



# Efficacy and Safety of Prostate Radiofrequency Thermotherapy in Elderly Patients with BPO and Nocturia Resistant to Alpha-Blocker Therapy: An Observational Study

## Prostat Radyofrekans Termoterapinin Alfa Bloker Tedaviye Dirençli Noktürisi Olan BPO' lu Yaşlı Hastalarda Etkinliği ve Güvenliği: Gözlemsel Çalışma

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### ABSTRACT

**Aim:** The purpose of this study is to investigate the effectiveness of the prostate bipolar radiofrequency thermotherapy method on the complaint of nocturia and its safety in elderly patients.

**Material and Methods:** The post-procedural results of 100 patients over the age of 65 with complaints of refractory nocturia were examined. The patients' pre-procedural Qmax values, prostate volumes, post-void residual amounts, IPSS scores, frequency of nocturia, and associated quality of life questionnaire scores were recorded and compared with the results at the 3rd month after the procedure.

**Results:** The pre-procedural and post-procedural nocturia frequencies of the patients were consecutively 4.1 (2-13) times and 2.1 (0-10) times ( $p=0.002$ ). There were significant improvements in the N-QOL scores of the patients by  $1.70\pm 0.7$  and in their discomfort caused by voiding at night ( $p<0.001$ ). The mean QOL score of the patients before the procedure was 4.2 (1-4), whereas it was calculated as 2.5 (1-5) 3 months after the procedure.

**Conclusion:** It was observed that this treatment method provided a significant improvement in terms of nocturia in patients over the age of 65 and a positive effect on their quality of life. It is thought that it can be a more effective and safer method in comparison to treatments that can have side effects or are not suitable for elderly patients.

**Keywords:** Nocturia, elderly, radiofrequency, thermotherapy, prostate

### ÖZ

**Amaç:** Bu çalışmanın amacı yaşlı hastalarda bipolar radyofrekans prostat termoterapi yönteminin nokturi şikayeti üzerine etkinliğini ve güvenliğini incelemektir.

**Gereç ve Yöntemler:** Altmış beş yaş üstü ve dirençli nokturi şikayeti olan 100 hastanın işlem sonrası sonuçları incelendi. Hastaların, işlem öncesi Qmax, prostat volümleri, işeme sonrası rezidü miktarı, IPSS skorları, nokturi frekansı ve Nocturia Quality of Life sorgulama formu kaydedilip işlem sonrası 3. ay sonuçları ile karşılaştırıldı.

**Bulgular:** Nokturi sıklığı ortalama 4,1 (2-13) kez görülürken işlem sonrası bu sayı 2,1 (0-10)'ya geriledi ( $p=0,002$ ). N-QOL yaşam kalitesi formunda  $1,70\pm 0,7$  oranında ve gece idrara çıkmanın vermiş olduğu rahatsızlıklarda anlamlı iyileşme görüldü ( $p<0,001$ ). Hastaların işlem öncesinde yaşam kalitesi indeksi skoru ortalama 4,2 (1-4) iken üçüncü ayda 2,5 (1-5) olarak hesaplandı.



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**Sonuç:** Bu tedavi yönteminin 65 yaş üzeri hastalarda nokturi açısından anlamlı derecede iyileşme, hastaların yaşam kalitelerine pozitif yönde etki sağladığı görüldü. Yaşlı hastalarda yan etkisi olabilen veya kullanımı uygun olmayan tedavilere göre daha etkili ve güvenilir bir yöntem olabileceği düşünülmektedir.

**Anahtar Sözcükler:** Noktüri, yaşlı, radyofrekans, termoterapi, prostat

## INTRODUCTION

Nocturia is defined by the International Continence Society as the complaint of having to wake up once or multiple times at night to urinate (1). Studies have reported that waking up especially two or more times at night to urinate leads to a noticeable reduction in quality of life. Increases in this number are associated with decreased quality of life and increases in the prevalence of potential problems (2). In cases where it is experienced more than twice per night, it can cause an increase of more than 20% in the risk of falling and problems such as limb fractures, daytime dysfunction, depression and reduced work performance (3). Especially considering comorbidities in elderly patients, it was seen that waking up two or more times at night to urinate was associated with increased mortality, and there was a dose-response model with an increasing trend in mortality along with an increased frequency of nocturia (4).

Nocturia can be stated as the most common urinary complaint in inquiries (5). It is believed that the most significant pathology that leads to nocturia, which is seen at a higher rate than 50% in male individuals over the age of 70, is benign prostate obstruction (BPO). The reasons for this are shown as bladder outlet resistance, lower bladder capacity, increased postvoiding residue and storage symptoms that are seen in BPO (6). In this patient group, alpha blockers are insufficient, and in patients resorting to surgery, the most persistent symptom after surgery is nocturia. Additionally, it was reported that anticholinergics and desmopressin that are used in the treatment of nocturia have serious side effects in elderly patients (7). Therefore, in the treatment of nocturia in this group of patients, there is a need for a treatment modality that can be effective in both solving obstruction and improving storage symptoms, with a lower rate of side effects in comparison to medical and surgical treatments.

The transurethral prostate bipolar radiofrequency (RF) thermotherapy method is an easily applicable method that is implemented to reduce rate of treatment-related complications in patients at advanced ages and those with severe comorbidities and does not require anesthesia. This method is expected to not only eliminate obstruction but also improve storage symptoms associated with denervation caused by obstruction in elderly patients (8).

Today, it is thought that treatment options and related studies are insufficient in the treatment of nocturia for the elderly

patient group. In this study, our aim is to examine the effect of RF thermotherapy on nocturia and related quality of life in elderly patients with persistent nocturia.

## MATERIAL and METHODS

The results of patients who received transurethral bipolar RF thermotherapy treatment at Ordu University Urology Clinic between January 2020 and December 2022 were retrospectively analyzed. Ethics committee approval was obtained from the local ethics committee of the Ordu University (approval No. 2021/274). Written informed consent was obtained from all participants before the procedure.

The patients who underwent the procedure were followed up for 3 months. The study included patients over the age of 65 who had received alpha blocker treatment due to the diagnosis of BPO, did not have a sufficient response to the treatment, had the complaint of persistent nocturia ( $\geq 2$  voids/night) and wanted to get treatment due to this complaint. Procedure was administered to total of 117 patients, while 100 patients who attended their follow-ups were included in the study. The uroflowmetry test (mL/sec), prostate volume ( $\text{mm}^3$ ), postvoiding residue volume (PVR) (mL), International Prostate Symptom Score (IPSS), nocturia frequency (per night) and Nocturia Quality of Life Questionnaire (N-QOL) score values of the patients were measured and recorded before the procedure and three months after the procedure. The American Society of Anesthesiologists (ASA) scores of all patients were calculated (9).

Patients with maximum urinary flow rate ( $Q_{\text{max}}$ ) of lower than 15 mL/sec, the presence of nocturia affecting the life of the patient to significant extent, prostate volume of 30-100 mL were included. The prostatic urethra lengths of all patients measured with the abdominal ultrasonographic probe were below 50 mm. The patients were treated with the TEMPRO direx transurethral RF ablation system (Direx Medical Systems Ltd., Petah Tikva, Israel). After the local anesthetic gel application, a urethral catheter with a sensor at the tip is placed. Transurethral RF ablation treatment was applied for 1 hour at 55°C with the middle model gradient method. A Foley catheter was inserted for each patient for 5 days after the procedure.

The IPSS form is a current information form that questions the lower urinary tract complaints of patients with 7 questions. Nocturia Quality of Life Questionnaire (N-QOL) is a form consisting of 13 questions and created to understand the effects of nocturia on quality of life.

Comorbidities that may be associated with nocturia such as active urinary tract infection, obstructive sleep apnea syndrome, restless legs syndrome and insomnia, uncontrolled hypertension, heart failure, abnormal serum electrolyte values, previous urinary surgery, radiotherapy in the pelvic region, suspected neurogenic bladder dysfunction patients were excluded from the study.

**Statistical Analyses**

SPSS 21.0 program (IBM, Chicago, USA) was used for statistical analysis and one sample Kolmogorov-Smirnov test was used to determine the fit of variables to normal data. Normally distributed variables were used as mean±standard deviation, while without normally distributed variables were used as median (interquartile range). Paired t test and Wilcoxon single rank tests were used for statistical analysis. p<0.05 was accepted as a statistically significant value.

**RESULTS**

In our study, bipolar radiofrequency thermotherapy was applied to a total of 117 patients over the age of 65 with persistent nocturia. At the end of the study, the results of a total of 100 patients who could be followed up for 3 months were evaluated. The mean age of the patients was 76.27±12.18 years and the body mass index was calculated as 26.28±3.99 kg/m<sup>2</sup>. The median ASA score was 3.0±1.0 (median (interquartile range)) in pre-procedural risk assessments. All included patients had been using alpha blocker treatment for at least 4 weeks.

The Qmax value of the patients showed a significant increase in the 3<sup>rd</sup> month compared to the pre-procedure (p=0.030). No significant change was observed in P. Vol and PVR values after the procedure. (Table 1). The mean total pre-procedural and post-procedural IPSS scores of the patients were found consecutively as 18.7 (12-34) and 11.4 (10-27) (p=0.002). While there was a significant decrease in the patients' mean score in the 2<sup>nd</sup> item of IPSS that questions the urge of urinating within 2 hours, there was

no significant difference in their mean score in the 4<sup>th</sup> item questioning the difficulty of resisting the urge to urinate. A significant improvement was observed in the mean quality of life (QoL) index score before the procedure in all patients at 3 months (Table 2).

While the mean frequency of nocturia was 4.1 (2-13) before the procedure, this frequency decreased significantly and was found to be 2.1 (0-10) times after the procedure (p=0.002). With this decrease in nocturia, in general, there was a statistically significant decrease by 1.7±0.7 in the mean N-QOL score of the patients (p<0.001). Among the daytime dysfunctions of the patients expected to develop in relation to nocturia, the frequencies of their difficulty in concentrating during the day and their feelings of lower energy were marked as 'most days' before the procedure, while these frequencies significantly decreased to the level of 'rarely' after the procedure (p<0.001). Complaints of having to sleep during the day and decrease in productivity also decreased statistically from 'most days' to 'rarely' (p<0.001). The rate of patients participating less in their favorite activities decreased from 'quite often' to 'moderate' (p<0.001). While the patients' attention to when or how much fluid they consumed was 'most days', it was determined as 'sometimes'. It was determined that the complaint of difficulty in getting enough sleep at night, which is one of the highest grade complaints and seen as 'every night', regressed to 'some nights' after the procedure (p<0.001). Significant regression in the patients' concerns about themselves, their environment and treatment caused by nocturia, and significant improvements in their nocturia-related quality of life were observed. In general, the patients' discomfort due to getting out of bed to urinate significantly decreased from the mean 'extremely' and 'quite a bit' to 'moderately' and 'a little bit' (p<0.001). While the fear of waking up at night due to the need to urinate was 'most days', it was detected as 'sometimes' after the procedure. Concerns that the situation on this subject would worsen in the future and that there was no effective method in its treatment decreased from

**Table 1:** Prostate volume, Qmax and post-voiding residual volume.

Parameters		Findings (n=117)	p
P. Vol (mm <sup>3</sup> ±SD)	Before	42.39±19.7	
	3 <sup>rd</sup> month	39.57±22.6	0.866
Qmax (mL/sec±SD)	Before	9.41±2.16	
	3 <sup>rd</sup> month	14.20±4.27*	<b>0.030</b>
PVR (mL±SD)	Before	82.6±31.7	
	3 <sup>rd</sup> month	56.9±29.5*	<b>0.041</b>

\* = Statistically significant (Paired t test)

**P.Vol:** prostate volume, **Qmax:** maximal uroflow rate, **PVR:** Post-voiding residual volume

**Table 2:** IPSS scores, Quality of Life score, Nocturia frequency.

IPSS	Before median (Q1-Q3)	3 <sup>rd</sup> month median (Q1-Q3)	P
Total	18.7 (12-34)	11.4 (10-27)*	<b>0.002</b>
Q2	2.58 (1-5)	1.87 (0-5)*	<b>0.021</b>
Q4	2.75 (0-4)	2.58 (0-5)	0.653
QoL	4.2 (1-4)	2.5 (1-5)*	<b>0.021</b>
Nocturia frequency	4.1 (2-13)	2.1 (0-10)*	<b>0.002</b>

\* = Statistically significant (Wilcoxon Sign Rank test)

**IPSS:** International prostate symptom score, **QoL:** Quality of life score

'quite' to 'moderately' in the 3<sup>rd</sup> month ( $p<0.001$ ). In the last 2 weeks, the patients' discomfort in getting out of bed at night for nocturia decreased from 'too much' to 'moderately'.

The patients' overall quality of life assessment improved from 'poor' to 'good' at 3 months after the procedure ( $p<0.001$ ). Regarding complications related to the RF thermotherapy procedure, only 6 patients experienced pain during the procedure, whereas 21 patients felt pain and discomfort due to the probe inserted after the procedure. No life-threatening complication was encountered in any patient.

## DISCUSSION

In our study, in elderly patients over the age of 65 who were diagnosed with BPO and had the complaint of persistent nocturia, it was observed that the RF thermotherapy procedure was significantly effective on nocturia. A statistically significant improvement was achieved in the effect of nocturia on the quality of life of the patients. The procedure provided a reduction in the nocturia-related difficulty of patients to concentrate, their need to sleep during the day, and their feelings of low energy. By getting more sleep at night with the reduction in the frequency of nocturia, there was an increase in the daytime social performance of the patient, whereas a reduction was seen in their disturbing thoughts related to the disease. Positive changes were observed in the quality of life of the patients after the procedure. Moreover, the procedure provided a decrease in the concerns of the patients about nocturia and the treatment of nocturia.

Nocturia is considered the most prevalent and distressing urinary symptom (10). It is seen at all ages in both sexes, and there is an increase in its prevalence especially by aging. While it is seen at rates up to 17% before 40 years of age, these rates reach up to 59% at older ages (11). Furthermore, as 25% of patients see nocturia as a natural outcome of aging, it is believed that the actual rate is higher than what is being reported (12). In the elderly population, it is seen more frequently in men, and the reason for this was reported as BPO. In the elderly patient group in general, the most significant cause of nocturia is BPO, and the most unpleasant BPO-related symptom in elderly patients is nocturia (6). It is an important cause of morbidity and mortality that threatens life due to the problems it may cause in patients at advanced ages, and it leads to severe deteriorations in the quality of life depending on the patient's frequency of waking up at night to urinate (13). In the elderly who experience nocturia more than 2 times at night, falls are observed at a rate of 5.8%, fractures occur at 7.2%, the condition causes sleep and mood disorders, and it increases the risks of fragility in the elderly (14). In our study, we observed a significant reduction in the frequency of the patients to urinate at night, and in relation to this, there was a decrease in the concerns and anxieties of the patients, an increase in the concentration of the patients and their par-

ticipation in social activities during the day, and a significant improvement in their sleep quality at night ( $p<0.001$ ).

Studies examining the etiology of nocturia in elderly male patients have reported the most prevalent causes as BPO and associated lower urinary system complaints (15). In addition to voiding complaints related to BPO, storage symptoms are frequently seen in patients over 65 years of age. With obstruction, detrusor muscle hypertrophy and increased collagen synthesis are observed in the bladder. After this, hypertrophy is seen in the afferent and efferent nerve fibers in the bladder and the urethra (16). New reflex pathways start to develop through the C fibers with the disruption of the spinal reflex mechanisms, and in combination with other anatomical changes, disorganization occurs in bladder functions. A significant decrease in the functional capacity of the bladder is observed (17). As a result of the increase in the physiological formation of urine throughout aging, the load on the bladder increases even further, while a large part of the daily urinary output of these patients is formed at night (18). Considering the treatment of BPO and associated symptoms in terms of nocturia, alpha blockers and 5-alpha-reductase inhibitors are highly inadequate against nocturia. It is known that mostly storage problems and nocturia persist in patients after these treatments (19). In studies conducted with anticholinergic agents, it has been reported that they are weaker and insufficient against nocturia compared to storage symptoms. Additionally, they were reported to have side effects in patients over the age of 65 varying from dry mouth to severe cardiac and neurological problems (20). It was stated that the effect of mirabegron, which is another recently used agent against storage symptoms, against nocturia is low (21). In studies conducted with alpha blockers and anticholinergic medications in combination, it has been seen that they are more effective in these combinations than their use alone, but they do not provide the resolution of nocturia (22). Another agent utilized in the treatment of nocturia, desmopressin, is not recommended for use in patients over the age of 65. The reasons for this were reported as a reduction in the response to desmopressin with age, metabolic insufficiencies, and the potential formation of hyponatremia (23). In BPO cases, the surgical removal of the obstruction is superior to medical treatments. However, although improvement is seen in patients after their prostatectomy, this effect was found to be limited (24).

If we look at all these treatment modalities together, it is seen that their effects are exerted usually on urinary symptoms or storage symptoms. However, considering the changes that may lead to nocturia, there is a need for a treatment modality that both aims to eliminate the obstruction and functions as an anticholinergic therapy that can cause inhibition in the bladder (25). At the same time, methods that are suitable for the elderly patient group over the age of 65

and safe in terms of their side effects are also needed. RF thermotherapy method has a significant effect on relieving the obstruction due to coagulation necrosis that develops with vascular thrombosis in the prostate parenchyma. In our study, significant improvements were seen in Qmax value and IPSS scores. Studies have determined that the surgical elimination of obstruction has an effect on nocturia, but this effect is not on a sufficient level (26). The difference of this study from other studies is that we investigated whether RF thermotherapy had an additional advantage against nocturia by utilizing the denervation effect it creates in addition to the elimination of obstruction. With coagulative necrosis developing after this procedure, denervation and axon loss are also observed, and this loss has an inhibitory effect on the muscle tissue (9). Studies have proposed the idea that afferent and efferent neuron damage in regions close to the prostatic lodge, urethra and trigone where irreversible nerve damage is seen may be effective in reducing the complaint of nocturia (27). While the mean frequency of nocturia in the patients in our study was 4.1 (2-13) times per night before the procedure, it significantly decreased after the procedure and was found as 2.1 (0-10) ( $p=0.002$ ). According to the N-QOL scores of the patients, the procedure reduced their complaints about difficulty in getting enough sleep at night, lowered the levels of their concerns about waking up at night to urinate and led to a noticeable decrease in their discomfort associated with nocturia. Overall, it has been observed that there is a significant increase in the quality of life of patients after the procedure. This method is considered a very safe option that is nonsurgical, does not require anesthesia, is a one-day treatment and can be easily implemented (28). In our study, only 6 patients experienced pain in the infrapubic area during the procedure, while 21 patients experienced pain and discomfort associated with the probe that was inserted following the procedure. Considering the side effects, its importance in terms of suitability in the elderly patient group can be understood.

The study was carried out as a single center and did not include a control group, and the 3-month follow-up of the patients was examined. There is no pre-procedural urodynamic examination of the patients. Since the patients included in the study were patients with moderate LUTS complaints, the study does not represent patients with severe LUTS complaints. These are considered as limitations of the study. In order to see the effects of RF thermotherapy on nocturia, studies with increased sample size and multicenter studies are needed.

Nocturia continues to be a serious problem for patients over 65 years of age. New treatment modalities are needed for refractory nocturia associated with lower urinary tract complaints in elderly patients. RF thermotherapy can be con-

sidered as an alternative minimally invasive option as a method that can be safely applied in elderly patients with its effect on the frequency of nocturia.

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#### Author Contributions

Concept: **Ahmet Yuce**, Design: **Ahmet Yuce, Ibrahim Yazici**, Data collection or processing: **Ahmet Yuce, Abdullah Cirakoglu**, Analysis or Interpretation: **Erdal Benli, Ismail Nalbant**, Literature search: **Ahmet Yuce, Ibrahim Yazici**, Writing: **Ahmet Yuce**, Approval: **Erdal Benli, Abdullah Cirakoglu, Ismail Nalbant**.

#### Conflicts of Interest

The authors declare no conflict of interest.

#### Financial Support

None to declare.

#### Ethical Approval

The present study was approved by the Ethics Committee of Ordu University (approval No. 2021/274). Written informed consent was obtained from all participants before the procedure.

#### Review Process

Extremely peer-reviewed and accepted.

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