

Association Between Mortality and Weight Loss in Critical Patients: A Propensity Matching Study

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Abstract

Background: Malnutrition is prevalent among critically ill patients and significantly impacts clinical outcomes. This study aimed to investigate the association between weight loss (a proxy for nutritional depletion) and mortality in intensive care unit (ICU) patients.

Methods: A retrospective cohort analysis was conducted using data from 29,217 ICU patients in the Medical Information Mart for Intensive Care III (MIMIC-III) database. Patients were stratified into weight-loss and non-weight-loss groups. Propensity score matching (PSM) was employed to balance baseline characteristics. Multivariable logistic and Cox regression analyses were performed to assess associations between weight loss and outcomes.

Results: Weight-loss patients exhibited significantly higher short- and long-term mortality rates compared to non-weight-loss patients (90-day: 18.9% vs. 13.6%, $P = 0.002$; 180-day: 21.8% vs. 16.9%, $P = 0.002$, 365-day: 31.3% vs. 24.2%, $P = 0.001$). Weight loss was also associated with prolonged mechanical ventilation (27.1% vs. 14.2%, $P < 0.001$), renal replacement therapy (4.1% vs. 0.9%, $P < 0.001$), and extended ICU/hospital stays. Adjusted regression models confirmed weight loss as an independent risk factor for short-term and long-term mortality.

Conclusions: Weight loss is significantly associated with mortality and adverse outcomes in critically ill patients. Early nutritional assessment and intervention are essential to improve prognosis.

Keywords: Weight loss; Mortality; Intensive care unit; Propensity score matching

Introduction

It is estimated that up to 60% of hospitalized patients are affected by malnutrition, which is defined as an imbalance between the availability of nutrients and the physiological demand for those nutrients [1–3]. Clinicians have challenges in meeting the calorie needs of critically ill patients due to gastrointestinal feeding intolerance, gastrointestinal dysmotility, gut microbial dysbiosis, and high energy demand [4]. In addition, malnutrition is made worse in critically ill populations due to metabolic stress, inflammation, and comorbidities [5, 6]. Therefore, malnutrition is more common in critically ill patients [7]. Weight loss, a key indicator of malnutrition, has been consistently linked to mortality in chronic diseases such as cancer, respiratory diseases, renal insufficiency, and heart failure [8–12]. The correlation between weight loss and death has been the subject of mixed findings in a number of research. After losing weight, the mortality rate is either higher [13–16] or stays the same [17], according to recent research. Among patients with life-threatening diseases, there is little evidence. In order to better guide our therapeutic intervention on the nutritional status of patients, we need to have a better understanding of the relationship between the nutritional status of patients in the intensive care unit (ICU) and the prognosis of the disease.

This study leverages the Medical Information Mart for Intensive Care III (MIMIC-III) database to evaluate the association between weight loss (defined by ICD-9 codes for malnutrition and abnormal weight reduction) and clinical outcomes in ICU patients [18].

Materials and Methods

Sources of data

The MIMIC-III is an open critical care medicine database that

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was collaboratively released by the Laboratory for Computational Physiology at Massachusetts Institute of Technology, Beth Israel Deacon Medical Center (BIDMC), and Philips Medical with the support of the National Institutes of Health (NIH). The MIMIC-III database gathered hospitalization information for more than 50,000 patients admitted to the ICU in BIDMC from June 2001 to October 2012.

Selection of participants

All patients admitted to ICU were extracted and were categorized into weight-loss and non-weight-loss groups based on ICD-9 diagnoses.

The exclusion criteria were as follows: 1) patients who were not admitted to ICU for the first time; 2) patients younger than 18 years old; 3) patients who died in hospital; and 4) patients with data missing more than 5%.

Data collection and definitions

Baseline features from the MIMIC-III database were obtained using a standard SQL query, encompassing fundamental information, critical illness scores, vital signs, comorbidities, laboratory test results from the first day of ICU admission, and clinical outcomes. Fundamental information included gender, age, ethnicity, admission and discharge times for the hospital and ICU, as well as the day of death. Critical illness scores comprised the Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS), and Oxford Acute Severity of Illness Score (OASIS). Vital indicators comprised heart rate, mean arterial pressure (MAP), respiratory rate, body temperature, pulse oxygen saturation (SpO₂), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Comorbidities encompassed congestive heart failure (CHF), hypertension, stroke, chronic obstructive pulmonary disease (COPD), diabetes, renal failure, liver disease, cancer, and coagulation problems. Laboratory analyses encompassed white blood cell count (WBC), hemoglobin, platelet count, hematocrit, international normalized ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT), blood urea nitrogen (BUN), creatinine, serum potassium, serum sodium, bicarbonate, chloride, glucose, and anion gap. Clinical outcomes encompassed both primary and secondary outcomes. The primary outcomes encompassed mortality rates at 90, 180, and 365 days. Secondary outcomes encompassed mechanical ventilation (MV, exceeding 72 h post-admission), renal replacement therapy (RRT), vasopressor utilization (exceeding 24 h post-admission), ICU stays (exceeding 3 days), and hospital stays (exceeding 14 days).

Statistical analysis

Continuous data were expressed as medians (interquartile ranges), whereas categorical variables were represented as frequency and percentage. The Shapiro-Wilk test was initially

conducted to assess the normality of continuous variables. The *t*-test or Mann-Whitney U test was utilized for comparing continuous variables, whereas categorical variables were assessed using Chi-square or Fisher's exact tests.

Logistic and Cox regression analyses were employed to illustrate the association between weight loss status in patients and clinical outcomes. Multivariate logistic and Cox regression analyses were conducted to compensate for all covariates listed in Table 1. To account for missing data mechanisms and reduce bias, we employed multiple imputations and repeated the primary outcome analysis as per Rubin's rules. Propensity score matching (PSM) was conducted to reduce confounding bias, incorporating all factors into the analysis. One-to-one nearest-neighbor matching was implemented using a caliper width of 0.2. A standardized mean difference (SMD) was employed to assess the outcome of PSM. A criterion of 0.1 was deemed acceptable. An inverse probability of treatment weighting (IPTW) model was employed to create a weighted cohort utilizing the predicted propensity scores as weights. Standardized mortality ratio weighting (SMRW), propensity score matching weighting (PSMW), and overlap weighting (OW) were employed to adjust the covariates, hence ensuring the robustness of our findings. We utilized Kaplan-Meier and log-rank analyses to differentiate 365-day survival curves, both before and following matching, PSMW, and IPWT.

The R package "MICE" was utilized to execute the neighbor interpolation method, subsequently employed to impute any missing data. All analyses were conducted utilizing the statistical software tool R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria). A P-value criterion of less than 0.05 (two-tailed) was deemed statistically significant.

Ethics approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The research protocol was authorized by the BIDMC and the Institutional Review Boards of MIT following completion of the CITI (Record ID# 40362987).

Results

Study population and baseline characteristics

Based on the ICD-9 diagnoses of weight loss, weight loss was defined mainly as malnutrition or low body weight. With data of 54,269 ICU patients in the MIMIC-III database reviewed, a total of 29,217 patients were included in the original cohort after applying the exclusion criteria. Among them, a total of 28,258 patients without weight loss were defined as group 1, while 959 patients with weight loss were defined as group 2. Before matching, there were significant differences in almost all variables between the two groups. After the PSM, 957 patients with weight loss and 957 patients without weight loss were successfully matched and included in this study. The flow chart of screening and matching is shown in Figure 1. After

Table 1. Comparisons of Characteristics Between the Original Cohort and Matched Cohort

Characteristic	Original cohort			Matched cohort		
	Group 1 (n = 28,258)	Group 2 (n = 959)	SMD	Group 1 (n = 957)	Group 2 (n = 957)	SMD
Basic information						
Female, n (%)	11,847 (41.9)	421 (43.9)	0.04	724 (75.7)	706 (73.8)	0.044
Age	65.20 (52.22, 77.38)	66.55 (53.79, 78.27)	0.095	68.09 (54.95, 79.59)	66.55 (53.81, 78.28)	0.058
Ethnicity, n (%)			0.094			0.044
White	20,415 (72.2)	707 (73.7)		724 (75.7)	706 (73.8)	
Black	2,095 (7.4)	87 (9.1)		79 (8.3)	87 (9.1)	
Other	5,748 (20.3)	165 (17.2)		154 (16.1)	164 (17.1)	
Admission, n (%)			0.382			0.054
Elective	4,815 (17.0)	52 (5.4)		41 (4.3)	52 (5.4)	
Emergency	22,711 (80.4)	890 (92.8)		900 (94.0)	888 (92.8)	
Urgent	732 (2.6)	17 (1.8)		16 (1.7)	17 (1.8)	
Weight, kg	79.00 (67.00, 93.00)	69.00 (58.00, 83.00)	0.425	77.00 (65.00, 91.00)	69.00 (58.00, 83.00)	0.380
Vital signs						
Heart rate, bpm	83.39 (73.92, 93.75)	86.84 (76.82, 99.18)	0.265	87.06 (76.45, 98.84)	86.80 (76.82, 99.00)	0.033
Respiratory rate, bpm	17.78 (15.81, 20.28)	18.48 (16.30, 21.55)	0.185	18.54 (16.32, 21.38)	18.48 (16.30, 21.54)	< 0.001
Temperature, °C	36.82 (36.49, 37.20)	36.80 (36.44, 37.23)	0.015	36.81 (36.44, 37.21)	36.80 (36.44, 37.23)	0.012
Spo2, %	97.64 (96.33, 98.73)	97.75 (96.33, 98.98)	0.022	97.69 (96.44, 98.80)	97.75 (96.33, 99.00)	0.022
SBP, mm Hg	117.35 (108.04, 129.40)	115.64 (105.72, 131.16)	0.041	116.86 (107.63, 129.71)	115.64 (105.72, 131.17)	0.049
DBP, mm Hg	60.08 (54.00, 67.15)	60.35 (53.62, 67.89)	0.064	60.56 (54.85, 68.00)	60.42 (53.61, 67.91)	0.022
MAP, mm Hg	77.23 (71.25, 84.76)	76.67 (69.68, 85.33)	0.026	77.06 (71.00, 85.44)	76.75 (69.71, 85.34)	0.04
Severity of illness						
GCS	15.00 (14.00, 15.00)	15.00 (13.00, 15.00)	0.184	15.00 (13.00, 15.00)	15.00 (13.00, 15.00)	0.046
SOFA	3.00 (2.00, 5.00)	4.00 (2.00, 7.00)	0.32	4.00 (2.00, 6.00)	4.00 (2.00, 7.00)	< 0.001
OASIS	30.00 (25.00, 36.00)	33.00 (28.00, 39.00)	0.382	34.00 (28.00, 39.00)	33.00 (28.00, 39.00)	0.006
Comorbidities, n (%)						
CHF	6,544 (23.2)	245 (25.5)	0.056	243 (25.4)	244 (25.5)	0.002
Hypertension	15,567 (55.1)	448 (46.7)	0.168	456 (47.6)	448 (46.8)	0.017
Stroke	971 (3.4)	80 (8.3)	0.21	77 (8.0)	79 (8.3)	0.008
COPD	4,861 (17.2)	196 (20.4)	0.083	182 (19.0)	195 (20.4)	0.034

Table 1. Comparisons of Characteristics Between the Original Cohort and Matched Cohort - (continued)

Characteristic	Original cohort			Matched cohort		
	Group 1 (n = 28,258)	Group 2 (n = 959)	SMD	Group 1 (n = 957)	Group 2 (n = 957)	SMD
Diabetes mellitus	7,187 (25.4)	229 (23.9)	0.036	224 (23.4)	229 (23.9)	0.012
Renal failure	3,409 (12.1)	156 (16.3)	0.121	165 (17.2)	156 (16.3)	0.025
Liver disease	1,698 (6.0)	141 (14.7)	0.288	135 (14.1)	141 (14.7)	0.018
Malignancy	2,317 (8.2)	128 (13.3)	0.167	113 (11.8)	126 (13.2)	0.041
Coagulopathy	2,636 (9.3)	182 (19.0)	0.28	165 (17.2)	181 (18.9)	0.043
Laboratory tests						
WBC, × 10 ⁹ /L	12.30 (9.10, 16.30)	12.50 (8.80, 17.35)	0.031	12.50 (9.10, 16.90)	12.50 (8.80, 17.30)	0.028
Hemoglobin, g/dL	10.10 (8.60, 11.80)	9.60 (8.40, 11.00)	0.21	9.70 (8.30, 11.30)	9.60 (8.40, 11.00)	0.012
Platelet, × 10 ⁹ /L	186.00 (134.00, 247.00)	201.00 (129.00, 282.00)	0.175	196.00 (129.00, 272.00)	201.00 (129.00, 282.00)	0.008
Laboratory tests						
Hematocrit, %	29.60 (25.20, 34.40)	28.50 (24.80, 32.55)	0.164	28.80 (24.70, 33.30)	28.50 (24.80, 32.60)	0.01
INR	1.30 (1.10, 1.50)	1.30 (1.20, 1.70)	0.122	1.30 (1.10, 1.70)	1.30 (1.20, 1.70)	0.042
PT, s	14.30 (13.10, 16.10)	14.70 (13.20, 17.85)	0.166	14.70 (13.30, 17.50)	14.70 (13.20, 17.80)	0.026
PTT, s	31.40 (26.80, 41.50)	32.80 (28.00, 43.20)	0.051	32.50 (27.00, 44.60)	32.70 (28.00, 43.20)	0.003
Bun, mg/dL	19.00 (14.00, 28.00)	22.00 (14.00, 37.00)	0.205	22.00 (15.00, 35.00)	22.00 (14.00, 37.00)	0.005
Creatinine, mg/dL	1.00 (0.80, 1.30)	1.00 (0.70, 1.50)	0.064	1.10 (0.80, 1.50)	1.00 (0.70, 1.50)	0.011
Potassium, mmol/L	4.50 (4.10, 5.10)	4.30 (4.00, 4.80)	0.218	4.30 (4.00, 4.90)	4.30 (4.00, 4.80)	0.013
Sodium, mmol/L	140.00 (138.00, 142.00)	140.00 (137.00, 143.00)	0.009	141.00 (138.00, 143.00)	140.00 (137.00, 143.00)	0.072
Bicarbonate, mmol/L	25.00 (23.00, 27.00)	25.00 (22.00, 28.00)	0.016	25.00 (23.00, 27.00)	25.00 (22.00, 28.00)	0.018
Chloride, mmol/L	107.00 (104.00, 111.00)	107.00 (103.00, 111.00)	0.005	108.00 (104.00, 111.00)	107.00 (103.00, 111.00)	0.068
Glucose, mEq/L	156.00 (125.00, 194.75)	150.00 (120.00, 196.50)	0.015	154.00 (125.00, 199.00)	150.00 (120.00, 197.00)	0.04
Anion gap, mmol/L	14.00 (12.00, 17.00)	15.00 (13.00, 18.00)	0.147	15.00 (13.00, 18.00)	15.00 (13.00, 18.00)	0.063

Group 1: patients without weight loss. Group 2: patients with weight loss, as defined by ICD-9 diagnoses. SMD: standardized mean difference; SpO₂: oxygen saturation; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; GCS: Glasgow Coma Score; SOFA: Sequential Organ Failure Assessment; OASIS: Oxford Acute Severity of Illness Score; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; WBC: white blood cell count; INR: international prothrombin time; PT: prothrombin time; PTT: partial thromboplastin time; BUN: blood urea nitrogen.

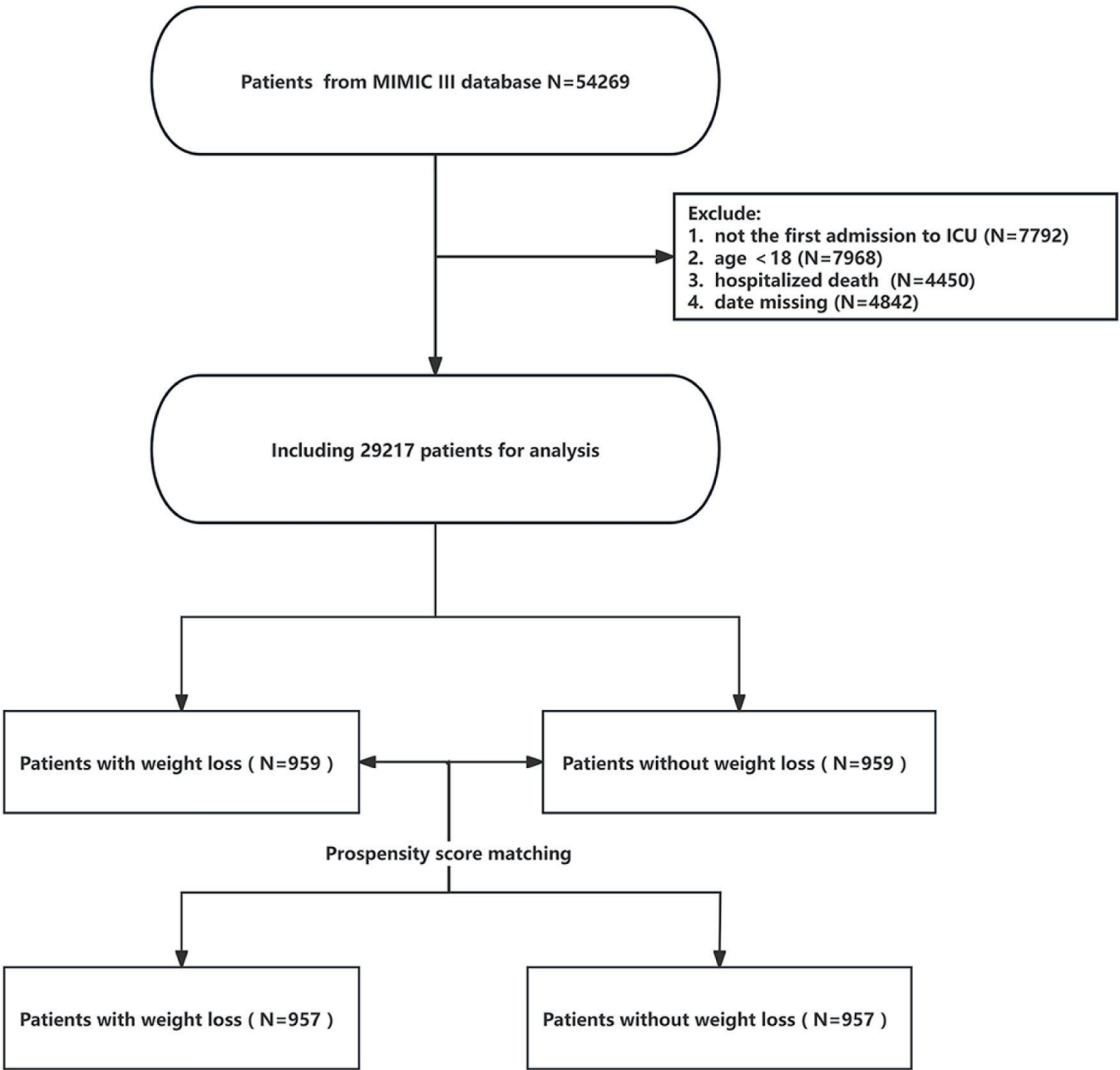


Figure 1. Flow diagram for data inclusion in the present study.

matching, there was a significant difference in body weight between the two groups, in addition to which almost all SMD were less than 0.1, showing the effectiveness of PSM. Baseline characteristics before and after matching are both presented in Table 1. Visualized comparison curves of weighted data before and after matching are shown in Figure 2.

Primary outcome

Statistically significant differences in mortality existed be-

tween the two groups both before and after matching, demonstrating that patients experiencing weight loss had elevated short-term and long-term mortality rates. Following propensity score matching, the 90-day mortality rates for patients with and without weight loss were 18.9% and 13.6%, respectively ($P = 0.002$), while the 180-day mortality rates were 21.8% and 16.9%, respectively ($P = 0.008$). The 365-day mortality rates were 31.3% and 24.2%, respectively ($P = 0.001$), indicating a substantial difference (Table 2). The outcomes of multivariate logistic regression and Cox regression, both prior to and during adjustment, exhibited statistical

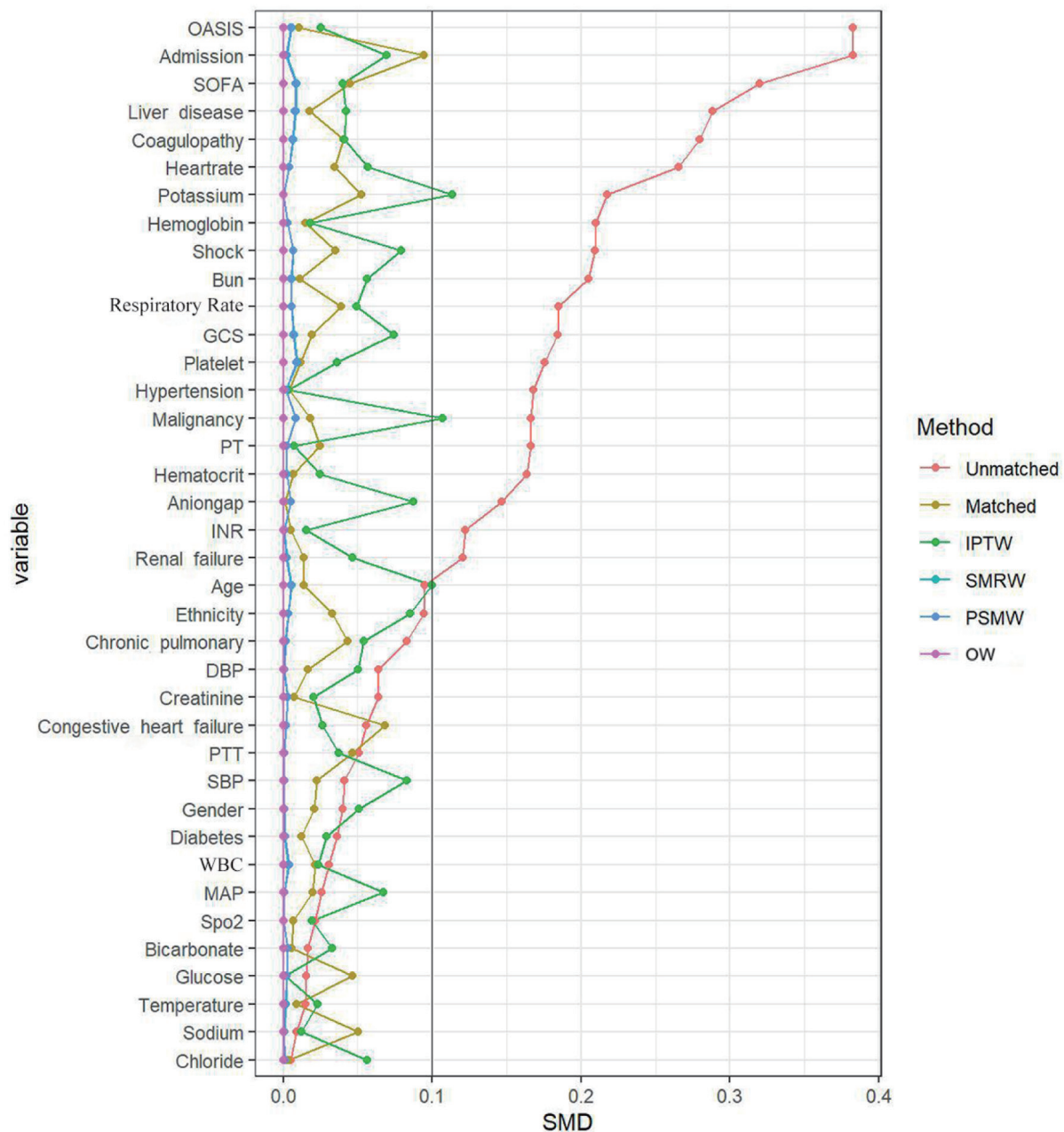


Figure 2. Plot of standardized mean difference after propensity score analysis. IPTW: inverse probability of treatment weighting; SMRW: standardized mortality ratio weighting; PSMW: propensity score matching weighting; OW: overlap weighting.

differences. Comorbid weight loss was identified as a risk factor for mortality at 90, 180, and 365 days in ICU patients (Tables 3 and 4). The Kaplan-Meier curves illustrated that the mortality rate among weight-loss patients exceeds that of non-weight-loss patients, with a statistically significant difference between the groups (Fig. 3).

Secondary outcomes

Following PSM, the proportion of patients requiring extended

MV in group 1 and group 2 was 14.2% (136/957) and 27.1% (259/957), respectively. The incidence of patients undergoing RRT was 0.9% (9/957) and 4.1% (39/957), respectively. In comparison to group 1, patients in group 2 exhibited a higher likelihood of being in the ICU for over 3 days (39.7% (380/957) vs. 55.5% (531/957), $P < 0.001$), and this trend was also observed for the duration of hospital stay longer than 14 days (22.5% (215/957) vs. 54.0% (517/957), $P < 0.001$). The usage of vasopressors between the two groups prior to matching was statistically significant; however, no statistically significant difference was observed between the groups post-matching. In

Table 2. Clinical Outcomes Analysis on the Original Cohort and Matched Cohort

Outcomes	Original cohort				Matched cohort			
	Total	Group 1	Group 2	P value	Total	Group 1	Group 2	P value
Primary outcome, n (%)								
90-day mortality	2,577 (8.8)	2,395 (8.5)	182 (19.0)	< 0.001	311 (16.2)	130 (13.6)	181 (18.9)	0.002
180-day mortality	3,209 (11.0)	3,000 (10.6)	209 (21.8)	< 0.001	371 (19.4)	162 (16.9)	209 (21.8)	0.008
365-day mortality	4,854 (16.6)	4,553 (16.1)	301 (31.4)	< 0.001	532 (27.8)	232 (24.2)	300 (31.3)	0.001
Secondary outcome, n (%)								
Vasopressor use (> 24 h)	3,559 (12.2)	3,388 (12.0)	171 (17.8)	< 0.001	315 (16.5)	145 (15.2)	170 (17.8)	0.139
RRT	271 (0.9)	232 (0.8)	39 (4.1)	< 0.001	48 (2.5)	9 (0.9)	39 (4.1)	< 0.001
MV (> 72 h)	3,176 (10.9)	2,917 (10.3)	259 (27.0)	< 0.001	395 (20.6)	136 (14.2)	259 (27.1)	< 0.001
ICU-stays (> 3 days)	10,214 (35.0)	9,681 (34.3)	533 (55.6)	< 0.001	911 (47.6)	380 (39.7)	531 (55.5)	< 0.001
Hospital-stays (> 14 days)	5,543 (19.0)	5,024 (17.8)	519 (54.1)	< 0.001	732 (38.2)	215 (22.5)	517 (54.0)	< 0.001

Group 1: patients without weight loss. Group 2: patients with weight loss, as defined by ICD-9 diagnoses. ICU: intensive care unit; MV: mechanical ventilation; RRT: renal replacement therapy.

logistic regression analysis, comorbid weight loss emerged as a significant risk factor for the extension of MV, utilization of RRT, prolonged ICU stay, and duration of hospital stay, both before and after adjustments were made. Comprehensive results are presented in Tables 3 and 4.

Sensitivity analysis

In the entire cohort, after adjusting for all covariates in Table

1, the risk factor for 365-day mortality in patients experiencing weight loss was 1.40 (95% confidence interval (CI), 1.25–1.58, $P < 0.001$), as corroborated by multivariate analysis using the Cox hazard model. The hazard ratio (HR) values consistently ranged from 1.28 to 1.74 across various adjustment and matching methods. Likewise, following the implementation of multivariate logistic regression analysis, it was determined that the risk factor for 365-day death in patients experiencing weight loss was 1.57 (95% CI, 1.34–1.84, $P < 0.001$), with odds ratio (OR) values consistently ranging from 1.34 to 1.87 using

Table 3. Logistic Regression Analysis of Clinical Outcomes on the Original Cohort and Matched Cohort

Outcomes	Original cohort				Matched cohort			
	Non-adjusted		Adjusted		Non-adjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Primary outcome								
90-day mortality	2.53 (2.14, 2.98)	< 0.001	1.59 (1.32, 1.91)	< 0.001	1.48 (1.16, 1.90)	0.002	1.65 (1.26, 2.17)	< 0.001
180-day mortality	2.35 (2.00, 2.74)	< 0.001	1.53 (1.28, 1.82)	< 0.001	1.37 (1.09, 1.72)	0.007	1.49 (1.16, 1.93)	0.002
365-day mortality	2.38 (2.07, 2.74)	< 0.001	1.57 (1.34, 1.84)	< 0.001	1.43 (1.17, 1.75)	0.001	1.56 (1.25, 1.96)	< 0.001
Secondary outcome								
MV (> 72 h)	3.21 (2.77, 3.72)	< 0.001	2.55 (2.13, 3.05)	< 0.001	2.24 (1.78, 2.83)	< 0.001	2.85 (2.17, 3.78)	< 0.001
RRT	5.12 (3.57, 7.15)	< 0.001	3.43 (2.19, 5.26)	< 0.001	4.47 (2.26, 9.90)	< 0.001	6.76 (2.64, 19.62)	< 0.001
Vasopressor use (> 24 h)	1.59 (1.34, 1.88)	< 0.001	1.36 (1.10, 1.67)	0.004	1.21 (0.95, 1.54)	0.124	1.29 (0.95, 1.75)	0.101
ICU-stays (> 3 days)	2.40 (2.11, 2.73)	< 0.001	1.93 (1.67, 2.24)	< 0.001	1.89 (1.58, 2.27)	< 0.001	2.23 (1.80, 2.75)	< 0.001
Hospital-stays (> 14 days)	5.45 (4.79, 6.22)	< 0.001	4.44 (3.85, 5.13)	< 0.001	4.06 (3.33, 4.95)	< 0.001	4.98 (4.00, 6.23)	< 0.001

CI: confidence interval; ICU: intensive care unit; MV: mechanical ventilation; OR: odds ratio; RRT: renal replacement therapy.

Table 4. Cox Regression Analysis of Clinical Outcomes on the Original Cohort and Matched Cohort

Outcomes	Original cohort				Matched cohort			
	Non-adjusted		Adjusted		Non-adjusted		Adjusted	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
90-day mortality	2.37 (2.04, 2.75)	< 0.001	1.44 (1.23, 1.68)	< 0.001	1.43 (1.14, 1.79)	0.002	1.43 (1.20, 1.70)	< 0.001
180-day mortality	2.22 (1.93, 2.56)	< 0.001	1.42 (1.23, 1.64)	< 0.001	1.34 (1.09, 1.65)	0.005	1.41 (1.15, 1.74)	< 0.001
365-day mortality	2.16 (1.93, 2.43)	< 0.001	1.40 (1.25, 1.58)	< 0.001	1.36 (1.15, 1.62)	< 0.001	1.53 (1.21, 1.92)	< 0.001

CI: confidence interval; HR: hazard ratio.

various adjustment and matching methods. The results were illustrated in a forest map, as depicted in Figure 4.

Discussion

This retrospective study provides evidence that weight loss,

as a marker of nutritional depletion, is significantly associated with increased short- and long-term mortality, prolonged MV, higher rates of RRT, and extended ICU/hospital stays among critically ill patients. Below, we contextualize these results, discuss potential mechanisms, and highlight implications for clinical practice and future research.

Our analysis revealed that weight-loss patients exhibited

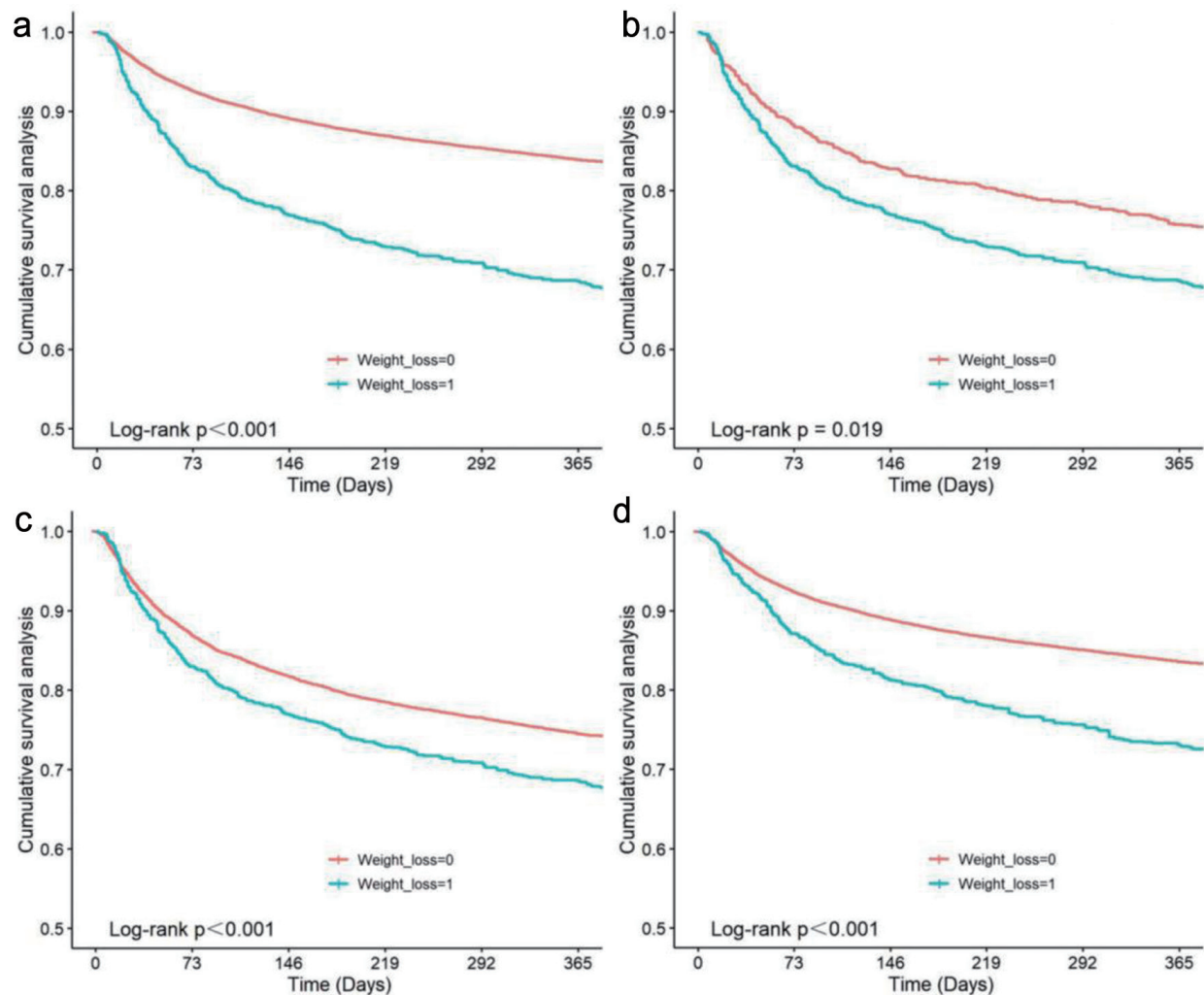


Figure 3. Kaplan-Meier curves for 365-day survival probability comparing two groups. (a) Before matched. (b) After matched. (c) Propensity score matching weighting (PSMW). (d) Inverse probability weighting (IPWT). The red line represents patients without weight loss and the blue line represents patients with combined weight loss.

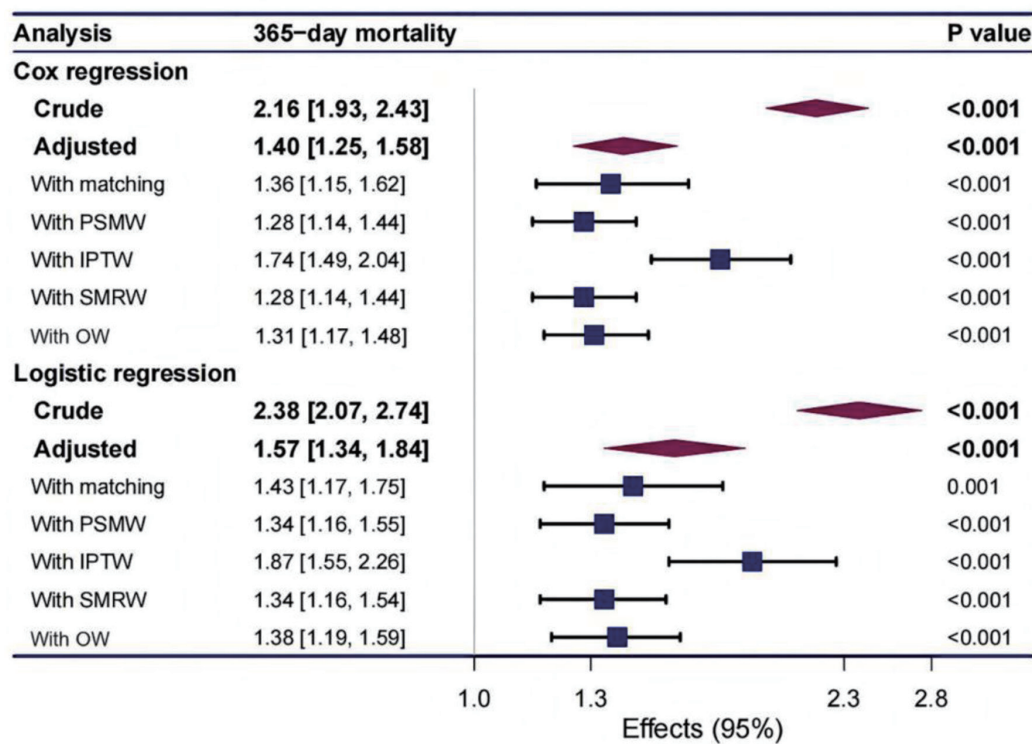


Figure 4. The forest plot of logistic and Cox regression analysis for 365-day mortality. PSMW: propensity score matching weighting; IPTW: inverse probability of treatment weighting; SMRW: standardized mortality ratio weighting; OW: overlap weighting.

markedly higher mortality rates at 90 days (18.9% vs. 13.6%), 180 days (21.8% vs. 16.9%), and 365 days (31.3% vs. 24.2%) compared to non-weight-loss patients. These findings are in line with previous research on chronic conditions, including heart failure and chronic obstructive pulmonary disease (COPD), which has shown that unintended weight loss is associated with a worse chance of survival [15, 19]. Multiple potential causes may account for the increased risk of ICU death in patients undergoing weight loss. Initially, the early stages of critical illness are marked by heightened energy consumption, leading to a state of hypermetabolism [20]. Any sickness can result in malnutrition, which may be exacerbated by critical illness if patients become immunocompromised and incapable of mounting an effective inflammatory response, rendering them vulnerable to adverse outcomes [21]. Second, weight loss often coexists with chronic comorbidities (e.g., heart failure, COPD, cancer), which independently increase mortality risk. Our regression model adjusted for these conditions, suggesting weight loss itself may contribute to poor prognosis beyond comorbidity burden [22]. The association between weight loss and secondary outcomes, such as prolonged MV (27.1% vs. 14.2%) and RRT (4.1% vs. 0.9%), further highlights the systemic impact of nutritional depletion. Multiple factors may explain the association between weight loss and the increased risk of extended mechanical breathing in ICU patients. Weight loss may impact ventilatory drive and pulmonary defense systems, drain energy reserves, result in muscle mass reduction, and potentially induce electrolyte imbalances such as hypophosphatemia, which can be linked to diminished muscular

contractile strength. Oxidative stress resulting from micronutrient deficits due to weight loss may significantly contribute to ventilator-induced diaphragmatic dysfunction. Weakness of the respiratory muscles may extend respiratory failure and hinder the weaning process from artificial support [23]. Likewise, weight reduction impacts renal function in ICU patients. Patients undergoing weight loss have demonstrated a reduced glomerular filtration rate and renal plasma flow, alongside diminished urine reabsorption capacity and acid excretion, potentially leading to increased reliance on renal replacement therapy [24]. Similar to other studies, the present study found weight loss as an independent risk factor for prolonged length of stay both in hospital and ICU [22, 25]. Weight-loss patients are in a state of nutritional loss, which increases their risk of infection, renal and liver dysfunction [26], and oxygen utilization deficiency [27], thereby affecting the prognosis. Notably, the non-significant difference in vasopressor use following propensity matching indicates that hemodynamic instability may be less directly linked to nutritional status than previously thought. This lack of difference likely reflects both the high baseline prevalence of vasoactive agents in the ICU population and propensity matching's efficacy in balancing underlying illness severity, thereby minimizing detectable between-group variation in pharmacologic support.

Strengths and limitations

Consistent with Yu et al's findings regarding BMI and mor-

tality, this study reveals that underweight is predictive of an elevated risk, while overweight or obesity is associated with a reduced mortality risk [28]. Our study's strengths include its large sample size ($n = 29,217$), rigorous adjustment for confounders via PSM, and sensitivity analyses using IPTW, SMRW, OW, and PSMW. The consistency of HRs (1.28–1.74) and ORs (1.34–1.87) across multiple models strengthens the validity of our conclusions. Furthermore, the use of the MIMIC-III database ensures standardized data collection, minimizing inter-center variability.

However, several limitations must be acknowledged. First, the retrospective design precludes causal inferences; weight loss may reflect underlying disease severity rather than directly causing mortality. Second, reliance on ICD-9-coded weight loss diagnoses may underestimate true nutritional risk due to four key limitations: 1) inability to capture subclinical malnutrition or dynamic changes (e.g., from admission to discharge), 2) lack of quantitative data on weight change magnitude, 3) no adjustment for fluid balance, and 4) dichotomous classification that overlooks etiology. This classification limitation inherently constrains mechanistic interpretation but strengthens the clinical relevance of our mortality association, as the codes reflect provider-recognized malnutrition with care implications. Third, we used body weight as a proxy for nutritional status due to inconsistent height data in MIMIC-III, which precluded reliable BMI calculation. Fourth, this may affect standardization but was unavoidable. Excluding patients with $> 5\%$ missing data may introduce selection bias, though multiple imputations mitigated this risk. Finally, the single-center nature of MIMIC-III limits generalizability to diverse healthcare settings. Future prospective studies are required to determine causality and evaluate the impact of dietary treatments in ICU populations. Research should incorporate BMI where possible and investigate the relationships among weight loss, inflammation, organ dysfunction, and medications with the aim of developing biomarkers to inform individualized treatment. Ultimately, integrating dynamic nutritional evaluations into the EHR may improve real-time monitoring and interventions.

Conclusions

Weight loss is a significant factor of mortality among critically ill patients. Nutritional assessment and intervention are needed to improve the prognosis from the patient's admission to the ICU.

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Financial Disclosure

None to declare.

Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

Due to the retrospective design and use of fully anonymized data from the MIMIC-III database, the requirement for informed consent from participants was waived by the institutional review boards. This waiver is consistent with ethical guidelines for secondary data analysis, where data cannot be linked to individuals.

Author Contributions

WH collected data, analyzed it, and wrote the manuscript. YZZ and XYW were involved in the study's conception, design, and coordination and helped draft the paper. XHC and QC was in charge of the entire project, reviewing the article, planning the study, and supervising it. All of the authors contributed to the paper and approved the final version.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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