

## Trunk Flexor and Extensor Muscle Strength Capacity in Healthy Individuals

### Sağlıklı Bireylerde Gövde Fleksör ve Ekstansör Kas Kuvveti Kapasitesi

Fatma Unver<sup>1</sup>, Elif Gur Kabul<sup>2</sup>, Meryem Buke<sup>3</sup>, Bayram Unver<sup>4</sup>

<sup>1</sup>Faculty of Physiotherapy and Rehabilitation, Pamukkale University, Denizli, Türkiye

<sup>2</sup>Physiotherapy and Rehabilitation, Faculty of Health Sciences, Uşak University, Uşak, Türkiye

<sup>3</sup>Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Van Yuzuncu Yıl University, Türkiye

<sup>4</sup>Faculty of Physical Therapy and Rehabilitation, Dokuz Eylül University, İzmir, Türkiye

#### ABSTRACT

**Objective:** Generating reference values of trunk muscle strength is of value for specific age groups and gender in every society. The aim of this study was to define flexor and extensor muscle strength of the trunk and the flexion/extension ratio in healthy individuals.

**Materials and Methods:** Hundred and two healthy individuals were included in this study. Isokinetic concentric strength of trunk flexor (Flex) and extensor (Ext) muscles of the participants were measured via an isokinetic dynamometer. Tests were performed at speeds of 60°/s and 180°/s. Maximum strength was characterized with peak torque (PT) (Flex<sub>abs</sub>, Ext<sub>abs</sub>; N·m), peak torque normalized to body weight (PTNBW) (Flex<sub>norm</sub>, Ext<sub>norm</sub>; N·m·kg<sub>bw</sub><sup>-1</sup>), and Flex<sub>abs</sub>/Ext<sub>abs</sub> ratio.

**Results:** For angular velocity of 60°/s, PT and PTNBW of flex and ext strength were higher in men; while for angular velocity of 180°/s, PTNBW of flex and ext strength were higher in women (p<0.05). Extensor strength for 60°/s and 180°/s angular velocities yielded lower values than flexor strength in both genders. The Flex<sub>abs</sub>/Ext<sub>abs</sub> ratios were 1.67±0.62 for 60°/s and 4.93±4.60 for 180°/s.

**Conclusion:** Trunk extensor strength was higher than flexor strength in men and women at 60°/s and 180°/s angular velocities. In this study, the ratio of Flex<sub>abs</sub>/Ext<sub>abs</sub> was not within the accepted range in non-active adults and there was no difference between men and women, indicating that muscle strength is not sufficient in this population. The data of this study can be used as a comparison parameter in future studies to get normative data, or common values in healthy individuals aged 18-30.

**Keywords:** Strength, gender, measurement

#### ÖZ

**Amaç:** Gövde kas kuvvetinin referans değerlerinin oluşturulması her toplumda belirli yaş grupları ve her iki cins için önemlidir. Bu çalışmanın amacı sağlıklı bireylerde gövdenin fleksör ve ekstansör kas kuvveti ile fleksiyon/ekstansiyon oranının tanımlanmasıdır.

**Gereç ve Yöntem:** Çalışmaya 102 sağlıklı birey alındı. Katılımcıların gövde fleksör (Flex) ve ekstansör (Ext) kaslarının izometrik konsantrik kuvveti izometrik dinamometre ile ölçüldü. Testler 60°/s ve 180°/s hızla gerçekleştirildi. Maksimum güç, zirve torku (PT) (Flex<sub>abs</sub>, Ext<sub>abs</sub>; N·m), vücut ağırlığına göre normalize edilmiş tepe torku (PTNBW) (Flex<sub>norm</sub>, Ext<sub>norm</sub>; N·m·kg<sub>bw</sub><sup>-1</sup>) ve Flex<sub>abs</sub>/Ext<sub>abs</sub> oranıyla karakterize edildi.

**Bulgular:** Erkeklerde 60°/s'lik açısal hız için fleksiyon ve ekstansiyon kuvvetinin PT ve PTNBW'si daha yüksek iken; 180°/s açısal hızda ise fleksiyon ve ekstansiyon kuvvetinin PTNBW'si kadınlarda daha yüksekti (p<0.05). Hem 60°/s hem de 180°/s açısal hız için ekstansör kuvvet, her iki cinsiyette de fleksör kuvvetten daha düşüktü. Flex<sub>abs</sub>/Ext<sub>abs</sub> oranları 60°/s için 1.67±0.62 ve 180°/s için 4.93±4.60 idi.

**Sonuç:** Erkek ve kadınlarda gövde ekstansör kuvvetinin 60°/s ve 180°/s açısal hızlarda fleksör kuvvetinden daha yüksek olduğu gözlemlendi. Bu çalışmada, Flex<sub>abs</sub>/Ext<sub>abs</sub> oranları aktif olmayan yetişkinlerde kabul edilen aralıkta değildi ve kadın ve erkekler arasında fark yoktu. Bu bulgu bu popülasyonda kas gücünün yeterli olmadığını göstermektedir. Bu çalışmanın verileri, 18-30 yaş arası sağlıklı bireylerde normatif veriler veya ortak değerler elde etmek amacıyla gelecekteki çalışmalarda karşılaştırma parametresi olarak kullanılabilir.

**Anahtar Sözcükler:** Kuvvet, cinsiyet, ölçüm

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Correspondence / Yazışma: Elif Gur Kabul · Uşak Üniversitesi Fizik Tedavi ve Rehabilitasyon Fakültesi, Uşak, Türkiye · elifgur1988@hotmail.com

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## INTRODUCTION

Isokinetic measurements have been thought to be the 'gold standard' for evaluation of muscle strength (1). Isokinetic assessment is used to measure the torque levels of different joints of the body, and typically contain the comparison of the agonist to antagonist ratio, and contralateral joint of the associated joint. Increased asymmetry amongst both sides may increase the risk of potential injury (2,3).

The interpretation of the normal values of flexor and extensor muscles of the trunk is considerably complex and difficult, because it is not possible to compare with the 'contralateral' side for the trunk, as for the extremities. For this reason, it is important to generate a series of reference values for the muscle strength of the trunk specific for age groups and each gender in any society. On the basis of these values, it will become possible to correlate a patient's muscle strength to a disability, and possible rehabilitation degree (4). Muscle strength plays a decisive role in deciding which of the low, moderate or high intensity exercises will be included in a program (5).

The identification of flexion and extension muscle strength of the trunk, and loss of strength at the Flexor/Extensor ratio (Flex/Ext ratio) is a valid method for evaluation of rehabilitation interventions or precautions (6). Especially, the weakness in extensor muscles, and the unbalance of extensor and flexor muscle strength it causes might predispose to chronic low back pain (7-9). The relationship between lower back pain and the weakness of lower back extensor and flexor muscles has been documented in some studies (10-14). The gold standard measuring equipment for objective muscle strength assessment is the isokinetic dynamometer. However, there are limited studies evaluating trunk strength with isokinetic measurements (15).

In the literature, various isokinetic dynamometer devices with different protocols were used in the isokinetic and isometric analysis of trunk muscles. In these studies, norm values were obtained through data on isokinetic muscle strength, and Flex/Ext ratio of trunk flexion and extension in the 10-150°/s angular speed range in healthy and in people with low back pain (10,12,13,16-23). However, there was only one study encountered using the 180°/s angular speed in sedentary individuals for the 18-30 age range (24). The test speed used in evaluating the isokinetic torque curve is important in diagnostic assessments. It is reported that choosing high velocities (180°-300°/s) as test speed is more reliable to reduce the load on the joint, when comparing to low velocity (25). Therefore, the use of high velocity is important in the evaluation of isokinetic muscle strength.

Young adulthood (ages 18-30) represents a transition period between adolescence and adulthood. During this period,

new skills are tried to be acquired, and interventions are very important to encourage positive orientations. Recognizing the deficiencies and taking action against them may affect behavioral changes. Muscle strength has an important place among health-related parameters in this period (26,27).

Normative parameters of various populations are needed in order to perform trunk muscle strength evaluations of individuals. There is a lack of normative data for trunk flexor and extensor muscles strength in the Turkish literature. In particular, trunk muscles' data on asymptomatic sedentary individuals is valuable in preventing problems that cause significant economic costs, such as low back pain. Besides, trunk muscles play serious roles in daily activities (28). Limited data prevents accurate assessment of trunk muscle strength, practical applications in general, and particularly during clinical rehabilitation and scientific research applications. Trunk muscle strength measurements are generally made concentrically (29-31).

In this study, we aim to analyze the maximum concentric isokinetic trunk flexion and trunk extension muscle strength capacity, and Flex/Ext ratio at 60°/s and 180°/s angular velocity in healthy individuals between 18-30 years old.

## MATERIAL and METHODS

### *Experimental approach*

A cross-sectional study design was used to evaluate trunk strength capacity in healthy individuals of each gender. Concentric muscle strengths of the individuals who were recruited were measured with an isokinetic dynamometer. Maximum strength was characterized with absolute maximum peak torque (Flex<sub>abs</sub>, Ext<sub>abs</sub>; N·m), peak torque normalized to body weight (Flex<sub>norm</sub>, Ext<sub>norm</sub>; N·m·kg<sub>bw</sub><sup>-1</sup>), and Flex<sub>abs</sub>/Ext<sub>abs</sub> ratio.

### *Participants*

Hundred and two healthy individuals (61 women and 41 men, mean age: 22.5±1.8 yrs) voluntarily participated in this study. Figure 1 displays a flow chart of the study design. Physical data is represented in Table 1.

Inclusion criteria for participation in the study were: (a) to volunteer to participate; (b) to be in the 18-30 age range. Exclusion criteria were: (a) having any surgical operation in the last six months; (b) being pregnant; (c) having any neurologic, cardiorespiratory, musculoskeletal or/and rheumatological disease; (d) regularly exercising within the last six months; (e) having idiopathic, congenital, developmental or neuromuscular spinal abnormalities; (f) a history

of severe back pain within the previous three months; (g) having received physical therapy, acupuncture or back strength training in the last six months. Withdrawal criteria from the study were: (a) not being able to complete all the tests; (b) individuals with missing or incomplete data.

**Table 1.** Characteristics of the study participants

Parameter	Women (n=61)	Men (n=41)	All (n=102)	p*
Age (yrs)	22.7±1.8 23 (19/28)	22.3±1.7 23 (19/26)	22.5±1.8 23 (19/28)	0.284
Height (cm)	163.2±5.4 163 (155/175)	175.5±5.6 174 (167/191)	168.1±8.2 168 (155/191)	0.001
Body weight (kg)	57.6±7.8 57 (43/80)	72.6±8.6 75 (53/91)	63.7±10.9 60 (43/91)	0.001
BMI (kg/m <sup>2</sup> )	21.6±2.6 21.2 (16.8/29.0)	23.6±2.8 24.2 (18.0/30.5)	22.4±2.9 22.0 (16.8/30.5)	0.001

As mean ± SD median (min/max); BMI: body mass index; \*: Mann-Whitney U test

The ethical permission of the study was obtained from Pamukkale University Noninvasive Clinical Research Ethical Board (60116787-020/8334). All the participants were informed verbally, and informed consent forms were signed.

### Procedure

Performance tests of the study were done in the company of two physiotherapists. No complaints (muscle spasm and/or pain and discomfort in the joints that make them feel unsafe, or/and dizziness, which may cause difficulty standing or walking) were reported by the participants during the study. All the participants completed the tests.

A form had been given to all participants before the study was started. Physical information and the status of surgery/injury within the last six months were filled in this form. After a 5 min warmup period at of 60-70 cycle/min in bicycle ergometer (Monark 818 Ergomedic), all participants performed static stretching exercises aiming the trunk flexor and extensor muscles for 20 s with five repetitions. Participants were fixed to the dynamometer at the lower leg and knee, and also were girded with two rigid belts from the thigh and upper trunk (Figure 2).

Dynamometer positioning was adjusted separately for each participant. After the height-weight values of the participants were entered into the system, measurements were taken. The anterior superior iliac spine was aligned with the dynamometer's mechanical axis. Since participants had no prior experience on isokinetic trunk tests; trunk strength measurement protocols were started with training trials as three repetitions for 60°/s velocity and five repetitions for 180°/s velocity, (isokinetic trunk flexion and extension), similar to the test to be applied. Then, concentric trunk flexor and extensor muscle strengths of the participants were measured by isokinetic dynamometry (Cybex, Humac Norm

Testing Rehabilitation System, CSMI Medical Solutions, USA).

Tests were performed as five repetitions at 60°/s velocity and 10 repetitions at 180°/s velocity for each direction. A 1 min rest interval was given in-between sets (32). Trunk flexion and extension muscles' strengths were recorded for both angular velocities. Maximum strength was characterized with absolute maximum peak torque (Flex<sub>abs</sub>, Ext<sub>abs</sub>; N·m), peak torque normalized to body weight (Flex<sub>norm</sub>, Ext<sub>norm</sub>; N·m·kg<sub>bw</sub><sup>-1</sup>) values, and Flex<sub>abs</sub>/Ext<sub>abs</sub> ratios. Verbal encouragements were done during performances to get the maximum strength of participants. The reliability of this measurement procedure was earlier analyzed in adults and reported as good (for 60°/s velocity, intraclass correlation coefficient (ICC) of trunk flexion was 0.89 and that of trunk extension was 0.86) (6).

### Statistical analyses

The GPower V3.1.9.6 (University of Kiel, Kiel, Germany) was used to determine the appropriate sample size. Depending on the concentric Flex<sub>abs</sub>/Ext<sub>abs</sub> ratio parameter -when the average expected value in the men group was 81.4 (with a standard deviation of 12.1) and the average expected value in the women group was 92.7 (with a standard deviation of 23.3)- based on the study results of Bernardelli et al (33), it was found that 40 of the individuals for each group must have been enrolled to have 85% power with 5% type 1 error level (d=0.609). The data were analyzed using IBM SPSS Statistics v22 software. Continuous variables were stated as mean (standard deviation) and median (minimum/maximum) values. The Mann-Whitney U-test was used to compare independent group differences, and the Wilcoxon paired-sample test was used to compare dependent group differences. Statistical significance was accepted as p<0.05.

## RESULTS

While the absolute maximum peak torque of all the participants at 60°/s angular velocity was 144.1±70.9 N·m for Flex<sub>abs</sub>, and 95.9±61.7 N·m for Ext<sub>abs</sub>; at 180°/s angular velocity, it was 71.6±40.0 N·m for Flex<sub>abs</sub>, and 21.3±13.2 N·m for Ext<sub>abs</sub> (Table 2). Flex<sub>norm</sub>, Ext<sub>norm</sub> and mean for gender are presented in Table 2.

### Absolute maximum peak torque and peak torque normalized to body weight

When concentric strength of the trunk flexion and extension was compared with regard to gender, while the absolute maximum peak torque (p=0.001) and peak torque normalized to body weight values (p=0.001) of men were statisti-

cally higher than those of women for 60°/s angular velocity; peak torque normalized to body weight values (p=0.014 and p=0.005, respectively) of women were statistically higher (p<0.05) than those of men for 180°/s angular velocity. When men and women were evaluated in their

own gender, trunk extensor strengths were lower than trunk flexor strengths in men and women at 60°/s (p=0.001) and 180°/s (p=0.001) angular velocities (Table 2).

**Table 2.** Results for absolute and normalized peak torque in trunk extension/flexion for 60°/s and 180°/s angular velocity

Group	Flexion absolute Flex <sub>abs</sub> , (N·m)	Extension absolute Ext <sub>abs</sub> , (N·m)	p**	Flexion normalized Flex <sub>norm</sub> , (N·m·kg <sub>bw</sub> <sup>-1</sup> )	Extension normalized Ext <sub>norm</sub> , (N·m·kg <sub>bw</sub> <sup>-1</sup> )	p**
<b>60°/s All participants</b>	144.1±70.9 125 (35/287)	95.9±61.7 76.5 (23/334)		2.18±0.83 2.08 (0.55/3.86)	1.45±0.78 1.26 (0.40/4.40)	
<b>Women</b>	97.3±38.7 94 (35/264)	62.7±27.8 57 (23/182)	<b>0.001</b>	1.68±0.57 1.60 (0.55/3.52)	1.09±0.45 0.96 (0.40/2.43)	<b>0.001</b>
<b>Men</b>	213.7±46.4 214 (66/287)	145.4±65.4 134 (53/334)	<b>0.001</b>	2.94±0.55 2.87 (0.97/3.86)	2.00±0.86 1.85 (0.69/4.40)	<b>0.001</b>
<b>p*</b>	<b>0.001</b>	<b>0.001</b>		<b>0.001</b>	<b>0.001</b>	
<b>180°/s All participants</b>	71.6±40.0 62 (1/187)	21.3±13.2 18 (1/85)		1.16±0.68 1.04 (0.01/3.67)	0.35±0.23 0.28 (0.01/1.49)	
<b>Women</b>	73.7±38.2 64 (7/187)	21.1±9.9 19 (5/50)	<b>0.001</b>	1.27±0.65 1.13 (0.15/3.67)	0.37±0.18 0.34 (0.07/0.85)	<b>0.001</b>
<b>Men</b>	68.5±42.9 58 (1/160)	21.6±17.1 18 (1/85)	<b>0.001</b>	0.98±0.70 0.74 (0.01/2.81)	0.31±0.28 0.22 (0.01/1.49)	<b>0.001</b>
<b>p*</b>	0.397	0.288		<b>0.014</b>	<b>0.005</b>	

Figures as mean±SD and median(min/max); \*: Mann-Whitney U-test, \*\*: Wilcoxon Signed rank test

### Ratio of Flex<sub>abs</sub>/Ext<sub>abs</sub>

Ratio of Flex<sub>abs</sub>/Ext<sub>abs</sub> overall was 1.67±0.62 for 60°/s angular velocity and 4.93±4.60 for 180°/s angular velocity. The ratios for 60°/s were 1.67±0.58, 1.67±0.68; and for 180°/s they were 4.98±4.75, 4.86±4.42 for women and men, respectively. When comparison was done based on gender, there was no statistical difference (p>0.05). (Table 3).

## DISCUSSION

In this study, normal isokinetic data of the trunk muscles in a population of healthy young men and women were obtained with a Cybex isokinetic dynamometer. Measuring the strengths of low back muscles quantitatively is important in assessing the muscular unbalance that can cause low back dysfunction (7-9). It is known that to strengthen the lower back area is important to prevent and rehabilitate lower back pain (12). When studies in the literature are examined according to gender differences for the absolute maximum peak torque and peak torque normalized to body weight values of concentric strengths of the trunk flexion and extension, it appears that the strength values of men are mostly higher than women (7,13,33,34).

In the study of Barlett et al. (16) on young and healthy people (mean age=24.3 yrs), the extension strength of the trunk was 198 N·m, 3.2 N·m·kg<sub>bw</sub><sup>-1</sup> in women, and it was 283 N·m, 3.5 N·m·kg<sub>bw</sub><sup>-1</sup> in men. In the study of Cowley et al. (18) on young and healthy people (mean age=24.3 yrs), flexor strength of women was 140 N·m, 2.3 N·m·kg<sub>bw</sub><sup>-1</sup>; extensor strength was 121 N·m, 2.0 N·m·kg<sub>bw</sub><sup>-1</sup>; while flexor strength of men was 248 N·m, 2.9 N·m·kg<sub>bw</sub><sup>-1</sup> and the extensor strength was 268 N·m, 3.1 N·m·kg<sub>bw</sub><sup>-1</sup> (18). In a study by Bernardelli et al. (33) on asymptomatic sedentary people (mean age=22.2 year), it was found that flexor strength of women was 110 N·m, extensor strength was 123 N·m; flexor strength of men was 168 N·m, and extensor strength was 210 N·m (33).

As seen from the results of these studies, there is a significant difference between men and women regarding the strength capacitance of the trunk. In accordance with the results in the literature, in our study; for 60°/s angular velocity, there is a statistical difference regarding gender in the absolute maximum peak torque and peak torque normalized to body weight of the concentric trunk flexion and extension values, and men had higher scores. However, trunk

**Table 3.** Results for Ratio of Flex<sub>abs</sub>/Ext<sub>abs</sub>

Group	Flex <sub>abs</sub> /Ext <sub>abs</sub> ratio	
	Mean±SD	Median (min/max)
<b>60°/s All participants</b>	1.67±0.62	1.61 (0.51/4.53)
<b>Women</b>	1.67±0.58	1.62 (0.51/3.36)
<b>Men</b>	1.67±0.68	1.57 (0.71/4.53)
<b>p*</b>		0.803
<b>180°/s All participants</b>	4.93±4.60	3.86 (0.06/21.40)
<b>Women</b>	4.98±4.75	3.86 (0.23/21.40)
<b>Men</b>	4.86±4.42	3.86 (0.06/20.71)
<b>p*</b>		0.918

\*: Mann-Whitney U test

strength values in the literature, especially regarding the trunk extensor strength, were quite higher than the values in our study. We think that this difference could be due to the test position used, isokinetic device difference or population characteristics such as the physical activity level which affects muscular strength.

To our knowledge, concentric trunk flexion and extension absolute maximum peak torque and peak torque normalized to body weight for 180°/s angular velocity were only studied by Grabnier et al. (24). In this study, 10 healthy and 10 sedentary women were evaluated. As the participants were only women, the results could not be evaluated in terms of gender difference. It is reported that choosing high velocity (180°-300°/s) as a test speed is more reliable to reduce the load on the joint, comparing with low velocity. Since there likely is a single study in the literature evaluating trunk muscle strength for 180°/s angular velocity by isokinetic measurement, we think that our results will make significant contribution to the literature. In addition, it has a significant number of sample groups that can contribute to obtaining normative data for healthy young adulthood in the Turkish population.

When men and women were separately evaluated regarding concentric strengths of trunk flexion and extension; it was hard to make a clear statement. In a study by Bernardelli et al. (33), absolute maximum peak torque values in the standing position were examined at 60°/s angular velocity. In contrary to our study, it was concluded that extensor strength was higher than flexor strength in both genders. In a study done by Cowley et al. (18), flexors were stronger than extensors in women, and extensors were stronger than flexors in men.

Apart from results revealing that trunk extensors are stronger than flexors, the opposite is also encountered in the literature: flexors are stronger than extensors at 120°/s; are equal at 90°/s, and weaker at 30°/s and 60°/s angular velocities (12,35,36). It is thought that gravitation is more effective at higher velocities. This situation helps flexion, and affects extension oppositely. Measurement position is as effective as gravitation on test results. Gravitation should especially be considered for measurements in a standing position.

In a study conducted by Grabiner et al. (25) in asymptomatic healthy women (mean age 26.3 yrs), the absolute maximum peak torques of concentric trunk flexion and extension for 60°/s and 180°/s angular velocities were given as 95.4 N·m, 47.5 N·m; 64.8 N·m, 37.3 N·m, respectively (25). The dynamometer mechanical axis in this study is the anterior superior iliac spine. The results of this study are closer

to ours, as in both studies, extensor strengths were found to be lower than that of flexors at 60°/s and 180°/s angular velocities.

In the previous studies, it is stated that most of the troubles of low back arise from muscular problems. The relationship between the weakness of extensor and flexor muscles of the trunk and chronic low back pain, and especially the decrease in extensor muscle strengths of the trunk, and the unbalance in the ratio of extensor to flexor muscle strength might be the predetermining factor for chronic low back pain and injuries (10,37,38). The ratio of Flex<sub>abs</sub>/Ext<sub>abs</sub> is generally between 0.71 and 0.92 in healthy, non-active adults (6,18,34,39). In our study, mean values given in Table 3 were not in this range. Only six participants were in this range for 60°/s angular velocity, and only two were in this range for 180°/s angular velocity. We think that the high Flex<sub>abs</sub>/Ext<sub>abs</sub> ratios in our study are due to the relatively low values of extension of the trunk when compared to literature. However, we believe that the limitation of our study is that the research population is only young people (18-25 years). In future studies, individuals can be tested during decades of adulthood to see how power changes over time.

Data obtained from this study can be used as a comparison parameter in future studies to get normative data, or common values in healthy individuals aged 18-30. Normative data or common values might enable to optimize specific muscle strengths of the trunk during rehabilitation, or determine the risk of injury with thorough examination. On the basis of this study, trunk muscle strength instabilities can be determined by measurements in larger populations in different age groups. People for whom the Flex<sub>abs</sub>/Ext<sub>abs</sub> ratio does not fit in the appropriate range can be followed in time, and their trunk pathologies be examined.

## CONCLUSION

When concentric strengths of trunk flexion and extension was compared regarding genders in our study; for 60°/s angular velocity, the values of absolute maximum peak torque and peak torque values normalized to body weight are found to be higher in men. Whereas for 180°/s angular velocity, peak torque values normalized to body weight are higher in women. Also when men and women were evaluated separately with regard to concentric strengths of the trunk flexion and extension, extensor strengths of the trunk were lower than flexor strengths for both 60°/s and 180°/s angular velocities. There were only six participants for 60°/s angular velocity and two participants for 180°/s angular velocity in the Flex<sub>abs</sub>/Ext<sub>abs</sub> ratio range, which is generally known to be 0.71 and 0.92 in healthy non-active adults. The

results of this study are partially in agreement with those of similar studies. For this reason, we think that research in a larger scale should be conducted to get normative data or common values specific to population characteristics.

#### **Ethics Committee Approval / Etik Komite Onayı**

The Ethics Committee of Pamukkale University approved all procedures and the experimental design (date: 01.02.2018 and number: 60116787-020/8334). The study protocol is in accordance with the latest version of the Declaration of Helsinki.

#### **Conflict of Interest / Çıkar Çatışması**

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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#### **Author Contributions / Yazar Katkıları**

FU and EGK designed the study. FU and EGK searched databases and performed the selection of studies. EGK and MB collected all the data. FU and EGK analyzed the data; EGK and MB wrote the manuscript; FU and BU contributed to writing and critically uprisng the manuscript and approved the last version.

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