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Original Research / Özgün Araştırma

Does bladder wall thickness have a place in the evaluation of male patients with lower urinary tract symptoms?

Alt üriner sistem semptomları olan erkek hastaların değerlendirilmesinde mesane duvar kalınlığının yeri var mıdır?

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Özet

Amaç: Mesane duvar kalınlığının (MDK), alt üriner sistem semptomları (AÜSS) olan erkek hastalarda, Uluslararası prostat semptom skoru (IPSS) ve üroflowmetri parametreleri ile ilişkisinin olup olmadığını araştırmaktır.

Gereç ve Yöntemler: Üroloji polikliniğine Haziran 2021- Ocak 2022 tarihleri arasında AÜSS ile başvuran erkek hastaların prostat spesifik antijen (PSA), prostat volümü, işeme sonrası rezidü idrar (PVR), IPSS, Maksimum akış hızı (Qmax), Ortalama akış hızı (Qort), üroflowmetri, MDK değerleri ve intravezikal prostatik protrüzyon dereceleri (İPP) kaydedildi. Hastalar MDK açısından 2 gruba ayrıldı (Grup: 1 MDK < 5 mm; Grup 2: MDK ≥ 5 mm). Bu iki grup arasındaki başlangıçta kaydedilen değerler arasındaki fark analiz edildi.

Bulgular: Dahil edilen 110 hastanın (Grup 1:65, Grup 1:45) ortanca yaşı 56.5(15); ortanca MDK 4.25(3.60) idi. Her iki grup arasında PSA, prostat volümü, üroflow toplam akım miktarı, Qmax, Qort, IPSS ve IPP değerleri istatistiksel anlamlı farklı bulundu. Her iki grup arasında yaş ve PVR değerleri benzer bulunmuştur. Mesane duvar kalınlığı ile IPSS ve Qort değerleri arasında güçlü, Qmax değeri arasında çok güçlü korelasyonel ilişki tespit edilmiştir.

Sonuç: Mesane duvar kalınlığı, üroloji pratiğinde IPSS ve üroflowmetri değerlerinin tahmini için kullanılabilen basit bir sonografik ölçümdür.

Anahtar Kelimeler: mesane duvar kalınlığı, alt üriner sistem semptomları, ultrasonografi

Abstract

Objective: To investigate whether bladder wall thickness (BWT) is associated with The International Prostatic Symptom Score (IPSS) and uroflowmetry parameters in male patients with lower urinary tract symptoms (LUTS).

Material and Methods: Prostate volume, prostate specific antigen (PSA), post-void residual (PVR) urine volume, IPSS, maximum and average urinary flow rates (Qmax, Qave), BWT and intravesical prostatic protrusion (IPP) grades of male patients who applied to the urology outpatient clinic with LUTS between June 2021 and January 2022 were recorded. .Patients were divided into 2 groups in terms of BWT (Group: 1 BWT < 5 mm; Group 2: BWT ≥ 5 mm). We compared IPSS, PVR, PSA, Qmax, Qave, prostat volume and IPP grades between two groups.

Results: A total of 110 patients were included in the study (Group 1: n= 65, Group 2: n=45). Median(IQR) age, and median BWT values of the patients were 56.5(15) years, and 4.25(3.60) mm, respectively. PSA, prostate volume, total urine volume, Qmax, Qave, IPSS and IPP values were found to be statistically different, while age and PVR were similar between two groups. In addition, a strong correlation was found between BWT and IPSS- Qave, and a very strong correlation between BWT and Qmax.

Conclusion: BWT is a simple sonographic measurement that can be used to estimate IPSS and uroflowmetry parameters in urology practice.

Keywords: bladder wall thickness, lower urinary tract symptoms, ultrasonography

The study was approved by Ethical Committee of Bursa Yüksek İhtisas Training and Research Hospital (Approval No: 2011-KAEK-25 2021/11-03 Date: 2021.11.17). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

INTRODUCTION

Lower urinary tract symptoms are a dynamic process that worsens with age. Although benign prostate enlargement is blamed for LUTS, disruption of bladder dynamics is responsible for most of the symptoms. Unless the bladder outlet obstruction is relieved, compensatory detrusor hypertrophy develops initially(1). If this compensatory mechanism is forced above its limits, renal decompensation and eventually renal insufficiency ensue.

Bladder outlet obstruction prevents voiding and is diagnosed by synchronized measurement of detrusor pressure and urine flow rate. The measurement of these dynamic parameters is made by urodynamic tests. However, since they are invasive, urodynamic investigations are avoided as much as possible and its application is recommended when conservative treatment methods fail. Since they cannot distinguish between detrusor hypoactivity and bladder outlet obstruction as is the case with urodynamic studies, uroflowmetry is one of the non-invasive tests frequently used in evaluating obstruction. When the threshold value is taken as 10 ml/sec, it has 70% specificity, 47% sensitivity, and 70% positive predictive value(2).

The idea of estimating bladder outlet obstruction with non-invasive imaging methods has been the subject of many studies. Prostatic configuration, intravesical prostatic protrusion, BWT, and ultrasonographically estimated bladder weight are the predictive parameters for obstruction as recommended in the European Association of Urology Guidelines to predict obstruction (1). Studies have shown that both BWT (3, 4) and IPP (5, 6) are associated with LUTS and bladder outlet obstruction. However, the level of evidence remains low due to the lack of standardization in threshold values.

In our study, we aimed to investigate whether BWT is associated with LUTS and uroflowmetry parameters in patients with LUTS.

MATERIAL AND METHODS

Ethics committee approval numbered 2011-KAEK-25 2021/11-03 was obtained for our study from the Ethics Committee of the University of Health Sciences Bursa Yuksek Ihtisas Training and Research Hospital. The study was conducted in two centers (University of Health Sciences Bursa Yuksek Ihtisas Training and Research Hospital and Nusaybin State Hospital). The study included male patients aged 40-90 years who applied to the Nusaybin State Hospital urology outpatient clinic between June 2021 and January 2022 with complaints of non-neurogenic LUTS. The study was conducted prospectively. Patients with a diagnosis of a bladder tumor, prostate cancer, history of bladder and prostate surgery or urethral stricture and a neurological disease were excluded from the study.

Age, medical treatment status, digital rectal examination findings, IPSS, PSA (ng/mL), uroflowmetry findings (Qmax (mL/sec), Qave (mL/sec)), ultrasonographically measured PVR (mL), BWT values (mm) and grades of IPP were recorded. All patients were using α-blockers, anticholinergics, 5-alpha reductase inhibitors, or a combination of these. The patients were divided into three groups according to IPSS as mild, moderate and severe LUTS.

Bladder wall thickness was measured transabdominally from the suprapubic region using a ultrasonograph with a convex 5–7 Mhz probe. Before uroflowmetry, measurements were made by a single clinician from the anterior wall when the patients felt urgent desire to pass urine. The thickness between the bladder mucosa and adventitia, which appears hyperechogenic, was measured(Figure 1,a-b). Calculation of the IPP grade was done by measuring the distance between the tip of the prostate median lobe and the bladder neck in the midsagittal plane by transabdominal USG while the bladder remained at the same level of distensio (Figure 1-c). The IPP was divided into 3 groups (< 5 mm grade 1, 5-10 mm grade 2, and >10 mm grade 3).

Patients were divided into two groups as having BWT<5 mm and ≥5 mm. The difference between LUTS and uroflowmetry parameters of the two groups was analyzed. In addition, the correlation between BWT and data used in the diagnosis of LUTS were analyzed.

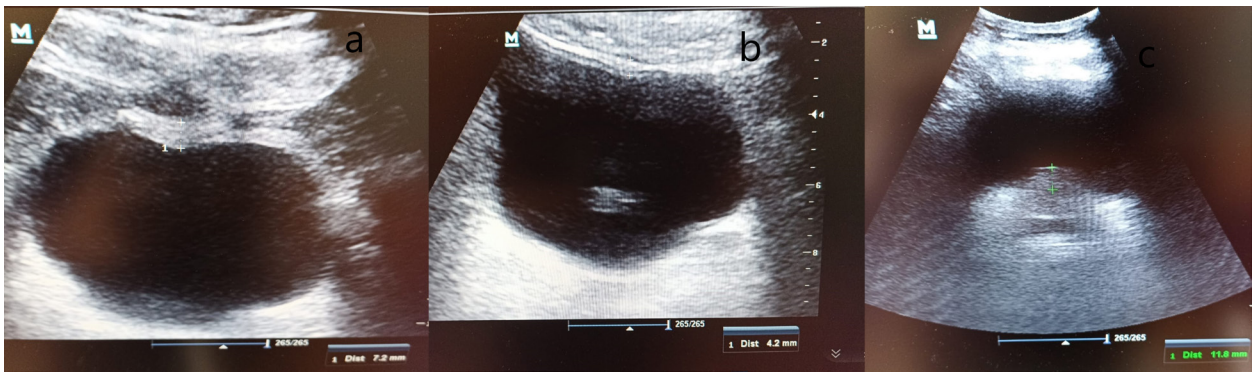

Figure 1. Ultrasonographic measurement of BWT and IPP in the transverse plane from the suprapubic area. a) The thickness of the anterior bladder wall that appears hyperechoic: 7.2 mm b) BWT of a patient with a lower IPSS: 4.2mm c) IPP measurement from the base of bladder: 11.8 mm(grade 3)

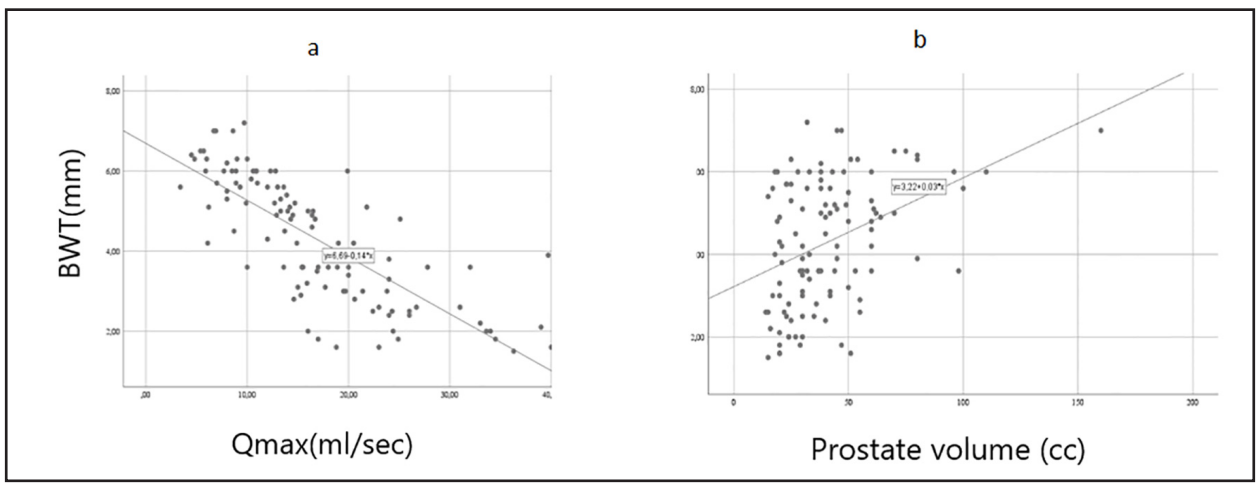

Figure 2. Relationship between bladder wall thickness and Qmax(a) and prostate volume(b)

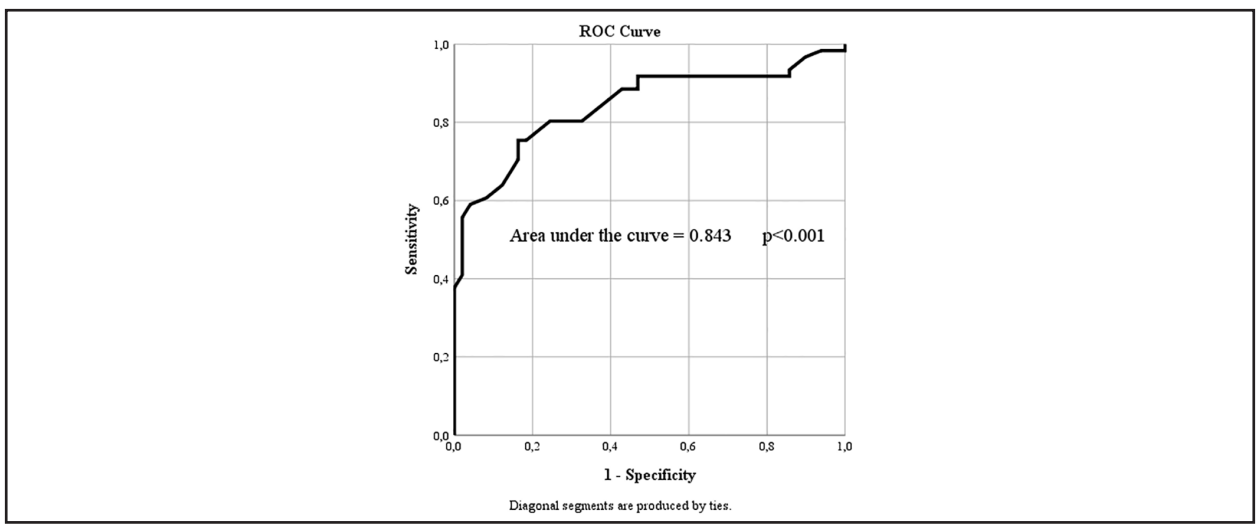

Figure 3. Roc curve analysis comparing bladder wall thickness and IPSS

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Normal distribution of the parameters was determined using analytical (Kolmogorov-Smirnov and Shapiro-Wilks analysis) and visual (histogram and probability graphs) methods. In descriptive statistics continuous variables were expressed as median (min-max) or mean±standard deviation while categorical variables in numbers and percentages. Mann-Whitney U test or Independent sample t test was used to compare the normally distributed continuous variables between the two groups. The difference between the categorical variables was calculated by the Fisher Exact test. Spearman Correlation test was used to investigate the correlation between bladder wall thickness and various parameters. A receiver operating characteristic (ROC) curve was applied to obtain the optimum cut-off value of bladder wall thickness in predicting severe IPSS. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 110 patients were included in our study. The mean age of the patients was 59.2 ± 9.3 years (median: 56.5 (15). Median(IQR) values for BWT 4.25(3.60) mm; total volume of voided urine 250.0(182.3) cc, Qmax 15.45(11.20) mL/sec, prostate volume 37(26) mL and IPSS 20.0(10.0) points were as indicated.

A total of 110 patients were included in Group 1 (n=65 ; 59%) and 2 (n=45 ; 41%) . There was no statistically significant difference between the two groups in terms of age and PVR. In the group with BWT ≥5 mm, PSA, prostate volume and IPSS were found to be significantly higher (p<0.05). Qmax, Qave and total volume of voided urine were found to be statistically significantly lower in the group with BWT 5≥mm compared to the group with BWT <5 mm (p<0.05). A significant difference was found between IPP grade and BWT (p<0.001) and BWT increased in line with IPP. While all of those with mild IPSS had BWT <5 mm, 86.7% of those with moderate and 36.1% of those with high had an BWT less than 5 mm. As IPSS increased, statistically significant increases were noted in BWT (p<0.001)(Table 1).

A statistically significant positive correlation was found between BWT and PSA, moderate correlations were detected between BWT, and prostate volume, BWT, and PVR, while a strong positive correlation was noted between BWT, and IPSS. A moderate correlation was observed between BWT and total volume of voided urine, and urine flow, while a very strong correlation between BWT, and Qmax and a strong negative and statistically significant correlation between BWT, and Qave were detected. There was no statistically significant correlation between age and BWT (p>0.05) (Table 2, Figure 2).

The area under the ROC curve was found to be statistically significant (0.843 with a confidence interval of 0.768-0.918), (p<0.001). When the BWT is 3.95 mm and above, the presence of higher IPSS can be predicted with 80.3% sensitivity, 75.5% specificity, 80.3 PPV and 75.5% NPV. When the BWT is 4.10 mm and above, higher IPSS indicating a severe bladder outlet obstruction can be predicted with a sensitivity of 78.7%, specificity of 77.6%, PPV of 81.4% and NPV of 74.5%. (Table 3) (Figure 3).

DISCUSSION

According to the guidelines, history, physical examination, symptom scores, urinalysis, PSA, and PVR measurement are recommended for diagnostic purposes in male patients with LUTS(1). Uroflowmetry is also recommended before medical or surgical treatment. Although the pressure flow study is thought to be the most useful method in the diagnosis of obstruction, it is recommended only in specific cases due to the lack of randomized controlled studies. Because urodynamic studies are invasive and can lead to various complications, many studies have been conducted to predict obstruction using non-invasive methods(7, 8). In our study, we showed that BWT is associated with LUTS and uroflowmetry parameters.

Because of methodological differences in studies and lack of standardization in measurements, the level of evidence for the use of BWT in the diagnosis of BPH is not strong enough for its inclusion in the guidelines. In their study evaluating the bladder neck obstruction using the urodynamic technique, Park et al. showed

Table 1. Comparison of two groups formed according to Bladder Wall Thickness in terms of parameters

	(BWT<5) mean±SD (n=65)	(BWT≥5) mean±SD n=45)	p
Age (year) median (IQR)	55.0(12)	63.0(18)	0.099**
PSA (ng/mL) median (IQR)	1.0(1.38)	2.05(3.1)	**0.002****
Prostate volume (cc) median (IQR)	30.0(24)	43.5(29)	**0.002****
Post voiding residual urine volume (mL) median (IQR)	30.0(50)	36.0(100)	0.204**
Total voiding urine volume (mL) median (IQR)	304.0(191.0)	217(155.0)	**0.001****
Qmax (mL/sec) mean±SD	21.4±7.6	10.3±4.0	**0001***
Qave(mL/sec) mean±SD	8.0±3.7	4.1±1.7	**0.001***
IPSS median (IQR)	16.0(8.0)	25.0(5)	**<0.001****
IPP, n (%)			
Grade 0 (<5mm)	57 (90.5)	6 (9.5)	**<0.001 ¥**
Grade 1 (5-10mm)	8 (30.8)	18 (69.2)	
Grade 2 (>10 mm)	-	21 (100.0)	
IPSS, n (%)			
Lower	4 (100.0)	-	**<0.001 ¥**
Mild	39 (86.7)	6 (13.3)	
High	22 (36.1)	39 (63.9)	

***SD:** Standart deviation *: t test in independent groups ** :Mann Whitney u **¥:** Fisher's Exact Test*
***PSA**: Prostate-specific antigen, **Qmax**: maximum urinary flow rate **Qave**: average urinary flow rate **IPSS**: International Prostatic Symptom Score **IPP**: Intravesical prostatic protrusion*

Table 2. Correlation between parameters and bladder wall thickness

(n=110)	Bladder Wall Thickness (mm)	
	r*	p
Age(year)	0.141	0.142
PSA (ng/mL)	0.332	**<0.001**
Prostate Volume (cc)	0.384	**<0.001**
Post voiding residual urine volume (mL)	0.271	**0.004**
Total voiding urine volume (mL)	-0.444	**<0.001**
Q max (mL/sec)	-0.826	**<0.001**
Q ave (mL/sec)	-0.668	**<0.001**
IPSS	0.733	**<0.001**

**: Spearman Correlation coefficient*
***PSA:** Prostate-specific antigen, **Qmax:** maximum urinary flow rate **Qave:** average urinary flow rate **IPSS:** International Prostatic Symptom Score*

Table 3. IPSS Prediction of Bladder Wall Thickness Evaluation of Strength

BWT (mm) Threshold value	Sensivity	Specifity	Positive Predictive Value	Negative Predictive Value
3.95	80.3	75.5	80.3	75.5
4.1	78.7	77.6	81.4	74.5

***BWT:** Bladder Wall Thickness*

that BWT and detrusor wall thickness (DWT) can be used in predicting bladder outlet obstruction in the patient group over 70 years of age(9). In this study BWT was measured after uroflowmetry. In their study Eze et al, found that mean PVR, IPSS, prostate volume and percentage of bladder emptying were statistically different between groups with BWT below and above 5 mm in symptomatic BPH patients(10). Azab and Elsheikh. evaluated the change in total IPSS, quality of life scoring, symptom scores, Qmax and PVR after 2 months of α-blocker therapy given to the patients in the study group. They found statistically significantly greater improvement in these values in the group with BWT <5 mm. Therefore, it was emphasized that BWT could be evaluated in determining the response to medical treatment (11). In their study, Karaköse et al. reported that BWT was significantly lower after alpha-blocker treatment. In addition, they found a significant difference in Qmax and PVR between the groups with BWT <5mm and ≥5mm, but not in terms of Qave, quality of life, PSA, prostate volume and IPSS(12).

As the bladder outlet resistance increases, the contraction force of the bladder increases. As the contraction force increases, detrusor hypertrophy occurs. Residual urine and increased pressure in the bladder cause edema and congestion in the interstitial space. With the combination of all these, an increase in BWT is observed. Detrusor hypertrophy contributes mostly to the increase in BWT. It may be possible to evaluate the development, progression of the disease and response to treatment of the disease by measuring the BWT with USG(13). Sonographically, hyperechoic mucosa and serosa of the bladder wall, while hypoechoic detrussor are seen. Although we measured all layers of the bladder wall in our study, only DWT was measured in some studies, considering that actually thickness of the detrusor muscle increased. For example, in their study including 102 patients, Kessler et al. measured detrusor wall thicknesses. They divided the patients into urodynamically obstructed, equivocal and non-obstructed groups. The mean detrussor wall thickness in the obstructed group was found to be statistically significantly higher compared to the eqivocal and non-obstructed groups. In addition, they found the cut-off value to be used in the diagnosis of obstruction as 2.9 mm (3). According to the authors, sonographically, the mucosa and serosa of the bladder wall appear hyperechoic which creates difficulties in distinguishing it from the surrounding tissues, and also leads to errors in making precise measurements of BWT.

The relationship between bladder wall thickness and LUTS was also investigated in other patient groups, such as female patients with symptoms of overactive bladder and pediatric patients with spina bifida.(14, 15). Blatt et al. included both genders in their study. According to the results of the study, BWT was not different between patient groups with bladder outlet obstruction, detrusor overactivity and normal urodynamics(16). Panayi et al included 379 female patients with lower urinary tract symptoms in their study. According to the classification of the International Continence Society, patients were divided into overactive bladder, stress urinary incontinence and mixed urinary incontinence groups. According to the analysis, mean BWT were significantly different in the stress urinary incontinence group compared to the mixed urinary incontinence and overactive bladder groups. They also reported that the group with daytime urinary frequency >7 had a greater mean BWT than the group with <7(17).

In similar research studies different ideas have been put forward about from where, and how to measure BWT, the device of the measurement, and the degree of bladder distension during measurements. In some studies, bladder wall thickness was measured when the bladder was not full(9), but the general consensus is that BWT decreases as bladder gradually distends. BWT reaches a plateau when bladder filling reaches 200-300 cc, or 46-60% of bladder capacity. Oelke et al. reported that BWT gradually decreased up to 250 cc of bladder filling, and then remained at the same level (13). Another question is related to the place of measurement BWT on the bladder wall. Although measurements are generally made from the anterior wall through the transabdominal route (18, 19), some authors measure BWT from several places and take their average (20). According to the report of the Incontinence-Research Society, the place where bladder wall

thickness is measured does not matter, entire bladder wall has the same thickness (13). On the contrary, in their study Anzia et al. measured BWT by MRI in both male ,and female patients, and, reported that there were differences in the values of bladder wall thickness depending on the place of measurements(21). Finally, the use of USG probes with higher Mhz is important in terms of detecting small changes. In our study, we made a single measurement with 5-7 Mhz USG from the anterior wall, through transabdominal route, when the patients felt urgent desire to pass urine before uroflowmetry.

Although our study emphasizes that BWT is closely related to IPSS and uroflowmetry parameters, it also has some limitations. First, diagnosis of bladder outlet obstruction of the patients was made with uroflowmetry test instead of pressure flow studies. Second, our study includes a small number of patients. Finally, measuring the bladder wall thickness during the patients' feeling of urgent desire to void urine may have resulted in measurement differences due to subjective nature of this approach.

CONCLUSION

According to the results of our study, BWT was found to be associated with IPSS and uroflowmetry parameters in male patients with LUTS. It can be used in daily urology practice as a non-invasive method for predicting the severity of symptoms and obstruction. Our results should be supported by studies with more patients in which the obstruction is evaluated urodynamically.

Conflict of Interest

The authors declare to have no conflicts of interest.

Financial Disclosure

The authors declared that this study has received no financial support.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethical Approval

The study was approved by Ethical Committee of Bursa Yüksek İhtisas Training and Research Hospital (Approval No: 2011-KAEK-25 2021/11-03), and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions

Conception and design; ÖE, SÇ, Data acquisition; ÖE, SZ, ÇB, Data analysis and interpretation; SZ, ÇB, Drafting the manuscript; ÖE, EB, Critical revision of the manuscript for scientific and factual content; ÖE, EB, Statistical analysis; EB, Supervision; SÇ, AG.

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