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FUNCTIONAL INDEPENDENCE AND MUSCLE STRENGTH IN ACUTE RESPIRATORY FAILURE WITH AND WITHOUT NON-INVASIVE MECHANICAL VENTILATORY SUPPORT

ORIGINAL ARTICLE

ABSTRACT

Purpose: Development of muscle weakness is common in the course of acute respiratory failure (ARF). This study aimed to compare muscle strength and physical function in subjects with ARF undergoing noninvasive mechanical ventilation (NIV) added to standard medical treatment (SMT) and SMT only in the intensive care unit.

Methods: Thirty-two subjects with ARF (19 NIV and 13 SMT) were included. Subject characteristics were recorded. Peripheral muscle strength was measured using the Medical Research Council Scale (MRC) and handgrip strength. Functional independence was evaluated using the Barthel Index (BI).

Results: In the NIV group, proximal muscle strength (shoulder abduction) was significantly lower than distal limb strength (wrist extension) (p=0.030). In both groups, proximal lower limb strength (hip flexion) was also significantly lower than distal limb strength (ankle dorsiflexion) (p=0.002). The BI total score was significantly lower in the NIV group than that of the SMT group (p=0.016). The BI score was significantly related to the MRC sum score (r=0.633) and handgrip strength (r=0.629, p<0.05).

Conclusion: Functional independence and proximal muscle strength compared to distal adversely affected in patients undergoing NIV for ARF. Weakness or functional limitations may prevent patients from functioning adequately in rehabilitation practices in intensive care.

Key Words: Intensive Care; Muscle Strength; Noninvasive Ventilation; Respiratory Failure.

NONİNVAZİV MEKANİK VENTİLASYON DESTEĞİ OLAN VE OLMAYAN AKUT SOLUNUM YETMEZLİĞİNDE FONKSİYONEL BAĞIMSIZLIK VE KAS KUVVETİ

ARAŞTIRMA MAKALESİ

ÖZ

Amaç: Akut solunum yetmezliği (ASY) sürecinde kas zayıflığı gelişimi sıktır. Bu çalışmanda yoğun bakımda ASY nedeni ile tek başına standart medikal tedavi (SMT) ve SMT'ye ek olarak noninvaziv mekanik ventilasyon (NIV) uygulanan olgularda kas kuvveti ve fonksiyonel bağımsızlığı karşılaştırılmak amaçlandı.

Yöntem: Çalışmaya ASY ile izlenen 32 olgu (19 NIV ve 13 SMT) dahil edildi. Olguların özellikleri kaydedildi. Periferal kas kuvveti için Medical Research Council Skalası (MRC) kullanıldı ve el kavrama kuvveti ölçüldü. Fonksiyonel bağımsızlık düzeyi Barthel İndeksi (Bİ) ile değerlendirildi.

Sonuçlar: NIV grubunda proksimal kas kuvveti (omuz abduktorleri) distal ekstremite kas kuvvetinden (el bileği ekstansorleri) anlamlı olarak daha düşüktü (p=0,030). Her iki grupta, proksimal alt ekstremite kas kuvveti (kalça fleksiyonu), distal ekstremite kas kuvveti (ayak bileği)'nden anlamlı olarak daha azdı (p=0,002). NIV grubunun Bİ toplam puanı SMT grubundan anlamlı olarak daha düşüktü (p=0,016). Bİ puanı, MRC toplam puanı (r=0,633) ve el kavrama kuvveti (r=0,629) ile ilişkiliydi (p<0,05).

Tartışma: ASY nedeni ile NIV uygulanan hastalarda fonksiyonel bağımsızlık ve distal kas kuvveti ile karşılaştırıldığında proksimal kas kuvveti olumsuz yönde etkilenmektedir. Yoğun bakımda rehabilitasyon uygulamalarında zayıflık veya fonksiyonel kısıtlılığın hastaların uygun fonksiyon görmesini engelleyebileceği göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Yoğun Bakım; Kas Kuvveti; Noninvaziv Ventilasyon; Solunum Yetmezliği.

INTRODUCTION

Muscle wasting and functional weakness are common after intensive care unit admission resulting from presenting illness, immobility, and treatments, including prolonged mechanical ventilation (1-2). Assessment of limb muscle strength is essential in subjects who are at risk of developing intensive care unit acquired weakness (3,4). Peripheral muscle weakness is associated with significant disability, mortality, and delayed rehabilitation (3,4).

Current practice in the intensive care unit has been changed to use less sedation, more physical activity, and mobilization. In acute respiratory failure, noninvasive mechanical ventilation (NIV) provides ventilatory support without a need for an invasive airway approach. The NIV has been shown to reduce mortality, need for intubation, and length of intensive care unit stay (5-7). The NIV has also been used to allow mobilization during the stay in the intensive care unit (8). It has been suggested that the NIV application might allow breathless subjects to exercise and prevent loss of muscle strength and function (9).

Although, the use of NIV is a common practice in the intensive care unit, to our knowledge, no previous study in the literature investigated whether muscle strength and physical function of subjects undergoing NIV were similar to less severe subjects receiving standard medical treatment (SMT). Therefore, the present study aimed to investigate muscle strength and functional capacity in subjects with acute respiratory failure undergoing NIV added to SMT compared to SMT alone. The secondary aim of the study was to investigate the association between peripheral muscle strength and functional independence in patients with acute respiratory failure.

METHODS

During two years (February 2009 and February 2011), we observed consecutive subjects with acute respiratory failure in a 9-bed adult medical intensive care unit of a university hospital. Hacettepe University Ethics Committee approved the study (Approval Date: 27.01.2009 and Approval Number: LUT 08/52-4). Subjects or relatives, as appropriate, gave informed consent to participate in this study. Intensive care subjects with acute respiratory failure (10), as judged by the attending physician, were included in this study. Exclusion criteria applied at intensive care unit admission were previous intubation before admission to intensive care unit, recruitment for invasive mechanical ventilation, previous neuromuscular weakness, stroke, postoperative status, pregnancy, injury preventing the evaluation of six muscle groups, inability to follow verbal instructions, and inability to provide informed consent. Hemodynamic instability (systolic blood pressure >200 mmHg and <80 mmHg, diastolic blood pressure >100 mmHg and <50 mmHg) was checked at the time of strength testing. Subjects' respiratory status (MV, oxygen therapy using a nasal cannula or venturi mask) was recorded from the nursing charts daily. The primary intensive care unit team provided the treatments. The attending physician took the decisions related to management. All subjects received SMT (antibiotics, bronchodilators, corticosteroids, mucolytics, theophylline, oxygen therapy with a nasal cannula, and venturi mask). The dose of corticosteroids was 20-40 mg/day. Subjects in the NIV group received noninvasive ventilatory support besides the SMT. Whether subjects received physiotherapy rehabilitation, applied by the primary physiotherapy team, in the intensive care unit, was recorded.

Patient characteristics, admission findings, chest radiography findings, and arterial blood gas tensions were recorded (10). Functional status before the development of acute respiratory failure was assessed using a 0-4 point category scale (0=working, 1=independent, 2=restricted, 3=housebound, 4=bed-or-chair bound). Lower scores were indicating a higher level of functional status (11). Illness severity and level of consciousness were evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) system and the Glasgow Coma Scale, respectively (10). The presence of delirium judged by psychiatric evaluation was recorded. Length of stay in the intensive care unit and duration of NIV were recorded.

Upper and lower extremity muscle strength was evaluated using the the Medical Research Council (MRC) scale. The range of MRC muscle test scores is 0 to 60 (six muscle groups, shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion, were examined on each side between 0 and 5 grade). A clinical diagnosis of intensive care-acquired weakness is made based upon a sum score of less than 48/60 (1,12). Handgrip strength was measured using a dynamometer (Baseline Standard Hydraulic Hand Dynamometer 90 kg, Baseline, USA) (13) upon subjects' clinical stability and obeying simple commands and when they were clinically stable, as judged by the attending physician, from clinical findings, hemodynamics, and arterial blood gases. A physiotherapist independent of clinical decisions for the subjects performed the measurements of strength and functional independence test.

Subjects' physical function and level of disability were assessed using the Barthel Index (14). Each item is rated on a 3-point scale (0=unable, 1=needs help, 2=independent). The final score is multiplied by five to get a number on a 100-point score. In Barthel Index, scores of 0-20 indicate "total" dependency, 21-60 indicate "severe" dependency, 61-90 indicate "moderate" dependency, and 91-99 indicate "slight" dependency. The Barthel Index was

Table 1: Characteristics of the Subjects.

Variables	NIV (n=19)	SMT (n=13)	p value
	Mean±SD	Mean±SD	
Age (years)	57.53±13.86	54.69±16.07	0.820
Gender (male/female), n	15/4	7/6	0.130
Height (cm)	169.58±6.17	165.23±7.80	0.140
Body Weight (kg)	76.79±17.11	77.61±19.82	0.850
Body Mass Index (kg/m^2)	25.46±6.29	28.70±8.54	0.430
Admission Findings			
Heart Rate (bpm)	102.53±19.71	106.08±24.39	0.880
Systolic Blood Pressure (mmHg)	122.21±28.72	125.23±32.15	0.650
Diastolic Blood Pressure (mmHg)	72.11±20.36	75.69±17.12	0.650
Respiratory Rate (bpm)	33.68±621.41	27.54±5.30	0.570
Blood Glucose (g/dL)	124.68±31.05	131.59±33.22	0.910
Albumin (g/dL)	3.28±0.56	3.67±7.68	0.075
Creatinine (mg/dL)	1.35±1.01	2.70±5.60	0.590
ALT (U/L)	84.75±158.89	99.87±258.16	0.320
APACHE II Score (0-71)	17.95±5.70	16.15±5.71	0.550
Acute Physiology Score	9.58±4.45	8.77±3.51	0.710
Glasgow Coma Scale (0-15)	14.58±1.02	15.00±00	0.470
Arterial Blood Gases			
pH	7.32±0.09	7.41±0.05	**0.011***
$PaCO_2$ (mmHg)	67.10±25.16	39.56±14.18	**0.002***
PaO_2 (mmHg)	52.67±15.14	60.81±25.36	0.570
Length of Stay in ICU (days)$^\phi$	7.91 (2.77-22)	5.01 (0.67-19.98)	**0.022***
Time for Evaluation (day) $^\phi$	5 (2-16)	2.5 (1-13)	**0.017***
MRC Sum Score (0-60)	55.68±3.67	57.85±3.00	0.180
Handgrip Strength (kg)	26.63±8.29	25.00±7.27	0.680
Barthel Index Total Score (0-100)	46.05±16.46	66.92±17.02	**0.016***

*p<0.05. $^\phi$Median (Min-Max). Mann Whitney-U test. NIV: Noninvasive Mechanical Ventilation, SMT: Standard Medical Treatment, ALT: Alanine Aminotransferase, APACHE II: Acute Physiology and Chronic Health Evaluation II, $PaCO_2$: Arterial Carbon Dioxide Pressure, PaO_2: Arterial Oxygen Partial Pressure, MRC: Medical Research Council, ICU: Intensive Care Unit.

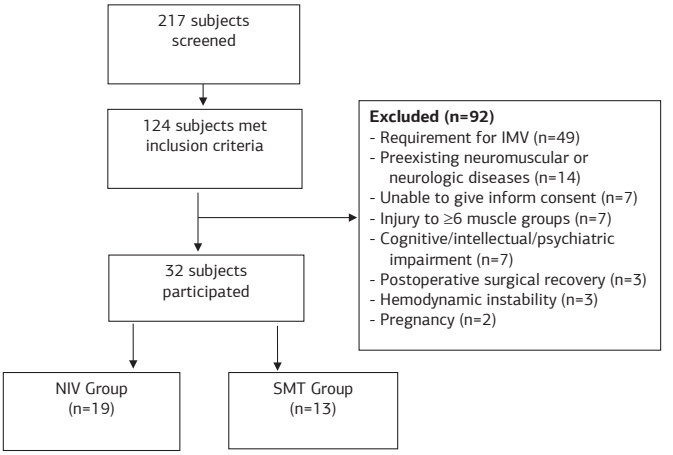

Figure 1: Flow Diagram of the Participants in the Study. (IMV: İntensive Mechanical Ventilations, NIV: Noninvasive Ventilation, SMT: Standard Medical Treatment).

applied on the same day as strength measurements.

Statistical Analysis

Statistical analysis was performed using SPSS 16.0 program (SPSS Inc, Chicago, IL, USA). Results were expressed as mean±standard deviation (mean±SD), median (mix-max) frequencies, and percentages. The normality of the data was checked using the Shapiro-Wilk test. Because of nonparametric test conditions, groups were compared using Mann Whitney u test and Chi-square test, as appropriate. Spearman rank correlation was used to analyze the relationship between the variables. Analyses were performed as a two-tailed, and the descriptive level of significance was set at $p<0.05$. According to the post hoc power analyses (G*Power, ver. 3.1, Heinrich Heine University Düsseldorf, Düsseldorf, Germany) based on the Barthel Index scores of two groups, the power of the study (1-β) was 90%.

RESULTS

Two hundred and seventeen subjects were screened during the study period. One hundred twenty-four subjects met the inclusion criteria, and 92 subjects were excluded (Figure 1). Thirty-two intensive care subjects with acute respiratory failure were included. Nineteen subjects were in the NIV group, and 13 subjects were in the SMT only group (served as controls). The NIV and SMT groups were similar in terms of age, gender, height, body weight, body mass index, and admission findings ($p>0.05$, Table 1), except arterial pH and arterial carbon dioxide

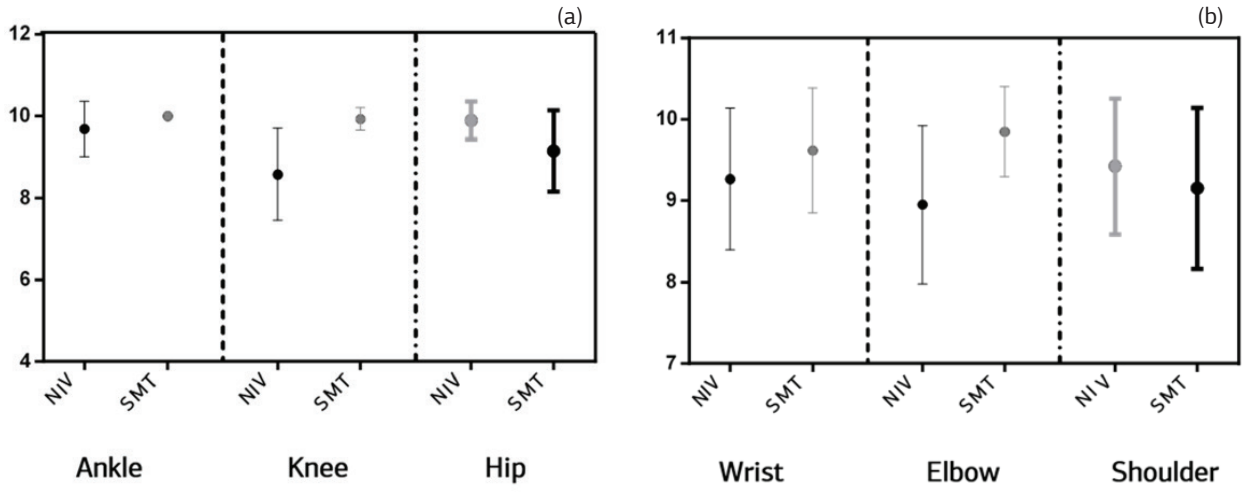

Figure 2: Strength Assessment by the Muscle Group. (a) Lower Extremity and (b) Upper Extremity in NIV and SMT Groups (NIV: Noninvasive Mechanical Ventilation, SMT: Standard Medical Treatment).

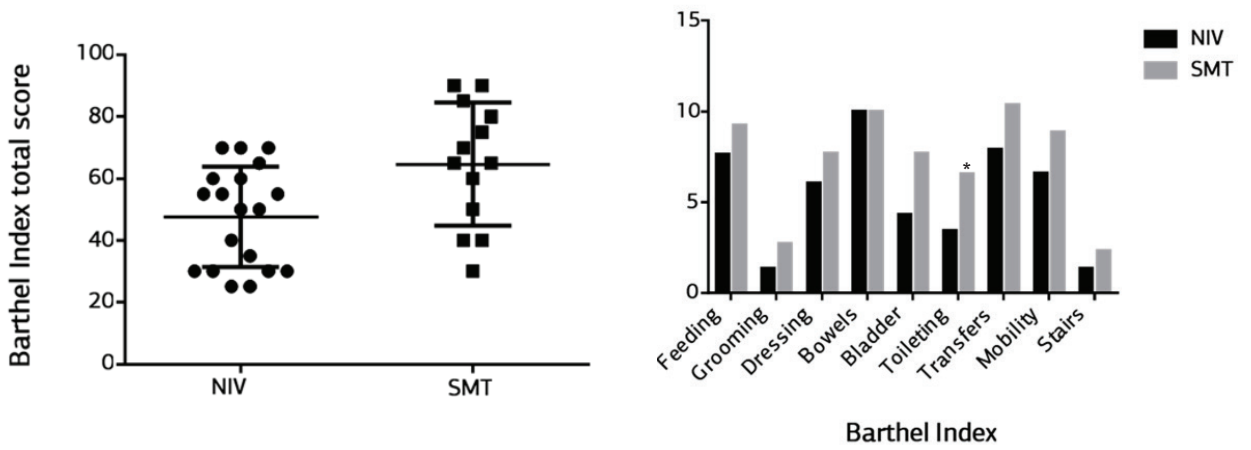

Figure 3: Distribution of Score of Barthel Index Total Score (a) and Individual Items (b) as well as the Barthel Index Total Score (b) in NIV and SMT Groups (p=0.016 for Barthel Index Total Score and *p=0.016 Toileting Score) (NIV: Noninvasive Mechanical Ventilation, SMT: Standard Medical Treatment).

pressure (p<0.05, Table 1). According to pre-admission functional capacity, 15.8% of patients were working, 31.6% of patients were independent, 26.3% of patients were restricted, 21.1% of patients were housebound, and 5.3% of patients were bed-or-chair bound in the NIV group. The 15.4% of patients were working, 23.1% of patients were independent, 46.2% of patients were restricted, and 15.4% of patients were housebound in the SMT group. There was no statistically significant difference in terms of pre-admission functional capacity between the groups (p=0,754). The 26.3% of patients had a type-I respiratory failure, and 73.7% of patients had type-II respiratory failure in the NIV group as admission diagnosis. In the SMT group, 61.5% of patients had a type-I respiratory failure, and 38.5% of patients had a type-II respiratory failure. No significant differences were found in the acute physiology score, APACHE II score, and Glasgow Coma Scale score between the two groups (p>0.05, Table 1). Drug therapy used was similar between the groups, and none of the subjects required sedation (p>0.05). One subject from NIV group had delirium (p=0.59). Ten subjects from the NIV group and six subjects from the SMT group received physiotherapy and rehabilitation during the intensive care unit stay (p>0.05, Table 1). In the NIV group, duration of ventilatory support was 2.66 (0.66-5.55) days, and pressure support (n=16) and pressure-controlled modes (n=3) were

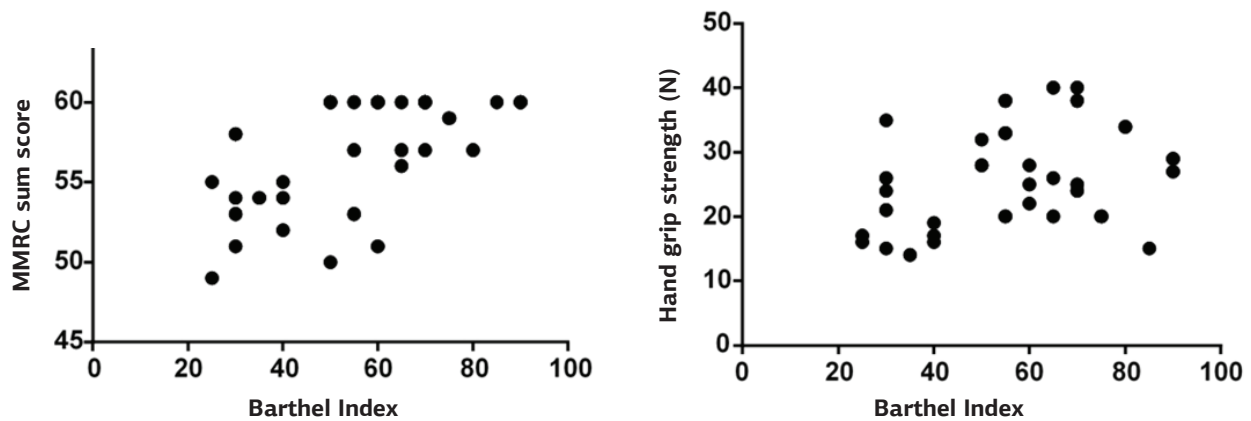

Figure 4: Relationship between the Barthel Index Total Score and (a) the MRC Scale Sum Score (r=0.633, p=0.004) and (b) Handgrip Strength (r=0.629, p=0.004) in NIV and SMT Groups (NIV: Noninvasive Mechanical Ventilation, SMT: Standard Medical Treatment).

used as ventilatory support.

Neither MRC scale sum score, upper and lower muscle strength, and handgrip strength nor MRC sum score and handgrip strength expressed relative to body weight were not significantly different between the two groups ($p>0.05$, Table 1). In the NIV group, proximal muscle strength (shoulder abduction) was significantly lower than distal limb strength (wrist extension) ($p=0.030$) and elbow flexion strength ($p=0.034$, Figure 2). In both NIV and SMT groups, proximal lower limb strength (hip flexion) was also significantly lower than distal limb strength (ankle dorsiflexion) ($p=0.002$, Figure 2).

Thirteen of NIV subjects and four of SMT subjects had a severe disability, and six of NIV and nine of SMT subjects had a moderate level of disability, based on the Barthel Index ($p<0.05$). The total Barthel Index score and toileting subscale score were significantly lower in the NIV group than those of the SMT group ($p<0.05$, Table 1, Figure 3).

The Barthel Index score was significantly related with MRC sum score ($r=0.633$, $p=0.004$, Figure 4), MRC upper extremity sum score ($r=0.597$, $p=0.007$) and lower extremity sum score ($r=0.584$, $p=0.009$), shoulder muscle strength ($r=0.681$, $p=0.001$) and hip muscle strength ($r=0.542$, $p=0.016$). Similarly, there was a significant relationship between Barthel Index score and dominant handgrip strength ($r=0.629$, $p=0.004$, Figure 4) and handgrip strength expressed relative to the body weight ($r=0.670$, $p=0.002$).

DISCUSSION

The main findings of the present study were that subjects undergoing NIV due to acute respiratory failure had lower proximal muscle strength and physical function as compared with the subjects receiving SMT only.

NIV is the first-line treatment for certain forms of acute respiratory failure in the intensive care. However, no previous study has investigated muscle strength in subjects undergoing NIV in the intensive care unit. In the current study, by measuring peripheral muscle strength using two different approaches, we found that subjects undergoing NIV had similar handgrip strength and MRC sum scores but had a lower proximal muscle group strenght both in the upper and lower extremities. Previously, a more reduction in proximal muscle strength compared with distal muscle strength has been observed (12). Underlying myopathic changes could affect mainly proximal regions of the limb (12,15). Despite having more severe acute respiratory failure, our subjects undergoing NIV did not develop severe total weakness. Application of NIV may allow functioning and might prevent muscle dysfunction in our subjects.

Acute illness, immobilization, mechanical ventilation, sedation, and corticosteroids are the parameters affecting functional capacity in the intensive care unit (16). The Barthel Index is relevant to assess functional status for subjects across their continuum of acute illness (4,17). Lower Barthel Index total score in the NIV group as compared with the SMT only indicated a different physical function in the intensive care unit. We found severe disability (<55 points) in 13 subjects and a moderate level of disability (55-90 points) in six subjects undergoing NIV plus SMT according to the Barthel Index. In contrast, the number of subjects having a severe and moderate level of disability in SMT only group was somewhat lower (four and nine subjects, respectively). These findings suggested that there were substantial differences between functional measurements, probably due to proximal muscle weakness. There is a lack of data linking muscle strength to objective measures of physical function in acute illness. We found that physical function measured using the Barthel Index scores was associated with global strength as well as proximal muscle strength. Determining muscle strength separately in upper and lower extremities and specific muscle groups using the MRC scale may help prognosticate a patient's ability to perform specific functional tasks (18). The ratio of muscle strength and muscle size (body mass) is known as a specific force and considered to be an expression of muscle quality (18). In our study, physical function was associated with the specific force determined using handgrip strength, and MRC sum score. Subjects with mild or no weakness, could still have either weakness relative to their baseline or limited function due to impairments in associated elements of neuromuscular control (19). Determination of factors affecting physical function and effects

application of an early individual activity training needs further investigation.

There are some limitations to our study. We used volitional tests to measure muscle strength, and this approach may affect the obtained results. However, these tests are frequently used in intensive care unit studies (1,11,18). In volitional tests, determination of the force generated by an isolated muscle group using electrical or magnetic neuromuscular twitch stimulation, are challenging to perform in an intensive care unit setting (expenses, time investment, and requirement of expert knowledge), and therefore have limited widespread clinical applicability (3,20). Secondly, the timing of strength and functional capacity assessments in NIV and SMT groups occurred within three and two days, respectively, which could create a difference in physical function between the groups, but it reflects transparent reporting practice. Third, there were more males in the NIV group, which was due to a higher number of chronic obstructive pulmonary disease subjects in this group that is a primary indication for the use of NIV in acute respiratory failure. In addition, the inclusion of subjects with respiratory failure from multiple causes of a variety of etiologies may have resulted in varying levels of functional capacity before illness (10) that may have an impact on the results, particularly if at a chronic level. However, there was no significant difference in pre-admission functional status at admission across the groups. Besides, this could reflect common practice in the acute care setting. The studies performed in the intensive care unit include subjects with diverse etiological factors and drive similar physiological derangements, which could be quantified in physiological scoring systems and used within variable success to predict intensive care outcomes. In addition, muscle biopsies from critically ill subjects demonstrate histopathological similarities across different disease groups (20).

In conclusion, subjects undergoing NIV due to acute respiratory failure have proximal muscle weakness and impaired physical function. The use of the Barthel Index could determine the functional loss in intensive care subjects. Either weakness or limited function due to impairments in associated elements of neuromuscular control may prevent subjects from functioning more efficiently in rehabilitation practices in intensive care. Further study is needed to clarify the mechanism of muscle dysfunction and functional independence in the intensive care.

Sources of Support: None.

Conflict of Interest: The authors have no conflicts of interest to declare.

Ethical Approval: Hacettepe University Ethics Committee approved the study (Approval Date: 27.01.2009 and Approval Number: LUT 08/52-4).

Peer-Review: Externally peer-reviewed.

Author Contributions: Concept - SC, Dİİ, AT; Design – SC, Dİİ, NVY, ECK; Supervision – Dİİ, AT, SS, HA; Resources and Financial Support–Dİİ, AT; Materials- SC, Dİİ; Data Collection and/or Processing - SC, NVY, MS, ECK, MBG; Analysis and/or Interpretation – SC, Dİİ, SS; Literature Research – SC, NVY, MS, ECK, MBG; Writing Manuscript - SC, Dİİ, NVY, MS, ECK; Critical Review - Dİİ, AT, SS, HA.

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