

# Do Malnutrition Scores Have a Role in Prediction of Non-Dipper Hypertension?

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## ABSTRACT

**Introduction:** Normally, blood pressure shows a circadian rhythm, in line with this, blood pressure at night falls by 10% compared to daytime blood pressure. Studies have shown that non-dippers have an increased mortality and morbidity of cardiovascular and cerebrovascular diseases. Malnutrition and obesity are associated with an increased risk of cardiovascular disease, and increased mortality in general population. This study was conducted to evaluate the value of controlling nutritional status (CONUT) and nutrition risk index (NRI) malnutrition scores in prediction of non-dipper status, compared with other measurements.

**Patients and Methods:** In this retrospective study, 167 patients who had ambulatory blood pressure measurements in our hospital were included. One hundred nine patients had previous diagnosis of hypertension; 58 patients were non-hypertensive. CONUT and NRI scores were calculated and their association between dipper and non-dipper patterns were examined.

**Results:** Patients were divided into two groups according to dipper or non-dipper status. The median age of patients with dipper and non-dipper were 50 (45-55, IQR), 51.5 (45-60) respectively. In addition, 109 (65.2%) subjects were hypertensive. Non-dipper status was seen in 93 (57%) patients. Max night blood pressure (BP) and mean night BP were higher in non-dipper group [144 (134-160), 133 (119-140)-126 (115-137); 111 (101-120),  $p < 0.001$ , respectively]. NRI was lower (low value denotes malnutrition) in non-dipper group [59 (55-63); 60.5 (56-72),  $p = 0.008$ , respectively]. CONUT any degree [25 (26.9%); 32 (43.2%),  $p = 0.027$ ]. We also performed ROC curve analysis for optimal cut-off threshold to predict non-dipper hypertension. Optimal cut-off according to Youden index was 0.297, analysis showed cut-off value 57.9, sensitivity 71%, specificity 58.06%, positive predictive value 57.61%, and negative predictive value 72%.

**Conclusion:** Our study showed that malnutrition status defined by CONUT or NRI scores are associated with non-dipper hypertension pattern.

**Key Words:** Malnutrition; hypertension; malnutrition score; dipper; non-dipper.

## Non-Dipper Hipertansiyonu Öngörmede Malnütrisyon Skorlarının Rolü Var mıdır?

### ÖZ

**Giriş:** Normalde kan basıncı sirkadiyen bir ritim gösterir, buna paralel olarak gece kan basıncı gündüz kan basıncına göre %10 düşer. Çalışmalar, dipper olmayanların artmış kardiyovasküler ve serebrovasküler morbidite ve mortalitesine sahip olduğunu göstermiştir. Yetersiz beslenme ve obezite, genel popülasyonda ölüme neden olabilecek artmış kardiyovasküler hastalık riskiyle ilişkilidir. Bu çalışma, “controlling nutritional status (CONUT)” ve “nutrition risk index (NRI)” malnütrisyon skorlarının dipper olmama durumunun öngörülmesindeki değerini diğer ölçümlerle karşılaştırıldığında değerlendirmek için yapılmıştır.

**Hastalar ve Yöntem:** Bu retrospektif çalışmada, hastanemizdeki ambulatuvar kan basıncı ölçümleri yapılan 167 hasta çalışmaya dahil edildi. Yüz dokuz hasta hipertansiyon tanısı olan hastaydı, 58 hasta hipertansif olmayan hastalara dahil edildi. CONUT ve NRI skorları hesaplandı ve dipper ve dipper olmayan hastalarla ilişkilendirildi.

**Bulgular:** Hastalar dipper ve dipper olmayan tansiyon paternine göre iki gruba ayrılmıştır. Dipper ve dipper olmayan hastaların ortanca yaşı sırasıyla 50 (45-55, IQR), 51.5 (45-60) idi. Ayrıca 109 (%65.2) hastanın hipertansiyon tanısı mevcuttu. Dipper olmayan 93 (%57) hastada görülmüştür. Dipper olmayan grupta maksimum gece kan basıncı ve ortalama gece kan basıncı daha yüksek bulunmuştur [sırasıyla 144 (134-160), 133 (119-140)-126 (115-137); 111 (101-120),  $p < 0.001$ ]. Dipper olmayan grupta NRI düşük (düşük değer yetersiz beslenmeyi gösterir) [59 (55-63), 60.5 (56-72) sırasıyla  $p = 0.008$ ]. Herhangi bir dereceye göre [25 (%26.9), 32 (%43.2),  $p = 0.027$ ]. Aynı zamanda optimum kesme tahmini dipper olmayan hipertansiyon için ROC eğrisi analizi yapılmıştır. Youden indeksine göre optik kesme değeri 0.297, analiz kesme değeri 57.9, duyarlılık %71, özgüllük %58.06, pozitif öngörü değeri %57.61 ve negatif öngörü değeri %72 bulunmuştur.

**Sonuç:** Çalışmamız, CONUT veya NRI skorlarıyla tanımlanan malnütrisyon durumunun dipper olmayan hipertansiyon paterni ile ilişkili olduğunu göstermiştir.

**Anahtar Kelimeler:** Malnütrisyon; hipertansiyon; malnütrisyon skoru; dipper; dipper olmayan.

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## INTRODUCTION

Normally, blood pressure shows a circadian rhythm, in line with this, blood pressure at night falls by 10% compared to daytime blood pressure. Ambulatory blood pressure measurement is a more sensitive risk predictor than office blood pressure of cardiovascular outcomes such as coronary events and stroke<sup>(1)</sup>. Studies have shown that patients with non-dipper hypertension have increased cardiovascular and cerebrovascular morbidity and mortality<sup>(2,3)</sup>. Therefore, early identification of non-dipper hypertensive patients might reduce risk of future cardiovascular events.

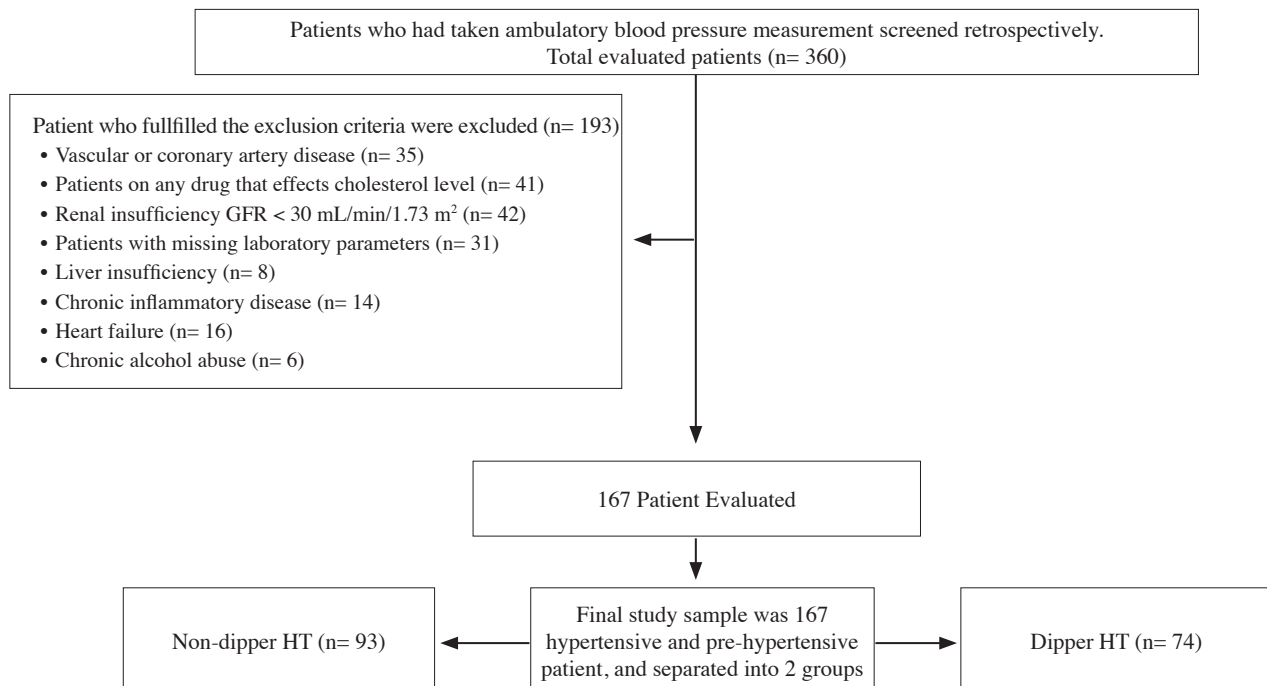
In a cross-sectional study conducted by Sesso et al., blood pressure is increased in malnourished children and in those who recovered from malnutrition. Malnutrition occurring during childhood may represent a risk factor for increased blood pressure later in life<sup>(4)</sup>. Malnutrition regardless of body mass index (BMI) is prevalent in patients with acute coronary syndrome, and associated with poor prognosis irrespective of the malnutrition index used<sup>(5)</sup>. Malnutrition and obesity are associated with an increased risk of cardiovascular disease, that can cause mortality in the general population<sup>(6-9)</sup>. Although different approaches have attempted to define malnutrition scores to date, these scores are objective indicators not only for malnutrition, but also for immune status<sup>(10)</sup>. Among patients undergoing general surgery, malnutrition is associated with delayed wound healing, postoperative complications, prolonged

hospital length of stay, hospital readmission, and death<sup>(11)</sup>. Pre-procedural nutritional status is associated with mortality in older adults following aortic valve replacement<sup>(12)</sup>.

Classification of malnutrition has been questioned in some studies<sup>(13)</sup>. Sze et al., found BMI > 30 kg/m<sup>2</sup> malnutrition according to controlling nutritional status (CONUT) score, and prognostic nutritional index (PNI) scores<sup>(9)</sup>. These results show us unmet need in high blood pressure patients to elaborate prognostic impact of malnutrition on long-term impact. Literature is scanty regarding the association of blood pressure and malnutrition status. The aim of the present analysis is to investigate this issue. As a result, this study was conducted to evaluate the value of CONUT and NRI in prediction of non-dipper status, compared with other measurements.

## PATIENTS and METHODS

In this retrospective study, 167 patients who had ambulatory blood pressure measurement (ABPM) in our hospital between October-December 2020 were included. One hundred nine patients had previous diagnosis of hypertension. Fifty eight patients were non-hypertensive. Diagnosis of hypertension was made by ABPM result or previous anti-hypertensive medication use. Hypertension criteria for ABPM was  $\geq 130/80$  mmHg over 24 hour,  $\geq 135/85$  mmHg for the daytime average, and  $\geq 120/70$  for the night-time average. Detailed inclusion and exclusion criteria given in Figure 1.



**Figure 1.** Detailed inclusion and exclusion criteria.

The ABPM device was programmed to record BP at 20 min in day-30 min at night intervals, and average blood pressure and max blood pressure values are provided for daytime, nighttime. Patients are defined as “dippers” when nighttime systolic and diastolic blood pressure fall is > 10%, and as “non-dippers” when night-time blood pressure fall is < 10%.

Clinical and demographic characteristics of patients such as age, gender, weight [weight in kg/height squared ( $m^2$ )], smoking status, anti-hypertensive drugs were gathered from hospital automation system. Hemogram, albumin, creatinine levels, blood glucose levels, and fasting serum lipid status, including low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were also noted from hospital databases. The study protocol was approved by our local ethics committee, the study complied with Helsinki amendment.

**The formula of NRI score:**  $[1.489 \times \text{albumin (g/L)}] + [41.7 \times \text{current body weight (kg)/ideal body weight (kg)}]$ .

The ideal body weight of patients was obtained by the Lorenz formulas:

**Formula for males:**  $\text{Height (cm)} - 100 - [(\text{height (cm)} - 150)/4]$

**Formula for females:**  $\text{Height (cm)} - 100 - [(\text{height (cm)} - 150)/2.5]$ .

When the current body weight was more than ideal body weight, we accepted weight as: current body weight/ideal body weight:  $1^{(5)}$ .

The CONUT score uses serum albumin, total lymphocyte count, and cholesterol. A score of 0 to 1 was considered as normal, scores of 2 to 4 as mild, 5 to 8 as moderate, and 9 to 12 as severe malnutrition<sup>(14)</sup>. We defined CONUT scores > 1 as “any degree malnutrition” for CONUT<sup>(5)</sup>.

### Statistical Analysis

Continuous data presented as median and interquartile ranges. Categorical data were defined as frequency and percentage. For the independent continuous data group comparisons, we used Mann-Whitney U test, and Pearson Chi-Square or Fisher-exact test for categorical data comparison. To determine independent predictors for dependent (non-dipper) variable, univariate (Crude) and multivariable (adjusted) logistic regression analysis was used. For correlation analysis between continuous variables Spearman test was used.

**Outcome variable:** Categorical non-dipper hypertension.

**Statistical modelling:** Multivariable logistic regression models of prognostic factors were used. The analyses were based on non-missing data. Predictors (confounders) of multivariable were selected according to a literature, consensus opinion by an expert group of physicians and focused variables. For all statistical analyses, p value less than 0.05 was defined as a statistical significance. Statistical analyses were performed by using R 4.00 software (Vienna, Austria) with “rms”, “ggplot” packages.

### RESULTS

Patients were divided into two groups according to dipper or non-dipper presence. The median age of the patients with dipper and non-dipper were 50 (45-55, IQR), 51.5 (45-60) respectively; in addition, 109 (65.2%) subjects was hypertension. Non-dipper was seen in 93 (57%) patients. Max night blood pressure and mean night blood pressure were higher in non-dipper group [144 (134-160), 133 (119-140)-126 (115-137); 111 (101-120)  $p < 0.001$ , respectively]. NRI lower (low value denotes malnutrition) in non-dipper group [59 (55-63), 60.5 (56-72) respectively  $p = 0.008$ ]. CONUT any degree [25 (26.9%), 32 (43.2%),  $p = 0.027$ ]. Sex, hypertension, diabetes mellitus, and anti-hypertensive drugs were not statistically different between groups. Other parameters are presented in Table 1. Besides we categorized two groups by any degree CONUT, as a result max night blood pressure and mean night blood pressure higher in any degree CONUT (+) group when compared to any degree CONUT (-) (0.04, 0.01), other presented in Table 2.

Crude logistic regression analysis depicted that white blood cell (WBC), NRI and any degree CONUT were associated with non-dipper (Table 3). Adjusted logistic regression analysis depicted only NRI was associated with non-dipper hypertension [Odds Ratio 0.93 (0.89-0.98),  $p = 0.002$ ] (Table 3).

We also performed ROC curve analysis for optimal cut-off threshold to predict non-dipper hypertension. Optimal cut-off according to Youden index was 0.297, analysis showed cut-off value 57.9, sensitivity 71%, specificity 58.06%, positive predictive value 57.61%, and negative predictive value 72% (Figure 2). We also performed Spearman correlation analysis between maximum night blood pressure with NRI scores which showed fair correlation  $r = 0.256$  (Figure 3).

**Table 1. Baseline clinical and laboratory parameters according to dipper, non-dipper status**

Variables	Dipper (n= 74)	Non-dipper (n= 93)	p value
Age	50 (45-55)	51.5 (45-60)	0.84
Sex (male) (n, %)	45 (48.4)	41 (55.4)	0.36
Hypertension (n, %)	58 (62.4)	51 (68.9)	0.37
Diabetes mellitus (n, %)	14 (15.1)	10 (13.5)	0.77
Max night BP (mmHg)	133 (119-140)	144 (134-160)	< 0.001
Max day BP (mmHg)	153(145-164)	157 (145-168)	0.39
Mean night BP (mmHg)	111 (101-120)	126 (115-137)	< 0.001
Mean day BP (mmHg)	129 (122-132)	126 (119-134)	0.58
ACEI/ARB (n, %)	36 (38.7)	31 (41.9)	0.67
Beta-blocker (n, %)	17 (18.3)	20 (27)	0.17
Diuretic (thiazide or indapamide) (n, %)	18 (19.4)	13 (17.6)	0.77
Calcium canal blocker (n, %)	35 (37.6)	19 (25.7)	0.10
WBC count (x10 <sup>9</sup> /L)	8.1 (6.4-10.0)	7.3 (6.1-8.2)	0.02
Lymphocyte count (x10 <sup>9</sup> /L)	2 (1.6-2.4)	2.2 (1.63-2.5)	0.34
Hb (g/dL)	13.4 (12.2-14.9)	13.5 (12.5-15.4)	0.35
Platelet count (x10 <sup>9</sup> /L)	257 (223-353)	263 (224-338)	0.78
CRP (mg/L)	0.3 (0.3-3)	0.4 (0.3-3)	0.57
AST (U/L)	18 (15-24)	21 (17-28)	0.004
Albumin (g/dL)	4.5 (4.2-4.8)	4 (3.7-4.4)	< 0.001
Creatinine (mg/dL)	0.76 (0.64-0.97)	0.77 (0.67-0.90)	0.75
Total cholesterol (mg/dL)	213 (154-238)	201 (166-253)	0.97
LDL (mg/dL)	136 (91-152)	129 (100-159)	0.73
Body mass index (kg/m <sup>2</sup> )	29.7 (27.3-33)	27.3 (26-32.9)	0.02
NRI	60.5 (56-72)	59 (55-63)	0.008
CONUT [(any degree) (n, %)]	25 (26.9)	32 (43.2)	0.027

ACEI/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker, WBC: White blood cell, Hb: Hemoglobin, CRP: C-reactive protein, AST: Aspartate transaminase, LDL: Low-density lipoprotein, NRI: Nutrition risk index, CONUT: Controlling nutritional status.

**Table 2. Blood pressure parameters and NRI comparison according to malnutrition status**

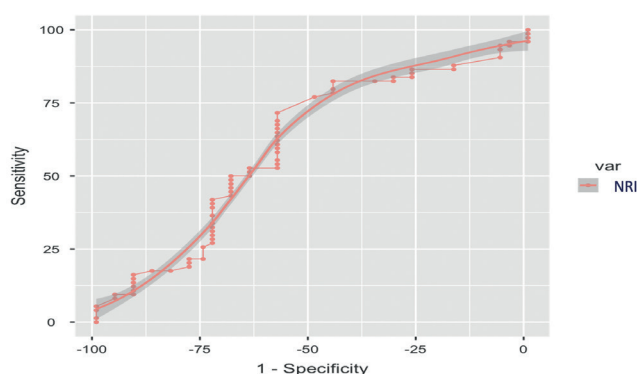
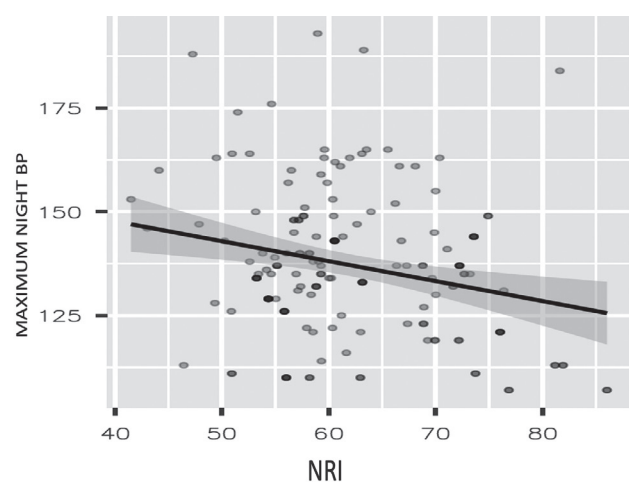
Variables	CONUT any degree (n= 110) (-)	CONUT any degree (n= 57) (+)	p value
Max day BP (mmHg)	154 (144-169)	154 (149-168)	0.48
Mean day BP (mmHg)	127 (119-135)	129 (120-134)	0.58
Max night BP (mmHg)	135 (121-145)	138 (130-148)	0.04
Mean night BP (mmHg)	115 (103 -122)	120 (113-129)	0.01
NRI	60.5 (56-72)	58.8 (55.2-66.8)	0.07
Non-dipper (n, %)	42 (38.2)	32 (56.1)	0.027

NRI: Nutrition risk index.

**Table 3. Multivariable logistic regression for prediction non-dipper status**

Variables	Crude OR CI	p value	Adjusted OR CI	p value
Age	0.99 (0.97-10.2)	0.65	0.98 (0.95-1.01)	0.11
Diabetes mellitus	0.88 (0.37-2.10)	0.78	1.09 (0.40-2.94)	0.85
Hypertension	1.34 (0.70-2.55)	0.70	1.18 (0.57-2.46)	0.65
WBC count	0.84 (0.71-0.99)	0.04	0.86 (0.71-1.05)	0.13
Hb	1.02 (0.87-1.19)	0.79	0.97 (0.81-1.15)	0.72
Creatinine	0.57 (0.22-1.42)	0.24	0.48 (0.17-1.39)	0.17
NRI	0.93 (0.90-0.97)	< 0.001	0.93 (0.89-0.98)	0.002
CONUT any degree	2.07 (1.08-3.96)	0.03	1.92 (0.91-4.07)	0.09

WBC: White blood cell, Hb: Hemoglobin, NRI: Nutrition risk index, CONUT: Controlling nutritional status.

**Figure 2.** Youden index.**Figure 3.** Spearman correlation analysis.

## DISCUSSION

In our study, we demonstrated that malnutrition status of is associated with non-dipper pattern on 24-hour ambulatory blood pressure measurement. The ABPM is an indispensable tool in the diagnosis of hypertension, and frequently used in daily practice. Not only to diagnose hypertension, it also

demonstrates blood pressure variation in the circadian rhythm. Twenty four-hour ABPM has been consistently shown to have a closer relationship with morbid or fatal events, and is a more sensitive risk predictor than office blood pressure of cardiovascular outcomes such as coronary morbid or fatal events and stroke<sup>(1)</sup>.

Blood pressure normally decreases during sleep. Dipping of blood pressure in the night is a physiological change and can be blunted by cardiovascular risk factors and the severity of hypertension. In most individuals, the highest pressures are seen during the morning hours, and the lowest during sleep. In hypertensive patients, this pattern is generally preserved, with an upward shift of the diurnal profile. Abnormal patterns of diurnal blood pressure variation have been reported to be related to advanced target organ damage and poor cardiovascular prognosis<sup>(14)</sup>. Studies have also demonstrated that night-time blood pressure is a stronger predictor of outcomes than daytime blood pressure. Moreover, patients with a reduced night time dip in blood pressure have an increased cardiovascular risk<sup>(15)</sup>.

Malnutrition includes both undernutrition and overnutrition and reflects the general condition of a patient, including physical condition, protein turnover, and immune-competence. Although it can be considered a modifiable condition, malnutrition is often overlooked in daily clinical practice. It is linked with poor prognosis in patients with cardiovascular disease, malignity, and patients who undergo surgery<sup>(5,16)</sup>. Since malnutrition is a continuous catabolic process, it affects patients' immune and endocrinologic status. Thus, it has a negative impact on many comorbidities<sup>(17)</sup>.

Hypertension, being one of the most important preventable cardiovascular risk factors, is a detrimental vascular disease regarding its effects on cardiovascular, cerebrovascular and other systems. Hypertensive disease could affect patient's



immunologic and endocrinologic functions. In our study, we aimed to demonstrate the malnutrition status defined by CONUT and NRI scores, as an immune-malnutrition index, is in association with dipper and non-dipper blood pressure patterns on 24-hour ABPM. We showed that increased degree of malnutrition is linked with non-dipper hypertension pattern.

Even though regulating patients' blood pressure is in the foreground in clinical practice, circadian blood pressure variation of these patients must be kept in mind. Malnutrition is usually an omitted diagnosis excluding geriatric patients, and it is known to be associated with many diseases. Assessment of malnutrition, and adequately treating it in hypertensive patients might help regulating blood pressure. Thus, hypertensive disease related complications might be prevented.

## CONCLUSION

Evaluation and treatment of malnutrition status in hypertensive patients might have an effect on regulating daily blood pressure variations.

## LIMITATIONS

As with the majority of studies, the design of the current study is subject to limitations. First, we couldn't evaluate patients whether they have orthostatic hypotension or autonomic dysfunction. This might complicate discrimination of dipper and non-dipper hypertension in elderly patients. The second limitation concerns the obstructive sleep apnoea, which couldn't have properly assessed in our population. Therefore, this might lead to misinterpretation of nighttime BP measurements. The last of our limitations is the high salt intake, we couldn't question our patients about their daily salt intake. That might have an effect on daily blood pressure variation. Thus, the findings of this study have to be seen in light of above-mentioned limitations.

**Ethics Committee Approval:** This study was approved by Kartal Lutfi Kırdar City Hospital Ethics Committee (514/192/60, Date: 30.12.2020).

**Informed Consent:** Informed consent was obtained.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept/Design - ÖA, UF, AK, SE, ST; Analysis/ Interpretation - AK, BU, BE, ZB; Data Collection - BU, BE, DÇ, CT; Writing - ÖA, BU, AK, ST, BE; Critical Revision - CK, NÖ, CD, ZB; Final Approval - UF, CK, NÖ, SE, ÖA; Statistical Analysis - AK, SE, CD; Overall Responsibility - All of authors.

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

**Financial Disclosure:** The authors declared that this study has received no financial support.

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