Özgün Çalışma / Original Article

Ankara Eğt. Arş. Hast. Derg., 2026 ; 59(1) :
DOI: 10.20492/aeahtd.1721510

Myostatin and BDNF as potential biomarkers of sarcopenia in ICU patients: A radiologic and biochemical correlation study

Yoğun Bakım Hastalarında Sarkopeninin Potansiyel Biyobelirteçleri Olarak Miyostatin ve BDNF: Radyolojik ve Biyokimyasal Korelasyon Çalışması

Ender ERGÜDER1, Jafar Nouri NOJADEH 4,5, Erdem ÖZKAN3, Ceren ÜNAL7, Ahmet Orçun KÖROĞLU6, Muhammed APAYDIN8, Esra ERIŞ2, Gürkan DEĞIRMENCIOĞLU1, Şener BALAS1, Mehmet Eren YÜKSEL2

ABSTRACT

AIM: Myostatin (MSTN) and Brain-Derived Neurotrophic Factor (BDNF) are muscle-related biomarkers involved in muscle metabolism, but their roles in detecting sarcopenia in critically ill patients remain unclear. Sarcopenia is common in intensive care unit (ICU) patients and is associated with poor outcomes. This study aimed to investigate the relationship between serum myostatin and BDNF levels and muscle mass assessed by radiologic evaluation, along with inflammatory and clinical severity markers, to evaluate their potential as biomarkers of radiologically defined low muscle mass in ICU patients.

MATERIAL AND METHOD: This prospective study included 44 adult ICU patients at Ankara Etlik City Hospital who underwent abdominal computed tomography (CT) scans. Skeletal muscle mass was assessed at the lumbar (L3) vertebral level using CT-derived Skeletal Muscle Index (SMI). Serum myostatin and BDNF levels were measured via Enzyme-Linked Immunosorbent Assay (ELISA) from blood samples collected during routine ICU care. Clinical, biochemical, and radiologic data were analyzed to assess the relationship between these biomarkers and sarcopenia, defined by established SMI cut-off values.

RESULTS: Serum BDNF levels showed a strong positive correlation with myostatin ($\rho = 0.764$, $p < 0.001$), and moderate correlations with skeletal muscle index (SMI) ($\rho = 0.377$, $p = 0.012$), C-reactive protein (CRP) ($\rho = 0.302$, $p = 0.046$), and tumor necrosis factor alpha (TNF-alpha) ($\rho = 0.315$, $p = 0.037$). Myostatin levels were positively correlated with SMI ($\rho = 0.464$, $p = 0.002$) and TNF-alpha ($\rho = 0.407$, $p = 0.006$), suggesting their involvement in both muscle metabolism and systemic inflammatory responses.

CONCLUSION: This study reveals significant correlations between biochemical, radiologic, and muscle-related parameters in critically ill patients. Myostatin and BDNF show promising biomarkers associated with CT-defined low muscle mass in ICU patients, potentially guiding early intervention strategies. The observed interplay between neurotrophic and muscle-regulating factors, along with CT-based evidence of age-related muscle loss, offers valuable insights into the pathophysiology of ICU-acquired muscle wasting and may guide future therapeutic approaches.

Keywords: Sarcopenia, intensive care unit, BDNF, myostatin, skeletal muscle index

ÖZET

AMAÇ: Miyostatin ve Beyin Kaynaklı Nörotrofik Faktör (BKNF), kas metabolizmasında rol oynayan biyomoleküllerdir; ancak kritik hastalarda sarkopeni tespitindeki işlevleri hâlen belirsizdir. Sarkopeni, yoğun bakım ünitesindeki (YBÜ) hastalarda sık görülür ve kötü klinik sonuçlarla ilişkilidir. Bu çalışmanın amacı, serum miyostatin ve BKNF düzeyleri ile radyolojik olarak değerlendirilmiş kas kütlesi ve inflamatuar belirteçler arasındaki ilişkiyi inceleyerek, bu biyobelirteçlerin YBÜ hastalarında BT ile tanımlanan düşük kas kütlesi tespitindeki potansiyelini değerlendirmektir.

GEREÇ VE YÖNTEM: Prospektif olarak tasarlanan çalışmaya, rutin YBÜ bakımı sırasında abdomen bilgisayarlı tomografi (BT) görüntülemesi yapılan 44 yetişkin hasta dâhil edildi. L3 vertebra düzeyinde BT kaynaklı İskelet Kas İndeksi (İMİ) ile iskelet kas kütlesi ölçüldü. Serum miyostatin ve BKNF düzeyleri, rutin kan alımı sırasında elde edilen örneklerden ELISA yöntemi ile belirlendi. Klinik, biyokimyasal ve radyolojik veriler, belirlenmiş İMİ eşik değerlerine göre tanımlanan sarkopeniyle ilişkilendirilerek analiz edildi.

BULGULAR: Serum BKNF ile miyostatin düzeyleri arasında güçlü bir pozitif korelasyon saptandı ($\rho = 0,764$, $p < 0,001$). BKNF; İMİ ($\rho = 0,366$, $p = 0,012$), CRP ($\rho = 0,302$, $p = 0,046$) ve TNF-alfa ($\rho = 0,315$, $p = 0,037$) ile orta düzeyde korelasyon gösterdi. Miyostatin düzeyleri ise İMİ ($\rho = 0,464$, $p = 0,002$) ve TNF-alfa ($\rho = 0,407$, $p = 0,006$) ile pozitif korelasyon sergiledi; bu sonuçlar hem kas metabolizması hem de sistemik inflamatuar yanıt ile ilişkisini göstermektedir.

SONUÇ: Çalışmamız, yoğun bakım hastalarında biyokimyasal, radyolojik ve inflamatuar parametreler arasında anlamlı korelasyonlar ortaya koymaktadır. Miyostatin ve BKNF, YBÜ kaynaklı sarkopeniyi tespit etmek için umut vaat eden biyobelirteçler olarak görünmektedir ve erken müdahale stratejilerine rehberlik edebilir. Nörotrofik ve kas düzenleyici faktörler arasındaki etkileşim ile yaşa bağlı kas kaybının BT kanıtı, YBÜ hastalarında düşük kas kütlesi patofizyolojisine dair önemli öngörü sunmaktadır ve gelecekteki tedavi yaklaşımlarını yönlendirebilme potansiyeline sahiptir.

Anahtar Kelimeler: Sarkopeni, yoğun bakım ünitesi, BKNF, miyostatin, iskelet kas indeksi

1Ankara Etlik City Hospital, Department of Surgery, Ankara, Türkiye
2Ankara Etlik City Hospital, Surgical Intensive Care Unit, Ankara, Türkiye
3Kastamonu Training and Research Hospital, Department of Radiology, Kastamonu, Türkiye
4Ankara University Faculty of Medicine, Department of Medical Biochemistry, Ankara, Türkiye
5Ankara University Graduate School of Health Sciences, Ankara, Türkiye
6Ankara Etlik City Hospital, Department of Radiology, Ankara, Türkiye
7Hacettepe University, Department of Statistics, Ankara, Türkiye
8Görele State Hospital, Department of Surgery, Giresun, Türkiye

Makale geliş tarihi / submitted: Haziran / June 2025

Makale kabul tarihi / accepted: Nisan / April 2026

Sorumlu Yazar / Corresponding Author:
Mehmet Eren YÜKSEL
Address: Varlık mah., Halil Sezai Erkut cad., Ankara Etlik Şehir Hastanesi, Genel Hastane, 1. Kat Cerrahi Yoğun Bakım Ünitesi, Yenimahalle /Ankara
Phone: +90 542 561 0755
E-mail: doctormehmeteren@yahoo.com

Yazar bilgileri:
Ender ERGÜDER: endererguder93@gmail.com, 0000-0001-5289-3718
Jafar Nouri NOJADEH: jafarnouri70@yahoo.com, 0000-0002-2468-2996
Erdem ÖZKAN: erdemozkan5454@gmail.com, 0000-0001-8120-7051
Ceren ÜNAL: cerenunal91@gmail.com, 0000-0002-9357-1771
Ahmet Orçun KÖROĞLU: ahmetkoroglu1996@gmail.com, 0009-0009-7063-1231
Muhammed APAYDIN: muhammet2893@gmail.com, 0000-0002-8554-7632
Esra ERIŞ: e.kurtulgu@gmail.com, 0000-0002-7234-5521
Gürkan DEĞIRMENCIOĞLU: drgurkangc@gmail.com, 0000-0003-1016-7085
Şener BALAS: senerbalas@yahoo.com, ORCID: 0000-0002-9154-3179
Mehmet Eren YÜKSEL: doctormehmeteren@yahoo.com, ORCID:000-0002-7110-0717

INTRODUCTION

Sarcopenia, defined as the loss of skeletal muscle mass, is a common and serious condition in critically ill patients, particularly those in intensive care units (ICUs). It is closely linked to poor outcomes, including prolonged hospital stays, delayed recovery, and increased mortality (1). ICU-acquired weakness (ICUAW), often manifested as critical illness myopathy (CIM) and critical illness polyneuropathy (CIP), is seen in over 40% of ICU patients and is associated with significant muscle atrophy and dysfunction (2, 3). Studies have shown that severe muscle atrophy in ICU patients results in a loss of 4% muscle mass per day, contributing to long-term recovery challenges (4). Myostatin, a transforming growth factor-beta (TGF-β) superfamily member, is expressed primarily in skeletal muscle. It inhibits muscle differentiation and development by promoting protein degradation and limiting protein synthesis, which act as a negative regulator of muscle growth (4). These findings have raised the hope that inhibiting myostatin may be a therapeutic strategy for treating muscle wasting diseases (5). However, the relevance of myostatin in the daily management of ICU patients to existing and well-established scoring systems remains controversial. Notably, myostatin has been implicated in the pathophysiology of cachexia, a syndrome commonly associated with severe illness and characterized by both muscle and fat loss. Serum myostatin concentrations are significantly decreased in critically ill patients and are associated with disease severity, suggesting a complex role for this biomarker in critical illness (6). In addition, Brain-Derived Neurotrophic Factor (BDNF), a myokine produced in skeletal muscle in response to exercise and muscle contraction, has gained attention for its potential role in muscle metabolism (7). BDNF plays a critical role in skeletal muscle maintenance and regeneration by regulating adaptation, plasticity, and metabolic flexibility in response to exercise. It also promotes myosatellite cell (muscle stem cell) proliferation and differentiation, which are essential for muscle repair and function (8). Research in patients with heart failure has shown that serum BDNF levels are significantly correlated with muscle strength and exercise capacity; however, no significant association was found between BDNF levels and muscle mass in these patients (9). While higher BDNF levels are associated with improved muscle function, current evidence does not conclusively support a direct relationship between BDNF levels and increased skeletal muscle mass. Herein, we explore the correlation of serum myostatin and BDNF with CT-based SMI and inflammatory severity markers in ICU patients. Therefore, more research is needed to determine the potential of BDNF as a biomarker or therapeutic target to mitigate muscle wasting. There are limited studies on the role of BDNF and Myostatin in critically ill patients, particularly those experiencing sarcopenia. However, muscle wasting in ICU patients is a significant factor influencing clinical outcomes, including prolonged recovery, increased morbidity, and higher mortality risk (3). Thus, this study correlated myostatin and BDNF levels with several clinical and biochemical parameters related to muscle mass, inflammation, and disease severity in ICU patients to explore their potential as biomarkers of muscle wasting and their association with ICU outcomes.

MATERIAL AND METHOD

Study design and setting:

Prospective observational cohort at the Surgical ICU of Ankara Etlik City Hospital. Inclusion: ICU patients who underwent contrast-enhanced abdominal CT within routine care within 24–48 hours of ICU admission. Exclusion: No abdominal CT, non-analyzable CT, missing key clinical/biochemical data, pregnancy, or prior major neuromuscular disorders. The local ethics committee approved the study protocol (Approval number: AEŞH-BADEK - 2024-648), which was conducted under the tenets of the Declaration of Helsinki. Written informed consent was obtained from conscious patients, and first-degree family consent was obtained from unconscious patients.

Study Procedures and Laboratory Measurements

Demographic data (age, sex, comorbidities) were collected from the hospital information system. Patients' morbidity and mortality were assessed using the acute physiology and chronic health evaluation (APACHE) score and the expected mortality rate score, both of which were recorded as part of the study. Routine biochemical data collected during daily clinical monitoring were also recorded. Blood samples were collected from ICU patients as part of their daily routine. The index blood draw for myostatin/BDNF was synchronized with the index CT time window (same day/within 24h). After collection, an additional 4-5 mL of blood was collected for biochemical analysis for muscle biomarkers. The sample was processed by the study team within one hour and transported to the central biochemistry laboratory at Ankara University Faculty of Medicine for analysis. The samples were centrifuged at 3000 rpm for 5 minutes, and the resulting supernatant (serum) was stored at -80°C until the ELISA assays for myostatin and BDNF were performed. During routine clinical follow-up, abdominal CT scans were performed when clinically indicated. Skeletal muscles at the level of the third lumbar vertebra (including the rectus abdominis, lateral abdominal wall muscles, psoas major, quadratus lumborum, erector spinae, and multifidus muscles) were evaluated using a single axial image, all segmentations were performed by two radiologist. To delineate muscle structures, manual segmentation was performed using the software available on the radiology workstation (Advantage Workstation 4.7 Revolution, GE, USA). The density range relevant to muscle tissue, spanning from –29 to +150 Hounsfield Units (HU), was used. The cross-sectional area of muscles within this density range at the L3 level was measured in square centimeters (cm^2) and defined as the Skeletal Muscle Area (SMA). The SMA was normalized by dividing it by the square of the patient's height in meters, resulting in the Skeletal Muscle Index (SMI), expressed as cm^2/m^2. SMI was treated as a continuous variable and used as an indicator of total body muscle mass, based on previous studies demonstrating a linear correlation between total skeletal muscle area at the L3 level and whole-body muscle mass (19,20). The presence or absence of sarcopenia was determined according to previously established sex-specific SMI cut-off values reported in the literature (21). Low SMI was defined as < 38 cm^2/m^2 (men) and < 42 cm^2/m^2 (women)

Statistical analysis and sample size

Statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA). Normality was assessed for BDNF, MSTN, Vascular Endothelial Growth Factor (VEGF), TNF-alpha, SMI, and APACHE score variables. Given the total sample size of 44 patients (n < 50), the Shapiro-Wilk test was used to assess normality. Based on the results, the normality assumption was not met for BDNF, MSTN, TNF-alpha, and SMI, while normality was observed for VEGF and APACHE score. Pearson's correlation coefficient was used to analyze relationships for normally distributed variables, while Spearman's rank correlation coefficient was used for variables that did not meet normality (The heatmap was generated using RStudio Desktop (Posit PBC, Boston, MA, USA)). All correlations were two-tailed. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 44 patients were included in the study, of which 21 (47.7%) were male and 23 (52.3%) were female. The demographic characteristics, specifically the age distribution of the patients, are summarized in Table 1.

Table 1. Baseline demographics at ICU admission.

	Number (n)	Percentage (%)	Mean ± SD	Min-Max
Age (Female)	23	52.3 %	74.48±12.763	49-94
Age (Male)	21	47.7 %	63.38±16.922	38-92
Age (Total)	44	100 %	69.18±15.747	38-94

SD: Standard Deviation

Spearman's rank correlation analysis assessed the relationships between various clinical, biochemical, and imaging parameters in a cohort of 44 patients. The APACHE score, laboratory markers (urea, CRP, creatinine, lactate dehydrogenase (LDH), procalcitonin, sodium), radiologic muscle-related indices (SMA, SMI, and Skeletal Muscle Density (SMD)), and other variables (BDNF, MSTN, VEGF, TNF-alpha, age) were analyzed. Results are shown using correlation coefficients (rho) and p-values, with statistical significance established at $p < 0.05$ and $p < 0.01$. Notable Spearman's rho correlations are summarized and visualized in the heatmap shown in tables

Table 2: Significant Spearman's rho correlations.

Variable 1	Variable 2	Correlation Coefficient (rho)	p-value
Biomarker-muscle correlations			
BDNF	MSTN	0.764**	<0.001
BDNF	SMI	0.377*	0.012
SMI	MSTN	0.464**	0.002
SMA	SMI	0.888**	<0.001
Inflammation-related correlations			
APACHE score	Procalcitonin	0.334*	0.027
Urea	Creatinine	0.752**	<0.001
Procalcitonin	Urea	0.448**	0.003
Procalcitonin	CRP	0.527**	<0.001
Procalcitonin	Creatinine	0.558**	<0.001
CRP	BDNF	0.302*	0.046
Sodium	BDNF	-0.376*	0.012
MSTN	TNF-alpha	0.407**	0.006
BDNF	TNF-alpha	0.315*	0.037
TNF-alpha	SMI	0.324*	0.032
Age-related correlations			
SMA	Age	-0.300*	0.048
SMD	Age	-0.388**	0.009

**p < 0.05 (significant at the 0.05 level, two-tailed). **p < 0.01 (significant at the 0.01 level, two-tailed). N = sample size for each correlation. Only correlations with p < 0.05 are included for brevity and relevance. SMA: Skeletal Muscle Area; SMI: Skeletal Muscle Index; SMD: Skeletal Muscle Density. BDNF: Brain-Derived Neurotrophic Factor; MSTN: Myostatin; TNF-alpha: Tumour Necrosis Factor-alpha; CRP: C-reactive protein ; APACHE: acute physiology and chronic health evaluation.*

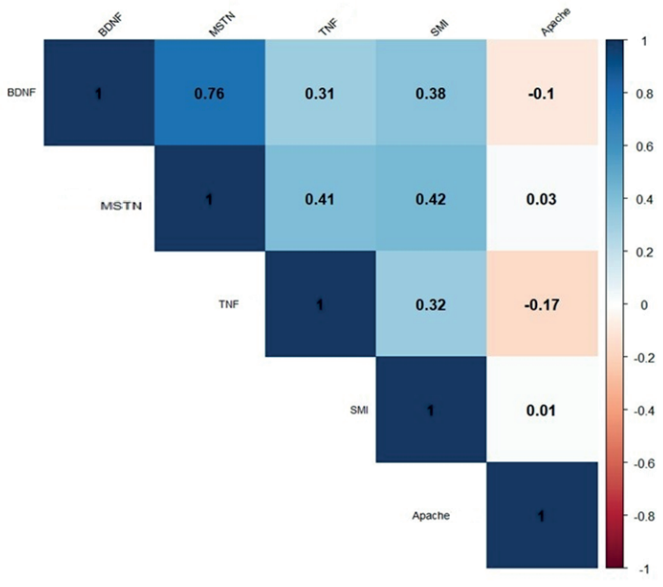

Figure 1. Heatmap of pairwise Spearman's correlation coefficients among key study variables. This heatmap illustrates the strength and direction of Spearman's rank correlations (rho) between serum BDNF, MSTN, TNF-alpha, SMI, and APACHE score. Each cell contains the correlation coefficient (rounded to two decimal places); coefficients reaching statistical significance ($p < 0.05$). The diverging color scale - ranging from deep blue (strong positive correlation, rho = +1) through white (no correlation, rho = 0) to deep red (strong negative correlation, rho = −1) - visually encodes the magnitude and direction of each relationship. Darker shades indicate stronger absolute correlations; sign is shown by axis labels/legend. *SMI: Skeletal Muscle Index; BDNF: Brain-Derived Neurotrophic Factor; MSTN: Myostatin; TNF-alpha: Tumour Necrosis Factor-alpha; APACHE: acute physiology and chronic health evaluation*

The APACHE score, a measure of disease severity, showed a statistically significant positive correlation with procalcitonin (ρ = 0.334, p = 0.027), suggesting that greater disease severity is associated with elevated procalcitonin levels, a known marker of systemic inflammation or infection (13). No additional biochemical or radiologic parameters showed significant correlation with the APACHE score at the 0.05 level, although a trend toward a positive association with urea (rho = 0.252, p = 0.103) and CRP (rho = 0.201, p = 0.19) was observed. Several strong and highly significant correlations were found among the laboratory markers. Urea and creatinine showed a strong positive correlation (rho = 0.752, p < 0.001). Procalcitonin showed positive correlations with urea (rho = 0.448, p = 0.003), CRP (rho = 0.527, p < 0.001) and creatinine (rho = 0.558, p < 0.001). CRP showed a positive correlation with BDNF (rho = 0.302, p = 0.046). Sodium showed a negative correlation with BDNF (rho = -0.376, p = 0.012), which warrants further investigation. SMD was negatively correlated with age (rho = -0.388, p = 0.009), suggesting a decline in muscle quality and quantity with age, with atrophied muscle tissue becoming richer in fat. SMI showed a significant positive correlation with MSTN (rho = 0.464, p = 0.002), suggesting an association between higher myostatin levels and greater skeletal muscle mass per unit area. SMA showed a significant negative correlation with age (rho = -0.300, p = 0.048), consistent with the age-related muscle loss known as sarcopenia.
BDNF showed a significant positive correlation with MSTN (rho = 0.764, p < 0.001), indicating a strong association between these two markers. A moderate positive correlation was also observed between BDNF and TNF-alpha (rho = 0.315, p = 0.037) and between BDNF and SMI (rho = 0.377, p = 0.012), suggesting that higher levels of BDNF are associated with greater muscle mass and inflammatory activity. However, no significant correlation was found between BDNF and VEGF (rho = -0.045, p = 0.770), nor between BDNF and APACHE score (rho = -0.100, p = 0.519). MSTN showed a significant positive correlation with TNF-alpha (rho = 0.407, p = 0.006) and with SMI (rho = 0.464, p = 0.002), indicating that higher myostatin levels are associated with increased inflammation and muscle mass. However, no significant relationship was observed between MSTN and VEGF (rho = -0.199, p = 0.195) or between MSTN and APACHE score (rho = 0.028, p = 0.856). A significant positive correlation was found between TNF-alpha and SMI (rho = 0.324, p = 0.032), reflecting that increased inflammation is associated with greater muscle mass. However, no significant correlations were found between TNF-alpha and VEGF (rho = -0.100, p = 0.518) or between TNF-alpha and APACHE score (rho = -0.166, p = 0.282).

DISCUSSION

The intensive care unit (ICU) presents a unique clinical environment marked by extended periods of immobility, systemic inflammation, and catabolic stress, all of which contribute to accelerated skeletal muscle wasting. This study, focused solely on ICU patients, utilized CT-derived skeletal muscle indices to quantify low muscle mass and characterized it biochemically through serum levels of myostatin and brain-derived neurotrophic factor (BDNF). According to European Working Group on Sarcopenia in Older People (EWGSOP2), sarcopenia is characterized primarily by low muscle strength, confirmed by low muscle quantity or quality, with physical performance indicating severity. In this study, we assessed radiologically defined low muscle mass (CT-derived SMI) rather than a full EWGSOP2 diagnosis (14). The results offer significant translational insights into the pathophysiology of low muscle mass and suggest the potential usefulness of these biomarkers in routine critical care evaluations especially in ICU. The observed relationships between myostatin, BDNF, and skeletal muscle index (SMI) highlight the importance of muscle-regulating and neurotrophic factors in the ICU setting. Although myostatin is traditionally recognized as a muscle growth inhibitor, its positive correlation with SMI in this group may indicate compensatory upregulation in patients with greater baseline muscle mass or those in the early stages of muscle catabolism. Myostatin plays a critical role in the regulation of skeletal muscle mass, influencing both embryonic development and pathophysiological adaptations, and its dysregulation contributes to muscle wasting in several diseases (15). Our results show a significant positive correlation between myostatin and TNF-alpha as well as between myostatin and SMI, suggesting that higher myostatin levels are associated with increased inflammation and musc-

le mass in critically ill patients. These results align with prior research demonstrating that myostatin overexpression has a role in muscle atrophy in several illness conditions, including chronic heart failure and chronic obstructive pulmonary disease (16, 17). The positive correlation between myostatin and SMI contradicts earlier findings indicating that myostatin predominantly functions as a negative regulator of muscle development (18). However, our results support the notion that higher myostatin levels are associated with greater muscle mass. This finding is consistent with the role of myostatin in regulating muscle mass, as evidenced by studies demonstrating increased muscle mass in myostatin knockout models (19). This hypothesis is consistent with previous research demonstrating reduced myostatin gene expression and plasma concentrations in critically ill patients with severe muscle wasting, suggesting a dynamic temporal regulation of myostatin during ICU stay. In addition, patients with ICU-acquired weakness (ICUAW) had lower myostatin gene expression than those without ICUAW, highlighting the complexity of myostatin regulation in critical illness (2). In addition, research in a sepsis model showed that myostatin deficiency prevented muscle wasting and improved survival, reinforcing the role of myostatin in muscle wasting during critical illness (20). These results suggest that myostatin regulation may depend on baseline muscle mass and the extent of muscle wasting, highlighting the need for further research into its potential as a therapeutic target in critically ill patients. BDNF also showed a significant positive correlation with myostatin, suggesting a strong interplay between these markers in critically ill patients. This association is intriguing because BDNF is traditionally recognized for its neuroprotective and myotrophic roles, promoting muscle regeneration and satellite cell activation (21), while MSTN is typically recognized as a negative regulator of muscle growth, inhibiting muscle cell proliferation and differentiation (18). As discussed above, the observed positive correlation between BDNF and MSTN may indicate a complex interplay between these factors in response to critical illness, possibly reflecting a compensatory mechanism to counteract muscle wasting. The positive MSTN–SMI correlation may reflect baseline mass–related regulation and/or early catabolic up-regulation; longitudinal sampling is required to resolve directionality. This is consistent with previous findings that both BDNF and MSTN are involved in muscle adaptation during pathological conditions (7), further supporting the idea of their dynamic regulation in critically ill patients. In addition, we observed a moderate positive correlation between BDNF and TNF-alpha, consistent with previous research identifying proBDNF as a myokine involved in inflammation following skeletal muscle injury (22), suggesting that elevated BDNF levels may be associated with increased inflammatory activity in critically ill patients. These findings align with prior evidence of BDNF's involvement in muscle repair and inflammation. BDNF may not only play a role in muscle maintenance and regeneration but also in modulating inflammatory responses in critically ill patients. The lack of significant correlation between BDNF and VEGF suggests that BDNF's role in critically ill patients may be more closely related to muscle physiology and inflammatory processes than to angiogenesis. This finding, alongside the observed interplay between BDNF, myostatin, and TNF-alpha, supports the hypothesis that these biomarkers reflect muscle-specific pathophysiological responses rather than overall disease severity, as neither was associated with the APACHE score. While myostatin is traditionally recognized as a negative regulator of muscle growth, its positive correlation with skeletal muscle index (SMI) in our cohort may indicate a compensatory upregulation in individuals with greater baseline muscle mass or during early catabolic states. Similarly, BDNF's association with both muscle regulation and inflammatory markers underscores its potential as a dual-function biomarker in critical illness. Notwithstanding prior links between these biomarkers and muscle biology, our study adds ICU-specific evidence by pairing serum BDNF/MSTN with CT-derived SMI in a critically ill cohort, a setting under-represented in the literature and directly relevant to risk stratification and early rehabilitation planning This study has several limitations. First, the relatively small sample size and single-center design may limit generalizability to broader ICU populations with diverse clinical profiles. Second, the cross-sectional design precludes causal inference regarding the observed associations between biochemical markers and CT-derived muscle indices. We did not assess muscle strength or physical performance; therefore, in line with EWGSOP2, we avoid diagnostic claims of sarcopenia and focus on radiologically defined low muscle mass. Biomarkers and SMI were captured at a single time point, which may not reflect their dynamic regulation over the course of critical illness; serial trajectories would better characterize temporal patterns. Moreover, potential confounders—such as differences in nutritional support, pharmacologic exposures (e.g., corticosteroids or neuromuscular blockers), pre-existing comorbidities, and duration of mechanical ventilation—were not systematically standardized, and could influence both muscle atrophy and biomarker concentrations. We also lacked validated bedside nutrition tools (e.g., NRS-2002, SGA, mid-arm circumference) and subcutaneous adipose tissue (SAT) metrics, which limits clinical granularity; accordingly, we frame our findings as biochemical–radiologic correlations rather than comprehensive sarcopenia phenotyping. Future multicenter, longitudinal studies with serial measurements are warranted to validate these findings and to define the temporal trajectory and prognostic significance of myostatin and BDNF in the ICU.

CONCLUSION

In conclusion, this study highlights significant associations between radiologic, biochemical, and clinical parameters in critically ill patients. Age-related declines in muscle quality were demonstrated through CT-based muscle metrics, while inflammatory markers such as procalcitonin and CRP correlated strongly with disease burden. Importantly, myostatin and BDNF emerged as promising biomarkers associated with CT-defined low muscle mass in ICU patients with potential applications in early detection, risk stratification, and personalized rehabilitation planning. Their combined use with imaging-based assessments could enhance current strategies for identifying and managing muscle loss in the ICU. Longitudinal studies are needed to confirm their prognostic value and therapeutic potential.

Yazar Katkıları

1.Ender Ergüder: Çalışma fikrinin oluşması, hasta sağlama, verilerin toplanması, kan örneklerinin taşınması, çalışmanın koordinasyonu, ana metnin yazılması
2.Jafer Nouri Nojadeh: Biyokimyasal analizlerin yapılması, ana metnin yazılması
3.Erdem Özkan: Radyolojik incelemelerin yapılması, ana metnin yazılması
4.Ceren Ünal: İstatistiksel analizlerin yapılması
5.Ahmet Orçun Köroğlu: Radyolojik incelemelerin yapılması
6.Muhammed Apaydın: Verilerin toplanması, kan örneklerinin taşınması
7.Esra Eriş: Hasta sağlanma, verilerin toplanması
8.Gürkan Değirmencioğlu: Hasta sağlama, metin düzenleme
9.Şener Balas: Hasta sağlama, metnin düzenlenmesi
10.Mehmet Eren Yüksel: Hasta sağlama, veri toplanması, çalışma fikrinin oluşması, metnin düzenlenmesi

REFERENCES

1.Mayer KP, Thompson Bastin ML, Montgomery-Yates AA, Pastva AM, Dupont-Versteegden EE, Parry SM, Morris PE. Acute skeletal muscle wasting and dysfunction predict physical disability at hospital discharge in patients with critical illness. Crit Care. 2020;24(1):637. doi:10.1186/s13054-020-03355-x
2.Grunow JJ, et al. Muscular myostatin gene expression and plasma concentrations are decreased in critically ill patients. Crit Care. 2022;26(1):237. doi:10.1186/s13054-022-04101-1
3.Schefold JC, et al. Muscular weakness and muscle wasting in the critically ill. J Cachexia Sarcopenia Muscle. 2020;11(6):1399–1412. doi:10.1002/jcsm.12624
4.Wollersheim T, et al. Dynamics of myosin degradation in intensive care unit-acquired weakness during severe critical illness. Intensive Care Med. 2014;40(4):528–538. doi:10.1007/s00134-014-3224-9
5.Pirruccello-Straub M, et al. Blocking extracellular activation of myostatin as a strategy for treating muscle wasting. Sci Rep. 2018;8(1):2292. doi: 10.1038/s41598-018-20524-9
6.Wirtz TH, et al. Low myostatin serum levels are associated with poor outcome in critically ill patients. Diagnostics (Basel). 2020;10(8):574. doi:10.3390/diagnostics10080574
7.Koito Y, et al. Serum brain-derived neurotrophic factor and myostatin levels are associated with skeletal muscle mass in kidney transplant recipients. Transplant Proc. 2021;53(6):1939-1944 doi:10.1016/j.transproceed.2021.04.021

8.Zhang J, et al. Localized release of muscle-generated BDNF regulates the initial formation of postsynaptic apparatus at neuromuscular synapses. Cell Death Differ. 2024;31(1):1–15. doi: 10.1038/s41418-024-01404-4
9.Nakano I, et al. Serum brain-derived neurotrophic factor levels are associated with skeletal muscle function but not with muscle mass in patients with heart failure. Int Heart J. 2020;61(1):96–102. doi: 10.1536/ihj.19-400
10.Ryan AM, Power DG, Daly L, Cushen SJ, Ní Bhuachalla Ē, Prado CM. Cancer-associated malnutrition, cachexia and sarcopenia: the skeleton in the hospital closet 40 years later. Proc Nutr Soc. 2016 May;75(2):199–211. doi: 10.1017/S002966511500419X
11.Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab. 2008 Oct;33(5):997–1006. doi:10.1139/H08-075
12.Ohashi K, Ishikawa T, Hoshii A, Hokari T, Noguchi H, Suzuki M, Yoshida T. Optimal skeletal muscle mass index cut-off values for presarcopenia evaluated by CT against dual-energy X-ray absorptiometry in patients with chronic liver disease. J Clin Med. 2021;10(7):1419. doi:10.3390/jcm1007141
13.Schuetz P, Christ-Crain M, Müller B. Procalcitonin and other biomarkers for assessment of disease severity and guidance of treatment in bacterial infections. Adv Sepsis. 2008;6(3):82–89.
14.Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber, C. C., Topinkova, E., Vandewoude, M., Visser, M., Zamboni, M., & Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2 (2019). Sarcopenia: revised European consensus on definition and diagnosis. Age and ageing, 48(1), 16–31. https://doi.org/10.1093/ageing/afy169
15.McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-β superfamily member. Nature. 1997;387(6628):83–90. doi:10.1038/387083a0
16.Hayot M, et al. Myostatin up-regulation is associated with the skeletal muscle response to hypoxic stimuli. Mol Cell Endocrinol. 2011;332(1-2):38–47. doi: 10.1016/j.mce.2010.09.008
17.George I, et al. Myostatin activation in patients with advanced heart failure and after mechanical unloading. Eur J Heart Fail. 2010;12(5):444–453. doi: 10.1093/eurjhf/hfq039
18.Thomas M, et al. Myostatin, a negative regulator of muscle growth, functions by inhibiting myoblast proliferation. J Biol Chem. 2000;275(51):40235–40243. doi: 10.1074/jbc.M004356200
19.Lee JH, Jun HS. Role of myokines in regulating skeletal muscle mass and function. Front Physiol. 2019;10:42. doi: 10.3389/fphys.2019.00042
20.Kobayashi M, et al. Myostatin deficiency not only prevents muscle wasting but also improves survival in septic mice. Am J Physiol Endocrinol Metab. 2021;320(1):E150–E159. doi: 10.1152/ajpendo.00161.2020
21.Brown AD, et al. Brain-derived neurotrophic factor drives muscle adaptation similar to aerobic training in mice. FASEB J. 2025;39(2):e70321. doi: 10.1096/fj.202402421R
22.Aby K, et al. ProBDNF as a myokine in skeletal muscle injury: role in inflammation and potential for therapeutic modulation of p75NTR. Int J Mol Sci. 2025;26(1):401. doi: 10.3390/ijms26010401