

Research Article

The Effect of Cuff Size on Blood Pressure Measurement in Obese Surgical Patients: A Prospective Crossover Clinical Trial

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ABSTRACT

Aim: This study aimed to determine the effect of a cuff properly sized for mid-upper arm circumference on blood pressure measurement in obese surgical patients.**Method:** This prospective crossover clinical trial was conducted with 100 patients who had body mass index ≥ 30 kg/m² and mid-upper arm circumference ≥ 27 cm and were admitted to the general surgery unit of a medical faculty hospital in İstanbul, Turkey between January 1, 2015, and December 31, 2015. Blood pressure of the patients was measured using a small-sized adult cuff and a cuff properly sized for mid-upper arm circumference.**Results:** Among the patients, 39% were morbidly obese and 67% had mid-upper arm circumference between 35 and 44 cm. Systolic blood pressure of the patients with a small adult cuff was 20.78 mmHg higher than that obtained with a cuff properly sized for mid-upper arm circumference, and their diastolic blood pressure was 10.15 mmHg higher on average ($p < 0.001$). Only 6% of those with systolic hypertension according to the small adult cuff readings were found to have hypertension according to the cuff properly sized for mid-upper arm circumference ($p < 0.001$).**Conclusion:** The results showed that, in obese surgical patients, blood pressure is measured inaccurately and found to be falsely high when measurements are not performed using a cuff properly sized for mid-upper arm circumference.**Keywords:** Blood pressure measurement, cuff size, mid-upper arm circumference, obese patients, obesity

INTRODUCTION

Arterial blood pressure (BP) is one of the most frequently measured physiological parameters in the clinical setting (Ostchega et al., 2013; Watson et al., 2011). Blood pressure measurement (BPM) is important in the perioperative care of all patients in surgery departments, especially in the treatment and evaluation of cardiovascular or respiratory complications associated with surgery and anesthesia and in the management of hypertensive patients (Eley, Christensen, Guy & Dodd, 2019; Stergiou et al., 2018; Watson et al., 2011). The most accurate BP value is obtained by direct intra-arterial measurement. However, noninvasive BPM is preferred globally because it is safe, cheap, and simple (Loenneke et al., 2016; Mishra, Sinha, & Rehman, 2017; Watson et al., 2011). Accuracy of noninvasive BPM is affected by the use of a cuff properly sized for mid-upper arm circumfer-

ence (MUAC), humerus length, and the shape of the arm (Bonso et al., 2010; Mishra et al., 2017; Palatini, Benetti, Fania, Malipiero, & Saladini, 2012; Palatini & Asmar, 2018). For accurate BPM, the cuff bladder length should be at least around 80% of the circumference of the upper arm, and the width of the cuff bladder should be 40% of the circumference of the upper arm (McFarlane, 2012; Palatini & Asmar, 2018; Ringrose et al., 2015). Evidence showed that BPM performed using a cuff properly sized for MUAC is as reliable as invasive BPM (Irving, Holden, Stevens, & McManus, 2016; Pickering et al., 2005).

In obese individuals, the circumference of the upper arm increases with increasing body mass index (BMI) (Akpolat et al., 2013; Irving et al., 2016). Therefore, the number of individuals with large MUAC (≥ 32 cm) increases in parallel with the increase in obesity

(Bilo et al., 2017; Irving et al., 2016; Ringrose et al., 2015). Studies also reported an increase in the number of patients with large MUAC and, therefore, an increasing need for large-sized adult cuffs (Akpolat et al., 2013; Irving et al., 2016; Ostchega et al., 2013). Moreover, some studies revealed that the use of small adult cuffs in obese individuals lead to falsely high BP measurements and, therefore, false HT diagnosis (Bilo et al., 2017; Fonseca-Reyes, de Alba-Garcia, Parra-Carrillo, & Paczka-Zapata, 2003; Mishra et al., 2017; Mourad et al., 2013), and overcuffing (use of a very large cuff) results in lower BP values (Ringrose et al., 2015). For this reason, a cuff properly sized for MUAC is required to create adequate pressure on the brachial artery in the measurement of BP of these individuals (McFarlane, 2012; Mishra et al., 2017; Pickering et al., 2005; Stergiou et al., 2018). However, research showed that BPM of 61% of patients who are referred to outpatient clinics (Türkoğlu et al., 2006) and 96.2% of individuals in community (Mishra et al., 2017) is measured with improperly sized cuffs.

Guidelines published by the American Heart Association (AHA) recommend use of different cuff sizes for different MUACs (Pickering et al., 2005; Whelton et al., 2018). Despite these recommendations, small adult cuffs are routinely used in nonbariatric surgery units, those units do not have proper cuffs for patients with MUAC ≥ 27 cm, and BP of these patients is measured by palpating the radial pulse from the upper cuff or forearm with small adult cuffs (Eley et al., 2019; McFarlane, 2012; Stergiou et al., 2018; Watson et al., 2011). Evidence showed that BP measured on the forearm in patients with large MUAC is significantly higher than BP measured on the upper arm (McFarlane, 2012; Watson et al., 2011), and this measurement is not appropriate for continuous BP monitoring in the intraoperative and postoperative periods (Eley et al., 2019). What is more, this literature suggests that problems related to accurate noninvasive BPM continue to exist in individuals with large MUACs. In the light of these considerations, this research was conducted to determine the effect of using a cuff properly sized for MUAC on the BP readings of obese general surgery patients with MUAC ≥ 27 cm.

Research Questions

1. Does the use of a cuff size inappropriate for the MUAC affect the systolic blood pressure (SBP) readings of obese surgical patients?

2. Does the use of a cuff size inappropriate for the MUAC affect the diastolic blood pressure (DBP) readings of obese surgical patients?

3. Does the use of a cuff size inappropriate for the MUAC lead to misdiagnosis of hypertension (HT) in obese surgical patients?

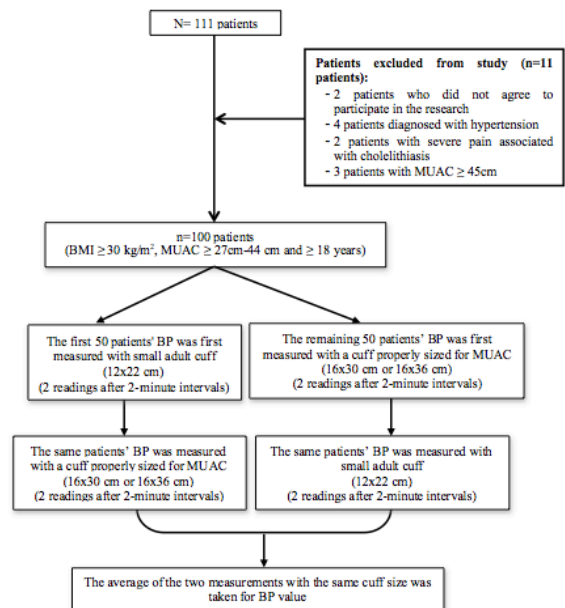
METHOD

Study Design

This research is a prospective crossover clinical trial. Each patient served as his or her own control in BPM with different cuff sizes.

Sample

The research population consisted of 111 patients who were 18 years old or older, were admitted to the general surgery unit of a medical faculty hospital in İstanbul, Turkey between January 1, 2015, and December 31, 2015, and had BMI ≥ 30 kg/m² and MUAC ≥ 27 cm (Figure 1). The minimum sample size was calculated as 74 for SBP and 67 for DBP values by taking the relevant study of Fonseca-Reyes et al. (2003) as a reference, the difference between standard and large cuffs for SBP values (11.2 mmHg) and DBP values (6.6 mmHg), and significance level at 0.05 and test power at 0.90 for Type I error in E-picos software (New York, NY, USA) into consideration.



BP: Blood pressure; BMI: Body mass index; MUAC: Mid-upper arm circumference

Figure 1. The sample and study protocol flow chart

Out of the subjects, two patients who did not agree to participate in the research, four patients with HT, two patients with severe pain associated with cholelithiasis, and three patients with MUAC ≥ 45 cm (adult thigh) for whom there were no proper cuff size for BPM were excluded from the research. Finally, the research was completed with a total of 100 patients (Figure 1).

Data Collection

Data were collected using a data collection form developed based on the relevant literature (Akpolat et al., 2013; Arıcı et al., 2015; Mancía et al., 2013; Mourad et al., 2013; Pickering et al., 2005; Watson et al., 2011). This form consisted of two parts: the first part included questions about the patients' descriptive characteristics, such as age, gender, marital status, diagnosis, classifications of obesity, and MUAC, whereas the second part included a table that aimed to collect data on the patients' anthropometric measurements (height, weight, and MUAC) and SBP and DBP readings.

Anthropometric Measurement Devices and Techniques:

Weights of the patients were measured in the morning with an empty stomach and bladder using a portable bathroom scale with a sensitivity of 0.5 kg. Their heights were measured using an inflexible tape measure and when the patients put their feet together and moved back until their heels touched the bottom of a wall and their heads were in the Frankfort plane (Akpolat et al., 2013). Their BMIs were calculated according to body weight (kg)/height (m^2) equation. Obesity was classified in accordance with the recommendations of the World Health Organization (WHO): Class I: BMI=30-34.99 kg/m^2 , Class II: BMI=35-39.99 kg/m^2 , and Class III: ≥ 40 kg/m^2 (WHO, 2018). MUAC measurements of the patients were made by determining the mid-point between the tip of the acromion process when their right arms were bent at the elbow at a 90° angle and the tip of ulnar process (Akpolat et al., 2013; Watson et al., 2011). In accordance with the AHA guidelines, MUAC was classified as small adult (22-26 cm), adult (27-34 cm), large adult (35-44 cm), and adult thigh (45-52 cm) (Pickering et al., 2005).

BPM Device and Techniques: BP was measured according to the recommendations of the AHA (Pickering et al., 2005), the European Society of Hypertension, the European Society of Cardiology (Mancía et al., 2013), and the Turkish Society of Cardiology (Arici et al. 2015). These recommendations remain

valid in recent guidelines and consensus reports, too (Aşık et al., 2018; Stergiou et al., 2018; Whelton et al., 2018).

Resting BP was measured in the morning in a quiet room at least 5 min after the patient sat on a chair (their legs on the ground and backs were supported) with an empty stomach and bladder. The patients refrained from smoking, exercising, or ingesting caffeine for 30 min before the measurement was made. During the rest period and during the measurement, the patients were not allowed to speak or sit with legs crossed. The clothes in the cuff placement location were removed. The right arms of the patients were supported at the right atrium level, and their palms were open. The brachial artery was palpated in the antecubital fossa, and the cuff bladder was placed so that the indicator arrow was 3 cm above the arterial pulsation. The radial pulse was then palpated, and the cuff was inflated 20 mmHg above this level. Cuff pressure was deflated by 2 mmHg every second, and the Korotkoff sounds were heard. The first Korotkoff sound was recorded as SBP, and the disappearance of Korotkoff sounds was noted as DBP (Arici et al., 2015; Mancía et al., 2013; Pickering et al., 2005). The HT threshold was accepted as ≥ 140 mmHg for SBP and ≥ 90 mmHg for DBP (Arici et al., 2015; Mancía et al., 2013).

BP was measured using three different-sized cylindrical cuffs that were calibrated and validated for use in adults (12x22 cm, 16x30 cm, or 16x36 cm; Amplestuff, Bearsville, NY, USA) (12x22 cm, 16x30 cm, or 16x36 cm); an aneroid sphygmomanometer (Omron Model 116; Omron, Hoffman Estates, IL, USA), and the auscultatory method. BP of all the patients was measured with a small-sized adult cuff (12x22 cm) that was routinely used in the general surgery unit and cuffs properly sized for MUAC (16x30 cm or 16x36 cm). A cuff properly sized for MUAC was determined according to the recommendations of the AHA. According to these recommendations, a cuff size of 16x30 cm (adult cuff) was used for those patients with MUAC of 27-34 cm, and a cuff size of 16x36 cm (large adult) was used for those patients with MUAC of 35-44 cm (Pickering et al., 2005).

Study Procedure

Upon their arrival to the general surgery unit, a clinical nurse (ND) performed height, weight, and MUAC measurements for each patient. After that, two nurse faculty members (SY, GAU) calculated BMI

for each patient. Also, the two clinical nurses (NA, ND) performed BP measurement on the right arm of each patient using a small adult cuff (12x22 cm) and a cuff properly sized for MUAC (16x30 cm or 16x36 cm). Both of the nurses were blinded to measurements of each other. Also, the patients were blinded to all of the readings.

All BP readings were taken by the two clinical nurses (NA and ND), who had more than 20 years of professional experience. Prior to study initiation, these two nurses were introduced to the recommended techniques for the correct BPM (Arıcı et al., 2015; Mancía et al., 2013; Pickering et al., 2005) in a half-day practical training, and at the end of the training, they were tested about their use of these techniques. For both of the nurses, the difference between the BP readings with the 12x22 cm cuff was 0.08 ± 0.75 mmHg for SBP and 0.02 ± 0.72 mmHg for DBP. Again, for both of the nurses, the difference between the BP readings with a cuff properly sized for MUAC was 0.04 ± 0.75 mmHg for SBP and 0.02 ± 0.67 mmHg for DBP. Intraclass correlation coefficients (ICCs) (i.e., two-way random effects model: consistency) were calculated, and it was determined that there was a perfect agreement (ICC value: >95%) between SBP (ICC: 99-100%) and DBP (ICC: 99-99%) readings taken by the nurses ($p < 0.001$).

To prevent repeated BP readings from affecting the research results, BP of the first 50 patients was measured with the 12x22 cm cuff, which is routinely used in the general surgery unit, followed by a second measurement with a cuff properly sized for MUAC (16x30 cm or 16x36 cm). BP of the remaining 50 patients was measured first with a cuff properly sized for MUAC (16x30 cm or 16x36 cm) and then with the 12x22 cm cuff. Following the recommendations that there should at least be a 1-min (Mancía et al., 2013; Mourad et al., 2013; Pickering et al., 2005) or 2-min time intervals (Arıcı et al., 2015) between repeated BP readings, there were 2-min waiting times between the consecutive measurements. A total of four BP readings (two consecutive readings for 12x22 cm cuff size, two consecutive readings for 16x30 cm or 16x36 cm cuff size) were taken on each patient's arm. The average of the two consecutive readings with the same cuff size was taken for the BP value (Figure 1).

Data Analysis

Descriptive data were analyzed using frequency, percentage, mean, and standard deviation. Because

SBP and DBP values were normally distributed, the means of SBP and DBP values measured with cuffs of different sizes were compared using the paired sample t test. The relationship between readings taken using cuffs of different sizes and systolic and diastolic HT percentages was analyzed with the Pearson Chi-square test. The reliability between SBP and DBP readings taken by the two nurses was assessed with the ICC, and there was a perfect agreement between them (≥ 95 -100%) (Alpar, 2018). Statistical significance was assessed at 95% confidence interval ($p < 0.05$).

Ethical Considerations

Before starting the research, written permission was obtained from the Ethics Committee of Istanbul University Cerrahpasa Faculty of Medicine (Number: 10998). Participation in the research was voluntary, and the enrolled patients were informed about the research. Written informed consent was obtained from all the participants.

RESULTS

The mean age of the patients was 52.82 ± 13.95 years, and 81% were female and married. The patients were admitted to the general surgery unit with the diagnosis of cancer (32%), cholelithiasis (37%), and multinodular goiter (31%). Among the patients, 61% had a BMI of 30-39.99 kg/m² and 39% were morbidly obese. The majority of them (67%) were in the MUAC range of 35-44 cm (large adult) (Table 1).

On average, SBP readings taken using a small adult cuff were 20.78 mmHg ($p < 0.05$) higher and DBP readings were 10.15 mmHg ($p < 0.05$) higher than readings taken using a cuff properly sized for MUAC (16x30 cm or 16x36 cm) (Table 2). According to readings taken using a cuff properly sized for MUAC, for the majority of the patients, SBP and DBP values were ≥ 10 mmHg higher than readings taken using a small adult cuff (93% and 66%, respectively), whereas there were fewer patients with SBP and DBP values ≥ 20 mmHg higher (53% and 18%, respectively) (Table 2).

Only 6% of patients with suspected systolic HT (≥ 140 mm Hg) according to readings taken using a small adult cuff were found to have HT according to readings taken using a cuff properly sized for MUAC ($p < 0.05$; Figure 2). In contrast, all the patients with suspected diastolic HT (≥ 90 mmHg) according to measurements performed using a small adult cuff

Table 1. Descriptive characteristics of patients (n=100)

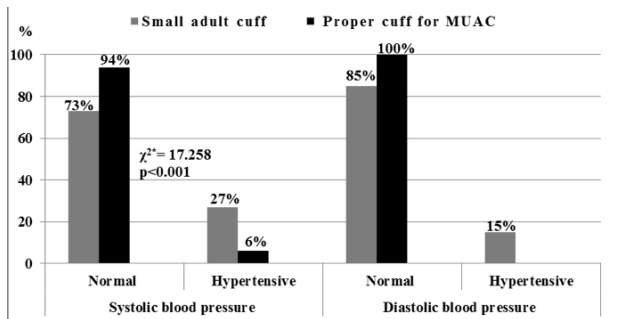
Characteristics (n=100)	n	%	
Age (Mean±SD) (Min-Max)	52.82±13.95	(22-75 years)	
Gender	Female	81	81.0
	Male	19	19.0
Marital status	Married	81	81.0
	Single	19	19.0
Diagnosis	Cancer	32	32.0
	Cholelithiasis	37	37.0
	Multinodular goiter	31	31.0
Classification of obesity	30–34.99 kg/m ² (Class I)	37	37.0
	35–39.99 kg/m ² (Class III)	24	24.0
	≥40 kg/m ² (Class III-Morbid obesity)	39	39.0
Classification of MUACd	27-34 cm	33	33.0
	35-44 cm	67	67.0

SD: Standard deviation; Min: Minimum; Max: Maximum; MUAC: Mid-upper arm circumference

Table 2. Comparison of blood pressure readings according to different cuff sizes

BP	Cuff size						Test*	p
	BP differences (%)		Small adult cuff	Proper cuff for MUAC	Difference			
	>10 mmHg	>20 mmHg	Mean (SD) mmHg	Mean (SD) mmHg	Mean (SD) mmHg			
Systolic	93	53	134.03 (18.74)	113.25 (16.09)	20.78 (11.07)	18.775	<0.001	
Diastolic	66	18	78.88 (11.93)	68.74 (7.88)	10.15 (10.26)	9.888	<0.001	

BP: Blood pressure; SD: Standard deviation; MUAC: Mid-upper arm circumference.
*Paired sample t test.



* Pearson Chi-square test
MUAC: Mid-upper arm circumference

Figure 2. Hypertension prevalence by different cuff sizes readings

(15%) were normotensive according to measurements performed using a cuff properly sized for MUAC (Figure 2).

DISCUSSION

The WHO reported that 13% of the world's adult population (>650 million) is obese, and that the prevalence of obesity has tripled during the 1975-2016

period (WHO, 2018). With the increase in obesity and the increase in the number of individuals with large MUAC (>34 cm), all health professionals, especially nurses, are faced with the problem of failure to perform accurate BPM with standard cuffs (MUAC=22-34 cm) within their departments and in community (Bilo et al., 2017; Eley et al., 2019; Mishra et al., 2017; Ringrose et al., 2015). Our research revealed that, in comparison with readings taken using a properly sized cuff, both SBP and DBP readings taken using a small-sized adult cuff were significantly higher. This finding supports the results from previous research emphasizing that MUAC measurement and use of a properly sized cuff is essential for accurate BPM (Bilo et al., 2017; Mishra et al., 2017; Mourad et al., 2013; Ringrose et al. 2015; Watson et al., 2011).

Inaccurate measurements made with small adult cuffs lead to SBP and DBP values that are too high to affect clinical results. A previous study reported that, in comparison with a large cuff (15.5x31 cm), a standard cuff (12.5x26 cm) causes higher SBP

(mean 9.08 mmHg) and DBP (mean 6.4 mmHg) values (Fonseca-Reyes et al., 2003). A study conducted in a post anesthesia care unit with no large adult cuffs found that measuring BP of patients with large arm circumferences using an extra-long adult cuff (slightly longer than the adult cuff) instead of a large cuff results in higher values of SBP (mean 6.3 mmHg) and DBP (mean 2.7 mmHg) (Watson et al., 2011). In a study conducted with HT patients, SBP measured by a standard cuff (MUAC=22-32 cm) is 6.9 mmHg higher and DBP is higher by 4 mmHg compared with a large cuff (MUAC=32-42 cm) (Mourad et al., 2013). In a similar study, it was determined that BPM is not affected even if the cuff position is incorrect when a cuff properly sized for MUAC is used, but BP values of the wrong cuff position are increased by 4-5 mmHg when an improperly sized cuff is used (Bilo et al., 2017). Mishra et al. (2017) found that SBP measured with a small adult cuff (MUAC=22-26 cm) is 9 mmHg higher than that measured with a large cuff (MUAC=35-44 cm) and 5.9 mmHg higher than that measured with an adult cuff size (MUAC=27-34 cm) on average. In the same study, DBP measured with a small adult cuff are 5.9 mmHg higher than that measured with a large cuff and 4.4 mmHg higher than that measured with an adult cuff size on average. Similarly, in our study, SBP and DBP values obtained using a small adult cuff are significantly different from those obtained using a cuff properly sized for MUAC (20.78 and 10.15 mmHg, respectively), but this difference is quite higher than the literature range. This difference could be due to the fact that the arm circumferences and/or cuff sizes used in previous studies (Bilo et al., 2017; Fonseca-Reyes et al., 2003; Mourad et al., 2013; Watson et al., 2011) are different from those used in this study, there are few patients with BMI>30 kg/m² and different cuff size readings are compared without taking MUAC appropriateness into consideration (Mishra et al., 2017), and their measurement times and measurement positions are different (Watson et al., 2011).

Another reason for the high difference in SBP and DBP values in this study may be the cylindrical cuffs used in the research. Research reported that using cylindrical cuffs in obese individuals with large arms (MUAC >30 cm) leads to higher BP readings (Bonso et al., 2010; Palatini et al., 2012), and particularly upper arms of most obese women are tronco-conical (Palatini et al., 2012). In our study, the majority of the patients were female, and almost two-thirds of them had MUAC > 30 cm. Therefore, those studies

in which the type of the cuff used was not specified (Bilo et al., 2017; Fonseca-Reyes et al., 2003; Mishra et al., 2017; Mourad et al., 2013; Watson et al., 2011) may have obtained lower BP values if they did use conical cuffs.

One of the important findings of this study is that SBP values obtained using a small adult cuff in nearly all of the patients and DBP values in more than half of the patients are ≥ 10 mmHg higher than the true BP values on average. A previous study similarly found that measurements made with an inappropriately sized adult cuff for MUAC result in ≥ 10 mmHg difference in SBP of 31% of the patients and in DBP of 23% of the patients (Watson et al., 2011).

A previous study determined that BP is associated with arm circumference, and every 5 cm increase in arm circumference over 35 cm results in 2-5 mmHg increase in SBP and 1-3 mmHg increase in DBP (Fonseca-Reyes et al., 2003). Accurate measurement of BP is particularly important in obese individuals, who have six times higher HT risk than lean individuals (Eley et al., 2019), because it prevents false diagnosis of HT and unnecessary drug treatment. Evidence showed that the incidence rate of HT significantly varies in obese individuals with large MUAC depending on cuff size (Mishra et al. 2017; Mourad et al., 2013) and arm shape (Bonso et al., 2010; Palatini et al., 2012; Palatini & Asmar, 2018), and that using a cuff properly sized for MUAC results in a two-fold decrease in the number of individuals with masked HT (Mourad et al., 2013). Ostchega et al. (2013) found that 52% of hypertensive men and 38% of hypertensive women need a larger BP cuff for accurate BPM. Mourad et al. (2013) found that the rate of HT, which is 56.6% compared with BP readings taken using a small cuff, is significantly higher than that of readings taken using a large cuff (41.5%). Similarly, Mishra et al. (2017) found that the rates of systolic and diastolic HT with small adult cuffs are 25.6% and 44.7%, respectively, but the rates are 20.8% and 29.7%, respectively, when measured with a cuff properly sized for MUAC. In parallel to related literature, in our study, the rates of systolic and diastolic HT according to readings taken using a small adult cuff (21% and 15%, respectively) are significantly higher compared with readings taken using a cuff properly sized for MUAC (6% and 0%, respectively). In this study, the reason for lower HT rates compared with measurements done using cuffs of different sizes in the literature could

be due to the fact that these studies (Mishra et al., 2017; Mourad et al., 2013) were conducted in the community at home, and they included individuals diagnosed with HT (37.5-35.8%). The guidelines of the AHA also reported that BP values in the clinical setting are higher than those in the home environment (Whelton et al., 2018).

Study Limitations

A significant limitation of this study is the lack of data on obese individuals with larger circumference (≥ 45 cm), as the research sample is limited to patients with MUAC=27-44 cm. Another important limitation is that it cannot provide information on the effect of under cuffing (use of a small cuff) in obese individuals with HT. Some studies reported that obese individuals mostly have conically shaped arms and that the shape of the cuff and the length of the humerus should be taken into account in the selection of appropriate cuffs (Bonso et al., 2010; Palatini et al., 2012; Palatini & Asmar, 2018; Stergiou et al., 2018). Another significant limitation of this study is that the appropriate cuff size for BPM was determined according to MUAC, the shape of the upper arm was not taken into consideration, and BP of all the patients was measured with cylindrical cuffs.

CONCLUSION AND RECOMMENDATIONS

The results of this research provide strong evidence for the literature that emphasize the importance of using a cuff appropriately sized according to MUAC for accurate BPM. In addition, our study reveals the necessity of having BPM devices with cuffs appropriately sized according to patients' MUAC in non-bariatric surgery departments too. BPM with a cuff properly sized for MUAC is important for patient safety because it prevents false diagnosis of HT and unnecessary drug treatment. Nurses providing care for patients with large arm circumferences in surgery departments should avoid performing BPM of these patients with small adult cuffs but provide cuffs appropriately sized for MUAC, arm shape, and humerus length of these patients. Future research is recommended to investigate the effect of MUAC, arm shape, and humerus length on accurate BPM measurement of patients with large MUAC (>30 cm).

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Date/Number: 2013/10998).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.Y.; Design – S.Y., G.A.U.; Supervision – S.Y., G.A.U.; Resources – S.Y., G.A.U.; Materials – S.Y., G.A.U.; Data Collection and/or Processing – S.Y., G.A.U.; N.A., N.D.; Analysis and/ or Interpretation – S.Y.; Literature Search – S.Y., G.A.U.; Writing Manuscript – S.Y., G.A.U.; Critical Review – S.Y., G.A.U.; Other – S.Y., G.A.U.; N.A., N.D.

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

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