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ORIGINAL RESEARCH

The effect of body mass index extremes on immune-inflammatory markers and outcomes in trauma patients

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Abstract

Background: Body mass index (BMI) extremes, including underweight and extreme obesity, are associated with unique health challenges and increased risk of complications in trauma patients. Immune-inflammatory markers, such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) are widely used prognostic indicators. However, their role in trauma patients with extreme BMI remains unclear. **Methods**: This retrospective cohort study analyzed trauma registry data from a single institution between 2009 and 2023. Adult trauma patients aged $\geq$20 years were categorized into underweight, normal weight, and extreme obesity groups (BMI, $<$18.5, 18.5–24.9, and $\geq$40 kg/m^2, respectively). NLR, MLR, PLR, and SII were calculated to evaluate the immune-inflammatory responses. Propensity score matching was performed to control for confounders such as age, sex, comorbidities, and injury severity. **Results**: Of 54,313 initially screened trauma patients, 19,967 were included. The underweight group exhibited higher MLR (0.45 *vs.* 0.39 *vs.* 0.41, $p = 0.001$), NLR (7.80 *vs.* 6.56 *vs.* 7.24, $p = 0.003$), and PLR (180.69 *vs.* 166.66 *vs.* 169.99, $p = 0.004$) than extreme obesity and normal weight groups. The underweight group also had the highest mortality rate (3.4% *vs.* 2.0% *vs.* 0.6%, $p < 0.001$), whereas the extreme obesity group had the longest hospital stay (10.7 *vs.* 8.7 days, $p = 0.029$). After propensity score matching, most immune markers showed no significant differences between the groups, except for monocyte counts, which remained significantly higher in the extreme obesity group (569.8 *vs.* 502.8/μL, $p = 0.032$). **Conclusions**: BMI extremes affect inflammatory profiles and trauma outcomes before matching, with patients having underweight demonstrating increased inflammatory ratios and mortality, and those with extreme obesity exhibiting prolonged hospital stay and elevated monocyte counts. Despite no significant differences in most immune markers after matching, these findings highlight the need for further studies on the interplay between BMI, immune response, and trauma recovery.

Keywords

BMI extremes; Trauma outcomes; Immune-inflammatory markers; Neutrophil-to-lymphocyte ratio; Propensity score matching

1. Introduction

Body mass index (BMI) is a key measure for assessing weight-related health risks. Accordingly, a BMI of $<$18.5 kg/m^2 indicates underweight, while BMI $\geq$40 kg/m^2 defines extreme obesity [1]. In 2022, 43% of adults were overweight, including 16% with obesity, reflecting a doubling in the global obesity rates since 1990 [2]. Obesity linked to chronic diseases, such as diabetes, cardiovascular issues, and cancer, has overtaken underweight globally, although underweight status remains significant in parts of South Asia and Africa [3]. These BMI extremes pose unique health risks and require integrated prevention strategies, particularly for trauma patients who face increased risks of complications and mortality. Both underweight and obesity patients experience significant challenges regarding trauma outcomes. Malnutrition, common in underweight individuals, compromises immune function, increases infection risks, slows wound healing, and exacerbates inflammation, particularly in older trauma patients, thereby leading to prolonged recovery and higher rates of complications and mortality [4, 5]. Similarly, obesity is associated with increased in-hospital complications, delayed recovery, and elevated mor-

tality risk [6]. For example, patients with extreme obesity face nearly double the morbidity rates of patients without obesity, with recovery rates reduced by nearly 48% and mortality rates increased by 30% [7]. Recovery was inversely related to BMI; each unit increase in BMI reduced recovery by 4% [7]. Compared with the general population, trauma patients with extreme BMI values may face additional and more complex health challenges [7, 8]. These patients are particularly vulnerable to delayed wound healing, altered pharmacokinetics, impaired mobility, and an increased susceptibility to infections. Acute physiological stress induced by trauma can exacerbate preexisting metabolic or nutritional imbalances, thereby prolonging recovery and increasing the likelihood of adverse outcomes. These findings underscore the dual burden of malnutrition and obesity in trauma care, and emphasize the importance of early nutritional assessment and tailored interventions to optimize outcomes in both underweight and obese trauma patients.

Complete blood count is a routine test that offers vital insights into immune status. White blood cell subtypes (neutrophils, lymphocytes, and monocytes) and derived ratios—neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and systemic immune inflammation index (SII)—are recognized as prognostic markers. Elevated NLR predicts poor outcomes in trauma, including intensive care unit (ICU) mortality in severe traumatic brain injury (TBI) (NLR $>$7.44), early mortality in severe hemorrhage, and in-hospital deaths (NLR $>$5.27) [9, 10]. Similarly, MLR reflects immune-inflammatory responses and predicts mortality, prolonged ICU stay, and complications. It is linked to poor outcomes in cerebral contusion and is an independent risk factor for 30-day mortality [11, 12]. PLR, another valuable marker, correlates with severe injuries, mortality, and the need for transfusions in abdominal trauma and traffic accidents [13–15]. Finally, SII, calculated as platelets $\times$ neutrophils/lymphocytes, predicts poor outcomes, including worse 6-month recovery in TBI, larger hematomas in intracerebral hemorrhage, and higher mortality in subarachnoid hemorrhage and ischemic stroke [16, 17]. Collectively, these indices are critical tools for risk stratification in trauma care.

Although these indices have been extensively studied in various diseases, their role in trauma patients, particularly those with extreme BMI values, remains unclear. This study aimed to address this gap by examining immune profiles, including white blood cell subtypes and derived ratios, in trauma patients categorized as underweight or extremely obese. Gaining insights into these relationships may enhance risk stratification and support tailored management strategies for trauma patients with extreme BMI values.

2. Materials and methods

2.1 Study design and patient enrollment

This retrospective cohort study was conducted in compliance with the regulations of the Institutional Review Board of the Chang Gung Memorial Hospital (IRB number: 202401825B0). Requirement for informed consent was waived by the Chang Gung Memorial Ethics Committee. Medical records and trauma registry data from the hospital's emergency department were analyzed over a 14-year period between 01 January 2009 and 31 December 2023. Adult trauma patients aged $\geq$20 years were included in the study. Exclusion criteria included patients with burns, hanging injuries, drowning incidents, incomplete laboratory data, and a BMI outside the range of 25.0–40.0 kg/m^2. Demographic and clinical data collected included sex, age, BMI, comorbidities, Glasgow Coma Scale score, Injury Severity Score (ISS), inflammatory markers, and in-hospital mortality rate. Laboratory parameters, including lymphocyte count, platelet count, monocyte count, NLR, MLR, PLR and SII (calculated as platelets $\times$ neutrophils/lymphocytes), were recorded for all the included patients.

2.2 Statistical analysis

Depending on data distribution, continuous variables are represented as medians with interquartile ranges or means with standard deviations. Categorical variables are presented as counts and percentages. Analysis of variance tests for continuous variables and chi-square tests for categorical variables were used for between-group comparisons, as appropriate. Propensity score-matched cohorts were analyzed to ensure balanced baseline characteristics. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS version 23 (IBM Corp., Armonk, NY, USA).

3. Results

3.1 Patient enrollment

This study initially evaluated 54,313 trauma patients included in the Trauma Registry System between 2009 and 2023. Of these, 47,922 patients met the age criterion of $\geq$20 years. We excluded 1192 patients with burns, 19 with hanging injuries, four with drowning incidents, and 13,880 with unavailable laboratory data. Additionally, 12,860 patients with a BMI outside the range of 25.0–40.0 kg/m^2 were excluded. Ultimately, 19,967 trauma patients were included in this study. The cohort was further categorized based on BMI: 2011 patients with BMI $<$18.5 kg/m^2, 17,794 patients with BMI between 18.5–24.9 kg/m^2, and 162 patients with BMI $\geq$40.0 kg/m^2, as illustrated in Fig. 1.

3.2 Patient demographics and clinical characteristics by BMI categories

Demographic and clinical characteristics of trauma patients, stratified by BMI categories, revealed significant differences across the groups (Table 1). The underweight group had a higher proportion of females than the extreme obesity and normal weight groups (55.4% *vs.* 42.0% *vs.* 48.3%, $p <$ 0.001). In contrast, the extreme obesity group showed a higher proportion of males than the underweight and normal weight groups (58.0% *vs.* 44.6% *vs*. 51.7%, $p < 0.001$). The extreme obesity group was the youngest, with a mean age of 41.4 years, compared with 55.0 years in the underweight group and 55.6 years in the normal weight group. Comorbidities varied

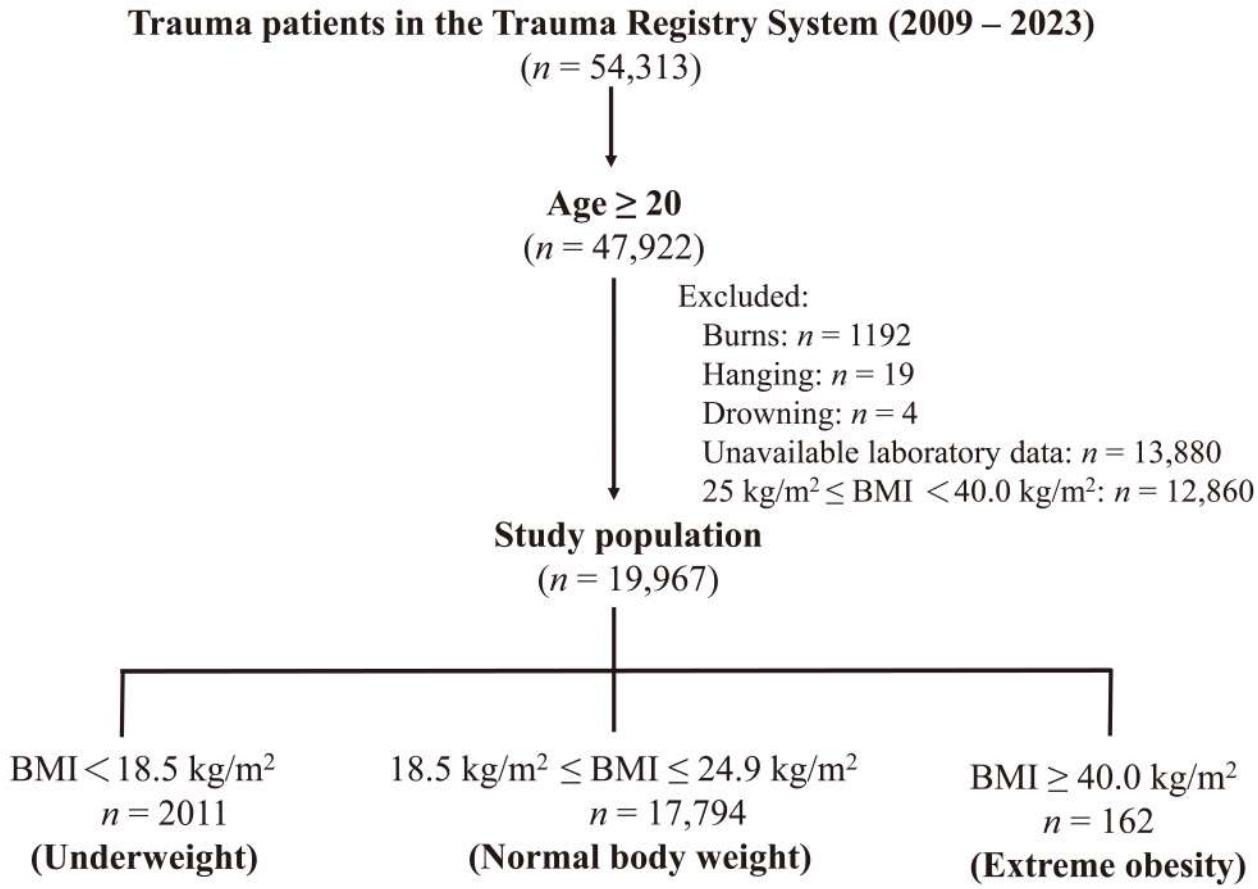

FIGURE 1. Flow diagram of patient enrollment process. BMI: Body mass index.

TABLE 1. Demographic and clinical characteristics of trauma patients stratified by BMI categories.

Variables	Underweight n = 2011	Extreme obesity n = 162	Normal body weight n = 17,794	*p*
Sex				
Male, n (%)	897 (44.6)*	94 (58.0)	9191 (51.7)	<0.001
Female, n (%)	1114 (55.4)*	68 (42.0)	8603 (48.3)	
Age in years	55.0 ± 24.4	41.4 ± 16.3*	55.6 ± 19.7	<0.001
Comorbidities				
CVA, n (%)	101 (5.0)	5 (3.1)	752 (4.2)	0.186
HTN, n (%)	473 (23.5)*	68 (42.0)*	5031 (28.3)	<0.001
CAD, n (%)	82 (4.1)	5 (3.1)	713 (4.0)	0.826
CHF, n (%)	19 (0.9)	3 (1.9)	119 (0.7)	0.081
DM, n (%)	220 (10.9)*	39 (24.1)*	2759 (15.5)	<0.001
ESRD, n (%)	59 (2.9)	3 (1.9)	408 (2.3)	0.182
GCS, median (IQR)	15 (15–15)*	15 (15–15)	15 (15–15)	0.001
≤8	91 (4.5)	3 (1.9)	685 (3.8)	0.133
9–12	95 (4.7)*	5 (3.1)	573 (3.2)	0.002
13–15	1825 (90.8)*	154 (95.1)	16,536 (92.9)	0.001
ISS, median (IQR)	9 (4–12)*	4 (4–9)*	9 (4–10)	<0.001
<16	1585 (78.8)*	145 (89.5)*	14,626 (82.2)	<0.001
16–24	308 (15.3)*	13 (8.0)	2288 (12.9)	0.001
≥25	118 (5.9)	4 (2.5)	880 (4.9)	0.066

TABLE 1. Continued.

Variables	Underweight n = 2011	Extreme obesity n = 162	Normal body weight n = 17,794	*p*
Monocyte (counts)	539.7 ± 311.8	572.4 ± 309.1	542.5 ± 497.7	0.707
Neutrophil (counts)	8737.8 ± 4426.5	9244.7 ± 4876.7	8744.0 ± 4652.2	0.390
Lymphocyte (counts)	1654.7 ± 1038.2	1938.6 ± 1186.8*	1716.1 ± 1364.5	0.014
Platelet (counts/μL)	220,647.6 ± 69,077.2*	236,814.8 ± 87,821.1	224,660.1 ± 82,030.4	0.016
SII	1,689,537.7 ± 2,007,806.8	1,529,757.6 ± 1,344,388.4	1,614,782.9 ± 2,106,890.2	0.270
MLR	0.45 ± 0.51*	0.39 ± 0.29	0.41 ± 0.43	0.001
NLR	7.80 ± 9.60*	6.56 ± 5.32	7.24 ± 7.11	0.003
PLR	180.69 ± 168.94*	166.66 ± 143.42	169.99 ± 132.52	0.004
Hospital stay (d)	8.9 ± 9.5	10.7 ± 11.9*	8.7 ± 9.7	0.029
Mortality, n (%)	69 (3.4)*	1 (0.6)	354 (2.0)	<0.001

*BMI: Body mass index; CAD: coronary artery disease; CHF: congestive heart failure; CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; IQR: interquartile range; ISS: injury severity score; MLR: monocyte to lymphocyte ratio; NLR: neutrophil to lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index. The count of subtype cells and derived ratio are expressed by mean ± standard deviation. *Indicated significant differences in comparison with those in the normal body weight group.*

significantly among the BMI categories. Hypertension (HTN) was more prevalent in the extreme obesity group than in the underweight and normal weight groups (42.0% *vs.* 23.5% *vs.* 28.3%, $p < 0.001$). Similarly, diabetes mellitus (DM) showed the highest prevalence in the extreme obesity group, followed by the normal weight and underweight groups (24.1% *vs.* 15.5% *vs.* 10.9%, $p < 0.001$). Clinical scores also showed significant trends. The ISS was significantly lower in the extreme obesity group than in the normal weight and underweight groups (4 *vs.* 9 *vs.* 9, respectively; $p < 0.001$).

Inflammatory and blood parameters exhibited notable differences. Lymphocyte counts were higher in the extreme obesity group than in the underweight and normal weight groups (1938.6 *vs.* 1654.7 *vs.* 1716.1/μL, $p = 0.014$). Platelet counts were also higher in the extreme obesity group than in the underweight and normal weight groups (236,814.8 *vs.* 220,647.6 *vs.* 224,660.1/μL, $p = 0.016$). The underweight group exhibited elevated inflammatory markers than the extreme obesity and normal weight groups, with higher MLR (0.45 *vs.* 0.39 *vs.* 0.41, $p = 0.001$), NLR (7.80 *vs.* 6.56 *vs.* 7.24, $p = 0.003$), and PLR (180.69 *vs.* 166.66 *vs.* 169.99, $p = 0.004$). The length of hospital stay was longer in the extreme obesity group than in the normal weight groups (10.7 *vs.* 8.7 days, $p = 0.029$). Mortality rates were higher in the underweight group than in the normal weight and extreme obesity groups (3.4% *vs.* 2.0% *vs.* 0.6%, $p < 0.001$).

3.3 Propensity score matched comparison of outcomes between underweight and normal body weight groups

After matching for sex, age, comorbidities, and ISS, no significant differences were observed between the underweight and normal-weight groups (Table 2). Inflammatory markers, such as lymphocyte counts (1670.0 *vs.* 1713.4/μL, $p = 0.225$), platelet counts (223,688.6 *vs.* 226,416.8/μL, $p = 0.286$), SII (1,665,934.6 *vs.* 1,750,360.3, $p = 0.413$), MLR (0.30 *vs.* 0.29, $p = 0.356$), NLR (7.60 *vs.* 7.63, $p = 0.894$), and PLR (179.38 *vs.* 174.64, $p = 0.441$), showed no significant differences. The mortality rates were also comparable between the underweight and normal body weight groups (2.3% *vs.* 2.7%, $p = 0.436$). This indicates that after matching, the clinical characteristics and outcomes were not significantly different between the two groups.

3.4 Propensity score matched comparison of outcomes between extreme obesity and normal body weight groups

After matching for sex, age, comorbidities, and ISS, lymphocyte counts (1947.8 *vs.* 1741.0/μL, $p = 0.099$), platelet counts (237,392.4 *vs.* 230,025.3/μL, $p = 0.415$), SII (1,519,797.6 *vs.* 1,739,575.3, $p = 0.256$), MLR (0.24 *vs.* 0.29, $p = 0.359$), NLR (6.47 *vs.* 7.75, $p = 0.137$), and PLR (167.16 *vs.* 175.91, $p = 0.594$) showed no significant differences (Table 3). However, monocyte counts were significantly higher in the extreme obesity group than the normal body weight group (569.8 *vs.* 502.8/μL, $p = 0.032$). The mortality rates were also comparable between extreme obesity and normal body weight groups (0.6% *vs.* 1.3%, $p = 0.562$).

4. Discussion

This study investigated the impact of BMI extremes on the immune profiles and clinical outcomes of trauma patients, with a specific focus on white blood cell subtypes and derived inflammatory markers. Our findings revealed significant differences in patient demographics, comorbidities, immune markers, and clinical outcomes across the BMI categories. Specifically, the underweight group had a higher proportion of females than the normal weight group, while the extreme obesity group was the youngest among all categories. Underweight is more prevalent among women, driven by cultural, social, and behavioral factors such as societal pressures on body image and dietary

TABLE 2. Propensity score matched comparison between underweight and normal body weight trauma patients.

	Propensity Score matched cohort				
	Underweight n = 1653	Normal body weight n = 1653	OR (95% CI)	*p*	SD
Sex					
Male, n (%)	740 (44.8)	741 (44.8)	1.00 (0.87–1.14)	0.972	0.10%
Age in years	52.7 ± 24.2	52.6 ± 24.2	-	0.893	0.50%
Comorbidities					
CVA, n (%)	50 (3.0)	47 (2.8)	1.07 (0.71–1.60)	0.757	1.10%
HTN, n (%)	342 (20.7)	331 (20.0)	1.04 (0.88–1.23)	0.635	1.70%
CAD, n (%)	27 (1.6)	28 (1.7)	0.96 (0.57–1.64)	0.892	0.50%
CHF, n (%)	2 (0.1)	1 (0.1)	2.00 (0.18–22.09)	0.564	2.00%
DM, n (%)	129 (7.8)	132 (8.0)	0.98 (0.76–1.26)	0.847	0.70%
ESRD, n (%)	12 (0.7)	13 (0.8)	0.92 (0.42–2.03)	0.841	0.70%
ISS, median (IQR)	9 (4–9)	9 (4–9)	-	0.927	0.30%
Monocyte (counts)	539.8 ± 305.2	543.1 ± 295.0	-	0.757	-
Neutrophil (counts)	8717.2 ± 4390.6	8982.2 ± 4363.4	-	0.082	-
Lymphocyte (counts)	1670.0 ± 1043.5	1713.4 ± 1013.6	-	0.225	-
Platelet (counts/μL)	223,688.6 ± 69,311.4	226,416.8 ± 77,442.5	-	0.286	-
SII	1,665,934.6 ± 1,648,235.9	1,750,360.3 ± 3,857,413.2	-	0.413	-
MLR	0.30 ± 0.58	0.29 ± 0.56	-	0.356	-
NLR	7.60 ± 7.20	7.63 ± 8.87	-	0.894	-
PLR	179.38 ± 130.34	174.64 ± 212.91	-	0.441	-
Mortality, n (%)	38 (2.3)	45 (2.7)	0.84 (0.54–1.30)	0.436	-

CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; HTN: hypertension; ISS: injury severity score; MLR: monocyte to lymphocyte ratio; NLR: neutrophil to lymphocyte ratio; OR: odds ratio; PLR: platelet-to-lymphocyte ratio; SD: standardized difference; IQR: interquartile range; SII: systemic immune-inflammation index. The count of subtype cells and derived ratio are expressed by mean ± standard deviation.

TABLE 3. Propensity score matched comparison between extreme obesity and normal body weight trauma patients.

	Propensity Score matched cohort				
	Extreme obesity n = 158	Normal body weight n = 158	OR (95% CI)	*p*	SD
Sex					
Male, n (%)	91 (57.6)	91 (57.6)	1.00 (0.64–1.56)	1.000	0.00%
Age, years ± SD	41.4 ± 16.5	41.5 ± 16.4	-	0.943	0.81%
Comorbidities					
CVA, n (%)	4 (2.5)	4 (2.5)	1.00 (0.25–4.07)	1.000	0.00%
HTN, n (%)	64 (40.5)	64 (40.5)	1.00 (0.64–1.57)	1.000	0.00%
CAD, n (%)	3 (1.9)	3 (1.9)	1.00 (0.20–5.03)	1.000	0.00%
CHF, n (%)	-	-	-	-	-
DM, n (%)	37 (23.4)	37 (23.4)	1.00 (0.59–1.68)	1.000	0.00%
ESRD, n (%)	1 (0.6)	1 (0.6)	1.00 (0.06–16.13)	1.000	0.00%
ISS, median (IQR)	4 (4–9)	4 (4–9)	-	0.778	3.18%
Monocyte (counts)	569.8 ± 310.5	502.8 ± 236.3	-	0.032	-
Neutrophil (counts)	9154.4 ± 4836.2	8770.0 ± 4320.6	-	0.457	-

TABLE 3. Continued.

Propensity Score matched cohort					
	Extreme obesity n = 158	Normal body weight n = 158	OR (95% CI)	*p*	SD
Lymphocyte (counts)	1947.8 ± 1198.0	1741.0 ± 1019.7	-	0.099	-
Platelet (counts/μL)	237,392.4 ± 88,706.5	230,025.3 ± 70,634.8	-	0.415	-
SII	1,519,797.6 ± 1,351,127.0	1,739,575.3 ± 2,018,790.6	-	0.256	-
MLR	0.24 ± 0.46	0.29 ± 0.52	-	0.359	-
NLR	6.47 ± 5.27	7.75 ± 9.40	-	0.137	-
PLR	167.16 ± 145.03	175.91 ± 146.05	-	0.594	-
Mortality, n (%)	1 (0.6)	2 (1.3)	0.50 (0.05–5.54)	0.562	

CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; HTN: hypertension; ISS: injury severity score; MLR: monocyte to lymphocyte ratio; NLR: neutrophil to lymphocyte ratio; OR: odds ratio; PLR: platelet-to-lymphocyte ratio; SD: standardized difference; IQR: interquartile range; SII: systemic immune-inflammation index. The count of subtype cells and derived ratio are expressed by mean ± standard deviation.

habits. In a previous study, approximately 65% of women had a normal BMI and many underweight women perceived themselves as heavier, influenced by cultural ideals linking thinness to beauty and success, often resulting in unhealthy dieting practices [18]. It also suggests potential underlying factors that influence body composition and health, which may be rooted in hormonal differences, metabolic variations, or physiological mechanisms contributing to weight status [19]. Age characteristics presented another intriguing dimension, with the extreme obesity group being the youngest among all the BMI categories. This potentially indicates that early onset obesity trends may be linked to contemporary lifestyle factors, including changing dietary patterns, reduced physical activity, genetic predispositions, or broader socioeconomic and environmental influences that affect weight management from an earlier age [20].

Comorbidities, such as HTN and DM, were more prevalent in the extreme obesity group than those in the normal body weight group. This correlation is consistent with the established medical understanding that excessive body weight causes substantial physiological stress. The increased incidence of these chronic conditions in the extremely obese group reflects the complex metabolic challenges associated with significant weight gain, including increased insulin resistance, cardiovascular strain, and systemic inflammatory processes. The inflammatory state disrupts insulin signaling and endothelial function, thereby contributing to HTN, dyslipidemia, and vascular dysfunction [21, 22]. Conversely, underweight individuals were less likely to develop metabolic comorbidities, and may have malnutrition-related conditions, including frailty and immune dysfunction, which can adversely affect their recovery from trauma.

Regarding immune markers, lymphocyte counts were significantly higher in the extreme obesity group than in the normal weight group, indicating an altered immune response. Although T lymphocytes maintain metabolic balance through anti-inflammatory Th2 responses in the lean state, obesity shifts this to a pro-inflammatory Th1 profile, leading to increased tissue inflammation and metabolic dysfunction [23]. The underweight group showed elevated MLR, NLR, and PLR compared with the normal weight group. Malnutrition disrupts immune function by suppressing lymphocyte production, and protein-energy malnutrition specifically impairs T-cell dynamics [24] and adaptive immunity [22, 25]. This triggers compensatory increases in monocytes, neutrophils, and platelets, thereby altering immune composition and increasing vulnerability to infection. However, after propensity score matching, most inflammatory markers and clinical outcomes were similar across BMI categories, suggesting a complex relationship between body weight and immune response in trauma patients rather than a direct correlation.

A unique exception to this pattern was the significantly elevated monocyte count in the extreme obesity group. Monocytes play a critical role in the immune-inflammatory response, particularly in the chronic low-grade inflammation characteristic of obesity. In inflamed tissues, such as the adipose tissue and liver, monocytes differentiate into M1 macrophages that secrete pro-inflammatory cytokines like Tumor necrosis factor alpha (TNF-α), thereby driving systemic inflammation and insulin resistance through monocyte chemoattractant protein-1 mediated recruitment [23]. Chronic obesity-induced inflammation activates monocyte production and maintains elevated circulating monocyte levels without acute infection [26]. This elevated baseline inflammatory state explains the persistently high monocyte levels observed in the extremely obese group after matching. Obesity-associated adipose inflammation alters monocyte function by increasing the expression of Cluster of Differentiation 16 (CD16), C-C Chemokine Receptor Type 5 (CCR5), and TLR pathway genes, thereby promoting sustained inflammation [27]. Obesity promotes a feed-forward cycle of monocyte activation and inflammation via adipocyte-released mediators and microparticles that target the TLR and CCR5 pathways [28]. Sustained systemic inflammation affects metabolic functions and can potentially influence trauma recovery and inflammatory complications. These findings have significant clinical implications.

Regarding clinical outcomes, the extreme obesity group had the longest hospital stay, whereas the underweight group had the highest mortality rate. The extreme obesity group had the longest hospital stay, reflecting the greater burden of in-hospital complications and delayed recovery often observed in obesity patients. Factors, such as impaired wound healing, increased risk of infection, and challenges in providing care for larger body sizes, contribute to prolonged hospital stays. In contrast, the highest mortality rate was observed in the underweight group. This finding underscores the vulnerability of underweight patients, who are often malnourished and immunocompromised, making them less resilient to the physiological stress of trauma. These findings emphasize the importance of tailored clinical interventions to address the unique needs of trauma patients across BMI extremes, despite the lack of significant differences observed after matching.

The selected BMI thresholds—underweight (<18.5 kg/m^2) and extreme obesity (≥ 40 kg/m^2)—represent clinically significant extremes with distinct immunological and metabolic profiles, justifying their use in stratifying risk in trauma populations. For underweight patients, early identification and targeted nutritional support may enhance immune function, reduce susceptibility to infection, and improve overall outcomes. In patients with extreme obesity, increased monocyte counts indicate chronic inflammation, underscoring the importance of inflammation-modulating strategies and tailored perioperative care to reduce the risk of complications and prolong hospitalization. Incorporating BMI-based risk assessments into trauma protocols can support more accurate prognostication, early intervention, and resource allocation, thereby improving patient recovery across the weight spectrum.

Overall, despite the absence of significant differences in most immune markers and outcomes between BMI categories after matching, evaluating both malnutrition and obesity remains essential, as these conditions affect health, immune function, and recovery, requiring tailored interventions to optimize outcomes for patients at BMI extremes.

This study has several limitations. First, its retrospective design relies on pre-existing data from the trauma registry, which may be subject to inaccuracies, missing values, or variations in data entry practices over a 14-year period. Such inconsistencies may introduce an information bias. Selection bias was also a concern, as patients with incomplete laboratory data or missing BMI values were excluded, which may have limited the representativeness of the study population. Additionally, unmeasured confounding variables, such as nutritional status, physical activity levels, prior inflammatory conditions, and medication use (*e.g.*, corticosteroids or immunosuppressants), were not captured in the registry and may have affected the immune-inflammatory markers or clinical outcomes. Second, this study was conducted at a single institution, which may restrict the generalizability of the results to other populations with different patient demographics, injury patterns, and management protocols. Third, although propensity score matching was employed to control for confounding variables, unmeasured factors, such as nutritional status, physical activity, and inflammatory history, could still affect the observed outcomes. Fourth, this study focused solely on BMI extremes without accounting for the broader spectrum of overweight and moderate obesity, which may provide a more comprehensive understanding of the relationship between BMI and trauma outcomes. Finally, although inflammatory markers, such as NLR, MLR, PLR, and SII, were analyzed, these are surrogate measures that may not fully capture the complexity of the immune response in trauma patients. Future studies should use prospective multicenter designs, including detailed assessments of nutrition, physical activity, and inflammation, and expand to overweight and moderate obesity. Interventional studies on tailored nutritional and immunological therapies for extreme BMI may provide deeper insights into the effects of BMI on trauma outcomes.

5. Conclusions

This study demonstrated the distinct effects of BMI extremes on trauma outcomes before matching, with patients that are underweight showing higher mortality and inflammatory ratios, and patients with extreme obesity experiencing prolonged hospital stays and elevated monocyte counts. There were no significant differences in most immune markers and outcomes between BMI categories after matching. These findings highlight the need for tailored interventions and further studies to develop targeted strategies for vulnerable populations.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

CYH—Writing. KCL—Article drafting and funding. CHT—Data curation. WTS—Database maintainence. SYH—Statistical analysis. CHH—Study design. CHL—Supervision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Chang Gung Memorial Hospital Institutional Review Board (approval number 202401825B0). Requirement for informed consent was waived by the Chang Gung Memorial Ethics Committee.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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