risk of 1-year mortality than non-malnutrition patients (adjusted HR (aHR)=2.141, 95% CI 1.275 to 3.594, p=0.004). Also, patients who had received nutrition intervention of blood products/colloid supplements had a significantly higher risk of 1-year mortality (aHR=2.004, 95% CI 1.202 to 3.341); patients with extreme disease severity had significantly higher risk of 1-year mortality (aHR=1.835, 95% CI 1.096 to 3.073) than did patients with major disease severity.

Factors associated with mortality stratified by gender

Further analyses were performed with patients stratified by gender. Results of univariate and multivariate Cox proportional regression analyses of in-hospital mortality and 1-year mortality in women are shown in table 3. Results of multivariate analysis showed that female malnutrition patients had significantly higher risk of 1-year mortality than non-malnutrition patients (aHR=2.592, 95% CI 1.081 to 6.218, p=0.033). Single women had significantly lower risk of 1-year mortality than women classified as married/life partner (aHR=0.124, 95% CI 0.016 to 0.962, p=0.046).

In men (table 4), after adjusting for significant factors from univariate analysis, patients with acute renal failure with malnutrition (aHR=1.928, 95% CI 1.002 to 3.710, p=0.049) who received nutrition intervention with blood products/colloid supplements had a significantly higher risk of 1-year mortality (aHR=1.903, 95% CI 1.003 to 3.611, p=0.049).

No significant differences were found in in-hospital mortality (p=0.949)) and 1-year mortality (p=0.051)

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Table 1 Subjects' demographic and clinical characteristics

Characteristics	Total (n=193)	Non-malnutrition (n=147)	Malnutrition (n=46)	p Value
Demographics				
Age (years) (median (IQR))	66.7 (56.3–77.7)	66.5 (56.6–77.8)	67.2 (56.0–77.6)	0.947
Age group				0.556
<65 years old	87 (45.1)	68 (46.3)	19 (41.3)	
≥65 years old	106 (54.9)	79 (53.7)	27 (58.7)	
Gender				0.530
Female	79 (40.9)	62 (42.2)	17 (37.0)	
Male	114 (59.1)	85 (57.8)	29 (63.0)	
Race				0.870
White	130 (67.4)	98 (66.7)	32 (69.6)	
Black	43 (22.3)	33 (22.4)	10 (21.7)	
Others	16 (8.3)	13 (8.8)	3 (6.5)	
Marital status				0.291
Married/life partner	91 (47.2)	74 (50.3)	17 (37.0)	
Single	54 (28.0)	38 (25.9)	16 (34.8)	
Divorced/separated/widowed	46 (23.8)	34 (23.1)	12 (26.1)	
Nutritional intervention				
Blood products/colloids supplement				0.479
No	138 (71.5)	107 (72.8)	31 (67.4)	
Yes	55 (28.5)	40 (27.2)	15 (32.6)	
Other nutritional supplement				0.494
No	173 (89.6)	133 (90.5)	40 (87.0)	
Yes	20 (10.4)	14 (9.5)	6 (13.0)	
Laboratory data				
BUN (mg/dL) (median (IQR))	67.0 (46.5–101.0)	62.0 (44.0–97.0)	75.5 (50.5–124.0)	0.101
Creatinine (mg/dL) (median (IQR))	3.6 (2.1–5.7)	3.6 (2.2–5.6)	3.0 (1.9–6.4)	0.517
Serum albumin (g/dL)				0.435
≥3.5	58 (30.1)	46 (31.3)	12 (26.1)	
<3.5	89 (46.1)	64 (43.5)	25 (54.3)	
Glucose (mg/dL)				0.989
<110	74 (38.3)	56 (38.1)	18 (39.1)	
110–140	46 (23.8)	35 (23.8)	11 (23.9)	
>140	73 (37.8)	56 (38.1)	17 (37.0)	
Sodium (mEq/L)				0.003*
≥135	104 (53.9)	88 (59.9)	16 (34.8)	
<135	89 (46.1)	59 (40.1)	30 (65.2)	
Hemoglobin (g/dL)				0.047*
≥12	61 (31.6)	41 (27.9)	20 (43.5)	
<12	132 (68.4)	106 (72.1)	26 (56.5)	
Potassium (mEq/L)				0.941
≤5.3	110 (57.0)	84 (57.1)	26 (56.5)	
>5.3	83 (43.0)	63 (42.9)	20 (43.5)	
Calcium (mg/dL)				0.937
≤10.2	185 (95.9)	141 (95.9)	44 (95.7)	
>10.2	8 (4.1)	6 (4.1)	2 (4.3)	
Phosphate (mg/dL)				0.559
≤5.0	99 (51.3)	78 (53.1)	21 (45.7)	
>5.0	93 (48.2)	68 (46.3)	25 (54.3)	
Severity				
DRG (disease) severity				0.169
Major severity	122 (63.2)	89 (60.5)	33 (71.7)	
Extreme severity	71 (36.8)	58 (39.5)	13 (28.3)	
Clinical outcomes				
In-hospital mortality				0.246
Survival	176 (91.2)	136 (92.5)	40 (87.0)	
Death	17 (8.8)	11 (7.5)	6 (13.0)	

Continued

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Table 1 Continued

Characteristics	Total (n=193)	Non-malnutrition (n=147)	Malnutrition (n=46)	p Value
1-year mortality				0.010*
Survival	127 (65.8)	104 (70.7)	23 (50.0)	
Death	66 (34.2)	43 (29.3)	23 (50.0)	

Continuous variables are shown as median (IQR); categorical variables are shown as counts and (%). Numbers may not equal full sample due to missing data.
*Represents significant difference between non-malnutrition and malnutrition patients, p<0.05.
BUN, blood urea nitrogen; DRG, diagnosis-related groups.

between men and women with malnutrition (online supplementary file 1).

DISCUSSION

In the present study of critically ill patients with acute renal failure, 1-year mortality was significantly more prevalent in malnutrition patients than in non-malnutrition patients. Although no significant differences were shown in in-hospital mortality between the two groups, starting at the 52nd day after ICU discharge, significant differences in mortality were shown between patients with malnutrition and non-malnutrition. No significant differences were found between men and women in in-hospital and 1-year mortality, although effects of malnutrition were more prominent among women.

Results of the present study are consistent with those of other studies regarding malnutrition as a significant factor associated

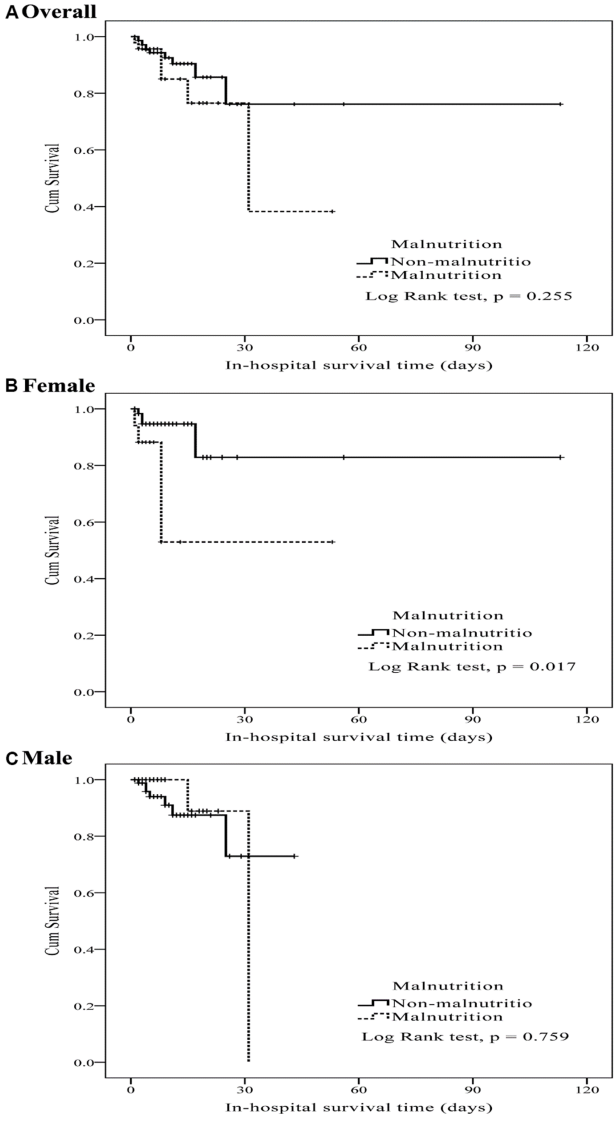

Figure 1 Kaplan-Meier analysis of in-hospital mortality (A) and gender-stratified female (B) and male (C) for non-malnutrition and malnutrition.

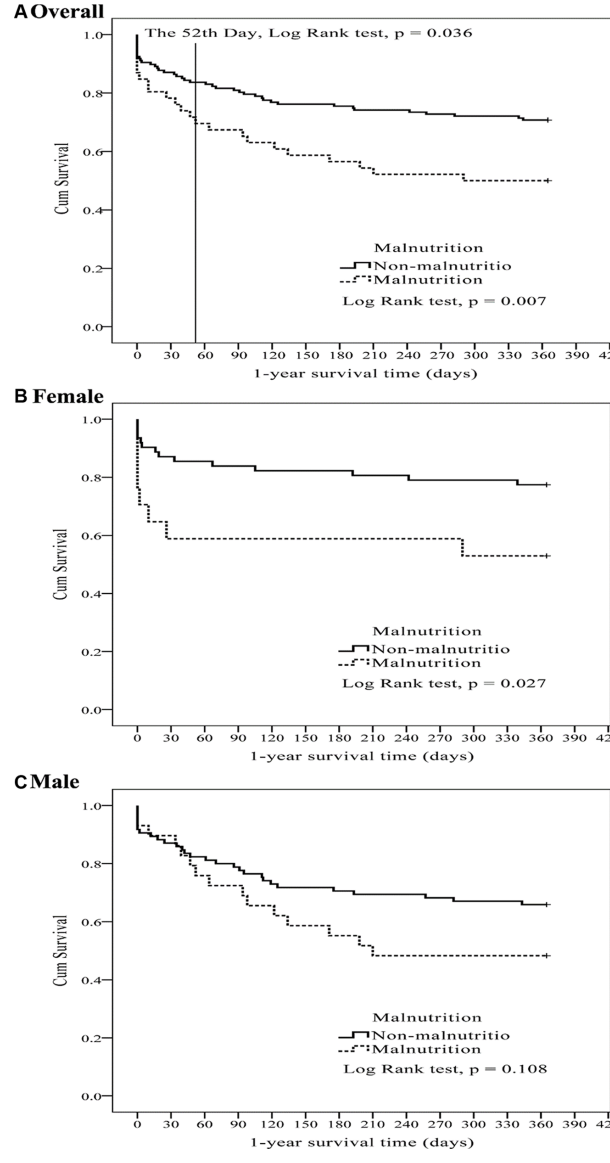

Figure 2 Kaplan-Meier analysis of 1-year mortality (A) and gender-stratified female (B) and male (C) for non-malnutrition and malnutrition.

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Table 2 Univariate and multivariate regression analyses of factors associated with in-hospital mortality and 1-year mortality

	In-hospital mortality		One-year mortality			
	Univariate		Univariate		Multivariate	
Characteristics	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Malnutrition						
No	Reference		Reference		Reference	
Yes	1.769 (0.653 to 4.796)	0.262	1.961 (1.181 to 3.256)	0.009*	2.141 (1.275 to 3.594)	0.004*
Demographics						
Age group						
<65 years old	Reference		Reference			
≥65 years	1.105 (0.419 to 2.913)	0.841	1.030 (0.634 to 1.675)	0.904		
Gender						
Female	Reference		Reference			
Male	0.699 (0.269 to 1.814)	0.462	1.415 (0.848 to 2.361)	0.184		
Race						
White	Reference		Reference			
Black	1.126 (0.361 to 3.510)	0.838	0.770 (0.408 to 1.453)	0.419		
Others	0.451 (0.058 to 3.516)	0.447	1.014 (0.433 to 2.375)	0.974		
Marital status						
Married/life partner	Reference		Reference			
Single	0.681 (0.181 to 2.569)	0.571	0.711 (0.379 to 1.332)	0.287		
Divorced/ separated/widowed	1.871 (0.645 to 5.426)	0.249	1.295 (0.734 to 2.285)	0.372		
Nutritional intervention						
Blood products/colloid supplements						
No	Reference		Reference		Reference	
Yes	2.221 (0.768 to 6.425)	0.141	2.448 (1.503 to 3.984)	<0.001*	2.004 (1.202 to 3.341)	0.008*
Other nutritional supplement						
No	Reference		Reference			
Yes	0.282 (0.052 to 1.533)	0.143	1.066 (0.487 to 2.333)	0.874		
Laboratory data						
Serum albumin (g/dL)						
≥3.5	Reference		Reference			
<3.5	5.892 (0.765 to 45.357)	0.089	1.757 (0.994 to 3.108)	0.053		
Glucose (mg/dL)						
<110	Reference		Reference			
110–140	0.759 (0.233 to 2.472)	0.648	0.742 (0.390 to 1.409)	0.361		
>140	0.532 (0.163 to 1.742)	0.297	0.844 (0.489 to 1.456)	0.541		
Sodium (mEq/L)						
≥135	Reference		Reference			
<135	1.376 (0.528 to 3.586)	0.513	1.579 (0.971 to 2.567)	0.066		
Hemoglobin (g/dL)						
≥12	Reference		Reference			
<12	5.677 (0.749 to 43.036)	0.093	1.586 (0.903 to 2.785)	0.109		
Potassium (mEq/L)						
≤5.3	Reference		Reference			
>5.3	2.117 (0.801 to 5.597)	0.130	0.870 (0.531 to 1.426)	0.582		
Calcium (mg/dL)						
≤10.2	Reference		Reference			
>10.2	†		1.213 (0.381 to 3.864)	0.744		
Phosphate (mg/dL)						
≤5.0	Reference		Reference			
>5.0	1.063 (0.409 to 2.761)	0.901	1.233 (0.760 to 1.999)	0.397		
Severity						
DRG (disease) severity						
Major severity	Reference		Reference		Reference	
Extreme severity	1.532 (0.531 to 4.418)	0.430	1.979 (1.221 to 3.207)	0.006*	1.835 (1.096 to 3.073)	0.021*

*Represents significant factor, p<0.05.
†Represents event of interest did not occur, thus data not available.
DRG, diagnosis-related groups.

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Table 3 Univariate and multivariate regression analyses of factors associated with in-hospital mortality and 1-year mortality in women

	In-hospital mortality		One-year mortality			
	Univariate		Univariate		Multivariate	
Characteristics	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Demography						
Age (years)	0.991 (0.939 to 1.045)	0.731	1.009 (0.977 to 1.041)	0.591		
Age group						
<65 years old	Reference		Reference			
≥65 years old	1.082 (0.258 to 4.534)	0.914	1.317 (0.537 to 3.230)	0.547		
Race						
White	Reference		Reference			
Black	1.071 (0.214 to 5.353)	0.934	1.113 (0.404 to 3.064)	0.836		
Others	†		0.441 (0.058 to 3.338)	0.428		
Marital status						
Married/life partner	Reference		Reference		Reference	
Single	0.610 (0.063 to 5.878)	0.669	0.127 (0.016 to 0.984)	0.048*	0.124 (0.016 to 0.962)	0.046*
Divorced/ separated/widowed	1.879 (0.420 to 8.405)	0.409	1.359 (0.577 to 3.203)	0.483		
Nutrition						
Malnutrition						
No	Reference		Reference		Reference	
Yes	4.660 (1.154 to 18.821)	0.031*	2.538 (1.062 to 6.065)	0.036*	2.592 (1.081 to 6.218)	0.033*
Blood products/colloid supplements						
No	Reference		Reference			
Yes	1.434 (0.330 to 6.238)	0.631	2.093 (0.893 to 4.905)	0.089		
Nutrition supplement						
No	Reference		Reference			
Yes	†		1.088 (0.322 to 3.677)	0.893		
Lab/biomarker						
Serum albumin (g/dL)						
≥3.5	Reference		Reference			
<3.5	†		3.396 (0.946 to 12.186)	0.061		
Glucose (mg/dL)						
<110	Reference		Reference			
110–140	1.595 (0.321 to 7.932)	0.568	0.944 (0.336 to 2.653)	0.913		
>140	0.951 (0.157 to 5.769)	0.956	0.790 (0.294 to 2.121)	0.640		
Sodium (mEq/L)						
≥135	Reference		Reference			
<135	1.894 (0.451 to 7.948)	0.383	1.545 (0.660 to 3.615)	0.316		
Hemoglobin (g/dL)						
≥12	Reference		Reference			
<12	2.793 (0.342 to 22.781)	0.337	0.967 (0.394 to 2.373)	0.942		
Potassium (mEq/L)						
≤5.3	Reference		Reference			
>5.3	3.066 (0.693 to 13.569)	0.140	1.019 (0.435 to 2.384)	0.966		
Calcium (mg/dL)						
≤10.2	Reference		Reference			
>10.2	†		0.652 (0.088 to 4.851)	0.676		
Phosphate (mg/dL)						
≤5.0	Reference		Reference			
>5.0	1.612 (0.385 to 6.754)	0.514	0.839 (0.352 to 2.001)	0.693		
Physical status						
DRG (disease) severity						
Major severity	Reference		Reference			
Extreme severity	0.965 (0.223 to 4.171)	0.962	2.153 (0.929 to 4.987)	0.074		

*Represents significant factor, p<0.05.
†Represents event of interest did not occur, thus data not available.
DRG, diagnosis-related groups.

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Table 4 Univariate and multivariate regression analyses of factors associated with in-hospital mortality and 1-year mortality in men

	In-hospital mortality		One-year mortality			
	Univariate		Univariate		Multivariate	
Characteristics	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Demographics						
Age (years)	0.993 (0.948 to 1.041)	0.775	0.994 (0.973 to 1.016)	0.593		
Age group						
<65 years old	Reference		Reference			
≥65 years old	1.156 (0.275 to 4.862)	0.844	0.974 (0.539 to 1.758)	0.929		
Race						
White	Reference		Reference			
Black	1.207 (0.240 to 6.073)	0.820	0.598 (0.263 to 1.358)	0.219		
Others	0.761 (0.088 to 6.540)	0.803	1.511 (0.587 to 3.888)	0.392		
Marital status						
Married/life partner	Reference		Reference			
Single	0.856 (0.165 to 4.435)	0.853	1.156 (0.579 to 2.308)	0.682		
Divorced/ separated/widowed	2.537 (0.422 to 15.235)	0.309	1.256 (0.575 to 2.743)	0.568		
Nutrition						
Malnutrition						
No	Reference		Reference		Reference	
Yes	0.781 (0.160 to 3.809)	0.760	1.653 (0.885 to 3.085)	0.115	1.928 (1.002 to 3.710)	0.049*
Blood products/colloid supplements						
No	Reference		Reference		Reference	
Yes	3.755 (0.724 to 19.485)	0.115	2.654 (1.463 to 4.815)	0.001*	1.903 (1.003 to 3.611)	0.049*
Nutrition supplement						
No	Reference		Reference			
Yes	0.684 (0.114 to 4.110)	0.678	1.106 (0.396 to 3.093)	0.847		
Lab/biomarker						
Serum albumin (g/dL)						
≥3.5	Reference		Reference			
<3.5	3.157 (0.391 to 25.465)	0.280	1.377 (0.724 to 2.616)	0.329		
Glucose (mg/dL)						
<110	Reference		Reference			
110–140	0.293 (0.035 to 2.438)	0.256	0.648 (0.283 to 1.480)	0.303		
>140	0.330 (0.066 to 1.650)	0.177	0.894 (0.465 to 1.721)	0.738		
Sodium (mEq/L)						
≥135	Reference		Reference			
<135	0.900 (0.232 to 3.485)	0.879	1.653 (0.913 to 2.994)	0.097		
Hemoglobin (g/dL)						
≥12	Reference		Reference		Reference	
<12	†		2.180 (1.047 to 4.539)	0.037*	1.910 (0.885 to 4.121)	0.099
Potassium (mEq/L)						
≤5.3	Reference		Reference			
>5.3	1.447 (0.387 to 5.412)	0.583	0.789 (0.430 to 1.447)	0.444		
Calcium (mg/dL)						
≤10.2	Reference		Reference			
>10.2	†		2.971 (0.715 to 12.342)	0.134		
Phosphate (mg/dL)						
≤5.0	Reference		Reference			
>5.0	0.657 (0.170 to 2.535)	0.542	1.430 (0.779 to 2.624)	0.248		
Physical status						
DRG (disease) severity						
Major severity	Reference		Reference		Reference	
Extreme severity	2.490 (0.476 to 13.033)	0.280	1.941 (1.074 to 3.510)	0.028*	1.685 (0.899 to 3.160)	0.104

*Represents significant factor, p<0.05.
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with 1-year mortality. A consensus statement by the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition emphasized that malnutrition was predictive of mortality and nutrition status was an independent prognostic indicator.[9] Given that approximately 30%–60% of hospitalized patients have evidence of undernutrition or malnutrition,[5] assessing the nutritional status of critically ill adult patients is integral to their overall care, and various methods have been proposed. The European Society for Clinical Nutrition and Metabolism[10] recommended that the standard method for evaluating adult malnutrition should be anthropometric measures such as weight loss and underweight status, and recent weight loss is still the single most important indicator of nutritional status.[2] Assessment of energy and protein needs in hospitalized patients led investigators to suggest that successful prevention and early detection of malnutrition must begin in the hospital with careful monitoring of food intake, even including evaluation of patients' menus for energy and protein quantities.[14] Jensen and Wheeler[6] proposed using acute and chronic inflammation to define and diagnose malnutrition in critically ill adults. Differences between malnutrition as a result of starvation versus disease-related malnutrition must also be distinguished, especially in chronic disease-associated malnutrition in which inflammation is chronic and may be associated with organ dysfunction—a frequent malnutrition syndrome seen in critical care patients.[15] It follows then that early identification of malnutrition and nutritional intervention would likely reduce the risk of mortality in critically ill patients.[16] Nutrition education may also be necessary to prevent malnutrition and its complications after discharge.

In the present study, patients who had received blood products or colloid supplements were at higher risk of 1-year mortality. Patients with malnutrition were receiving nutrition intervention after admission to ICU because healthcare professionals will do everything possible to improve patients' health status. This also may help to explain why no significant differences were found in *in-hospital* mortality and why, beginning at 52 days after ICU discharge, significant differences were found in mortality. Patients' dietary behavior did not likely change after discharge and malnutrition was still present. Further research is needed to determine whether the effects of nutrition intervention may last for 52 days, as seen in our results.

Results of the present study show that the effects of malnutrition on survival time were somewhat more prominent in women even though significant differences were not found between genders in in-hospital mortality (with borderline significance) or 1-year mortality. The gender difference in malnutrition effects on mortality is due to the better (baseline) survival in non-malnutrition women than in men, including 95.8 days for women and 35.9 days for men for in-hospital survival, and 299.0 days for women and 268.0 days for men for 1-year survival. One study of malnutrition in patients with cancer reported that gender differences were possibly related to the role of nutritional status in survival.[17] But additional larger studies may be required to further examine the gender differences of malnutrition on survival in critically ill patients with acute renal failure. Also, because critical illness is a physiologic stressor that alters patients' metabolic and energy demands, and these demands differ between men and women and their respective BMI and levels of excess body fat, the generally smaller female physique may succumb more to a hypercatabolic state.[18] Male waist circumference >40 inches and female waist circumference >35 inches, even if their BMI is normal, are indicators of nutrition status and fat content and are known risk factors for chronic disease. Since ICU patients do not always take food by mouth, and patients' preadmission dietary habits may not be known, we also do not know if the risk of malnutrition may be greater among critically ill women and differences between malnourished and not malnourished may simply be more obvious. Single women in our study also had a significantly lower risk of 1-year mortality than married women, contradicting a generally recognized benefit of marriage on mortality. Results of a previous study indicated that married women have a higher death rate than single women in those aged 20–30 years, which was explained as the influence of childbearing during these years and the trend of delayed marriage.[19]

The prevalence of anemia (hemoglobin less than 12 g/dL) was significantly higher in non-malnutrition patients than in malnutrition patients. This is difficult to explain except for the fact that iron deficiency resulting from low transferrin levels is common in older adults,[18] and that MIMIC patients with malnutrition were already receiving nutrition intervention that may help to correct iron deficiency. Also, in some non-malnutrition patients, an imbalance between the supply of nutrients and energy and the body's demand for them may not yet have progressed to BMI-detectable malnutrition status. This points again toward the necessity of evaluating nutrition status in critically ill patients, whose status is precarious and always evolving. Evaluation of nutrition status should include transferrin levels, which indicate acute changes in nutrition better than albumin levels, and renal disease especially will reduce transferrin levels.[20]

In the present study, the prevalence of low serum sodium (less than 135 mEq/L) was significantly higher in malnutrition patients than in non-malnutrition patients, which is consistent with renal failure but may not be noted in association with other disease states. In patients with chronic malnutrition, serum electrolytes, including sodium, may remain stable; however, imbalances in body sodium may be associated with the increased mortality of critically ill patients,[21] although not necessarily associated directly with malnutrition. Using an etiology-based approach to evaluating malnutrition, patients with chronic renal disease and acute renal failure will have mild to moderate inflammation, which is the most significant factor in disease-associated malnutrition.[22] Nutritional deficiencies and loss of muscle mass characteristic of malnutrition contribute to functional decline in critically ill patients, and baseline impairment must be understood before improvement can be expected from interventions.[16] Our results suggest that defining and diagnosing malnutrition is essential in selecting the appropriate nutrition interventions and supporting functional outcomes.

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Strengths and limitations

The present study used a high-quality database that encompasses a diverse and exceptionally large population of ICU patients. It provided high temporal resolution data, including lab results, electronic documentation, and bedside monitoring trends and waveforms, which all helped to give credence to our analysis and results. However, this study also has certain limitations, mainly on the data from only one medical center, and that the results are not generalizable to other populations. The MIMIC data set provided no information on patients' status prior to ICU admission; therefore, the impact of pre-existing malnutrition on the outcomes in ICU patients could not be evaluated. The MIMIC database also does not have lifestyle and dietary information, environmental exposure, and family medical history, factors that may have influenced our results if they had been included in analysis. Also, no information was available on medical utilization after discharge, and only in-hospital data from patients' ICU stays were included. Additional study is needed to corroborate our results relative to the influence of nutritional status on the mortality of critically ill patients with acute renal failure.

CONCLUSIONS

Nutritional status is a predictive factor of mortality among critically ill patients with acute renal failure, particularly 1-year mortality after ICU discharge. Longer, more detailed follow-up of critically ill patients with acute renal failure is needed from the time of ICU discharge, emphasizing nutritional assessment and intervention. Future study must include baseline nutrition assessments to support more accurate analysis. Effective strategies for reducing the negative effects of malnutrition in acute renal failure and other critical disease states are dependent on reliable nutrition assessment.

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