Bipolar radiofrequency thermotherapy vs. transurethral resection of the prostate: Effect on nocturia as a result of benign prostatic obstruction

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Abstract

Introduction: The purpose of this study was to investigate and compare the effects of radiofrequency thermotherapy (RF) thermotherapy and transurethral resection of the prostate (TURP) on nocturia and associated quality of life in patients diagnosed with benign prostatic obstruction (BPO) under medical treatment who have complaints of persistent nocturia.

Methods: The results of patients who underwent RF thermotherapy and TURP procedures between February 2019 and February 2022 were examined, and their three-month results were compared based on their uroflowmetry values, International Prostate Symptom Score (IPSS) values, nocturia frequency, and Nocturia Quality of Life Questionnaire scores.

Results: While the frequency of nocturia in the RF thermotherapy group that was 4.5±1.6 before the procedure decreased to 2.3±1.4 after the procedure (p=0.002), this value in the TURP group decreased from 5.1±2.42 to 3.9±2.1 (p=0.044). RF thermotherapy was found to be more effective than TURP (p<0.005). Significantly more...
noticeable improvements were observed in most nocturia-related next-day complaints and nocturia-related concerns in the RF thermotherapy group than the TURP group.

**Conclusions:** It was observed that RF thermotherapy had a more acceptable effect on obstructive complaints in comparison to TURP, and it could be more effective on nocturia and associated quality of life. RF ablation treatment may be offered as an appropriate option to treat nocturia complaints in suitable patients.

**Introduction**

Nocturia is defined as the need of a person to wake up at night once or multiple times to urinate. The higher the frequency of nocturia is, the higher its effects on quality of life and the emergence of associated problems will be. It was reported that especially in elderly patients, urinating at night more than twice may lead to problems such as falling in the dark, limb fractures, depressive mood the next day, and reduced productivity. Nocturia is stated to be the most distressing and treatment-resistant symptom among lower urinary tract symptoms (LUTS). It was stated that it is at a higher rate than 50% in men of advanced age, and in this patient group, nocturia is mostly related to benign prostate obstruction (BPO). Due to bladder outlet resistance, increased amounts of residue urine and changes in the detrusor muscle that are observed in BPO, it is the most frequently observed permanent complaint after both medical and surgical treatments. Medical treatments for nocturia remain inadequate, and a reduction in the frequency of nocturia is more noticeable, especially after surgical treatments. In comparison to alpha-blockers and other medical treatments, transurethral resection of the prostate (TUR-P) is seen as a superior treatment in terms of nocturia response. However, it is thought that the reduction in nocturia frequency achieved with TUR-P is not sufficient. Therefore, for BPO-related nocturia, in addition to existing treatments, there is a need for new treatment methods.

The transurethral bipolar radiofrequency (RF) thermotherapy method not only reduces bladder outlet resistance with its coagulative necrosis and denervation effects on prostate tissue and surrounding tissues but also shows an inhibitory effect on detrusor functions through denervation. Studies conducted with BPO patients have shown that it is not as effective as TUR-P in the removal of the obstruction. However, it was reported that it is more effective on storage complaints due to its denervation effect that distinguishes it from TUR-P. Regarding its effects on nocturia, there are still lacking data in the literature. Today, there are not enough studies in the elderly patient group about treatment options for BPO-related nocturia, and especially the effects of minimally invasive methods. As the first example in the literature, the purpose of this study is to investigate the outcomes of the TUR-P and transurethral bipolar radiofrequency thermotherapy methods in patients who have received at least 4 weeks of alpha-blocker treatment but continue to have persistent nocturia complaints and compare their 3-month results in terms of nocturia frequency and nocturia-related quality of life.
Methods
In this study, the results of patients who presented to the Urology Clinic of Ordu University between February 2019 and February 2022 and underwent transurethral bipolar RF thermotherapy and TUR-P procedures were prospectively recorded and retrospectively examined. This study was performed according to the Declaration of Helsinki and approved by local ethics committee of the Ordu University, Turkey. (approval No. 2022/31). All participants provided written informed consent before participating in this study. Before the procedures, the patients were given detailed information about TUR-P and RF thermotherapy procedures, and the groups were planned accordingly. It was aimed to examine both obstructive and nocturia and related complaints between both groups. The measurements and records of the patients were taken by the same physician. All patients were called to follow-ups at the 3rd month after the procedures. The study included patients who had received alpha-blocker treatment due to BPO for at least 1 month but required surgical treatment, had persistent nocturia (≥2 voids/night) and wanted to be treated for this complaint. The uroflowmetry results, prostate volumes (P.vol), residue urine volumes after voiding (PVR), international prostate symptom scores (IPSS), nocturia frequencies, and Nocturia Quality of Life Questionnaire (N-QOL) scores of the patients were measured and recorded before and after their procedures.

The study included patients with nocturia complaints that affected their lives severely, a maximum urinary flow rate (Qmax) under 15 ml/sec, a prostate volume in the range of 30-100 ml, and a prostatic urethra length (from the bladder neck to the verumontanum) shorter than 50 mm. The procedure was performed on the patients with the TEMPRO direx transurethral thermotherapy radiofrequency ablation system. Before the procedure, under local anesthesia applied to the urethra, an applicator attached to a silicone-covered probe with a diameter of 16 Fr (5.5 mm) that had 3 different sensors for different parts of the prostate was inserted into the urethra of the patient. The transurethral bipolar radiofrequency ablation treatment was performed on each patient with the middle model gradient method at 55°C for 1 hour. After the TUR-P and RF thermotherapy procedures, the patients used Foley catheters for 5 days.

The IPSS form is a current questioning form that is used to examine lower urinary tract complaints in patients. It is a fast and validated test that also questions quality of life index values while questioning the obstructive voiding complaints and nocturia frequencies of patients. Consisting of 13 items, the Nocturia Quality of Life Questionnaire (N-QOL) is the most frequently used validated form to understand the effects of nocturia-related daytime and nighttime symptoms on the patient’s quality of life.

Based on the exclusion criteria of the study, patients with active urinary tract infections, urinary incontinence, conditions requiring urodynamic examination related to lower urinary tract complaints, uncontrolled hypertension, serum sodium levels of <135 mM/L, clinically significant irregularities in serum potassium and creatinine values, comorbidities that could affect nocturia (e.g., insomnia, obstructive sleep apnea syndrome, restless leg syndrome), a history of prostate surgery, suspected bladder dysfunction with neurogenic origins, of a history of radiotherapy in the pelvic region were not included.
Statistical analysis
Statistical analyses used SPSS 21.0 (IBM, Chicago, USA). The one simple Kolmogorov-Smirnov test was used to determine the fit of variables to normal data. Variables with normal distribution are given as mean±standard deviation, while variables without normal distribution are shown as median±interquartile range. For statistical analysis, the Mann-Whitney U test and Wilcoxon rank test were used. A value of p<0.05 was accepted as statistically significant. The effect size in this study was calculated using the Cohen (2013) criteria. For the simple effect size of intragroup and intergroup comparisons, with the alpha value of 0.05 and statistical power of 0.80, the recommended sample size was calculated as approximately 106 (n=53+53) (this value was obtained using the G*Power 3.1 software). Our study sample includes 204 (102+102) patients.

Results
In the sample of the study, there were 102 patients who received bipolar RF thermotherapy and 102 patients who received TUR-P procedures. The mean age of the RF thermotherapy group was 75.81±11.34 (66-93) years, and the mean age of the TUR-P group was 72.68±12.51 (65-88) years (p=0.514). The mean BMI values were found as 26.63±3.47 (18.4-31.7) kg/m² in the RF thermotherapy group and 23.56±4.84 (18.5-30.2) kg/m² in the TUR-P group (p=0.31). The median ASA score of both groups was similarly calculated as 3.0±1.0 (median±IQR) (p=0.72).

In the RF thermotherapy group, while the mean Qmax value was 9.3±3.1 (ml/sec) before the procedure, it was calculated as 14.2±3.2 (ml/sec) after the procedure, which was significantly higher (p=0.034). There was no statistically significant difference between the prostate volumes measured before the procedure as 53.8±26.6 cm³ and after the procedure as 45.4±21.3 cm³ (p=0.79). On the other hand, the PVR value measured as 84.5±36.2 ml before the procedure was measured as 58.9±33.5 ml after the procedure, and the second measurement was significantly lower (p=0.046). The mean total IPSS value of the patients significantly fell from 17.5±6.3 to 11.8±4.1 (p<0.001). In the IPSS values, the mean score of the 2nd question about storage symptoms significantly declined from 2.61±1.5 to 1.92±1.1 (p=0.028). There was no significant difference in the mean score of the patients in the 4th question about difficulty in postponing urination (p=0.854) (Table 1).

In the TUR-P group, while the mean Qmax value was 8.6±2.5 ml/sec before the procedure, it was calculated as 19.6±5.4 ml/sec after the procedure, which was significantly higher (p<0.001). There was a significant decrease in the PVR values after the procedure (p=0.014). As opposed to the case in the RF thermotherapy group, there was a significant reduction in the prostate volumes of the patients in the TUR-P group (p=0.02). The mean total IPPS of 21.7±6.1 before the procedure significantly decreased to 8.7±4.3 (p<0.001). While there was a significant decrease in the mean score of the 2nd question in the IPSS form from 3.12±1.9 to 2.83±1.6 (p=0.045), there was no significant difference in the mean score of the 4th question (Table 2).

The mean frequency of nocturia in the RF thermotherapy group before the procedure was 4.5±1.6 times, whereas this number was found as 2.3±1.4 times after the procedure,
which was significantly lower (p=0.002). There was also a significant decrease in the mean frequency of nocturia in the TUR-P group from 5.1±2.4 times before the procedure to 3.9±2.1 times after the procedure (p=0.044). Nevertheless, the degree of reduction in the frequency of nocturia in the RF thermotherapy group was significantly higher than that in the TUR-P group (p=0.005). In the N-QOL form addressing nocturia-related quality of life, while difficulty in concentration during the day, need for sleep during the day, and reduced energy and productivity, which are next-day complaints, were seen ‘most days’ in the RF group before the procedure, they significantly decreased to the level of ‘rarely’ (p<0.001). Similarly, there were evident reductions in these complaints in the TUR-P group, but the responses after the procedure were usually as ‘some days’ (p=0.04). The improvement in these complaints was significantly higher in the RF thermotherapy group than the TUR-P group (p<0.001) (Figure 1). The changes in the improvement rates in terms of lowered productivity on the next day were not significantly different between the groups (p=0.57). The increase in the status of the patients to participate in the activities they like and the reduction in their concerns about when and how much they consumed fluids were more pronounced in the RF thermotherapy group compared to the TUR-P group (p<0.001). In comparison to the TUR-P group, the RF thermotherapy group had significantly lower levels of being occupied by thoughts of waking up at night (p=0.006), the worsening of the disease in time (p=0.002), and concerns about not being effectively treated for nocturia (p=0.003). The reductions in the extent to which they raised discomfort in other due to nocturia were similar between the two groups (p=0.55). The reduction in the discomfort of the patients associated with getting up from the bed at night and the general improvement in their quality of life were significantly more noticeable in the RF thermotherapy group than the TUR-P group (p<0.001).

Discussion
In this study, the effects of RF thermotherapy and TUR-P on nocturia and associated quality of life in patients diagnosed with BPO who were under medical treatment and had complaints of persistent nocturia. The frequency of nocturia in the RF thermotherapy group that was 4.5±1.6 times before the procedure decreased to 2.3±1.4 time after the procedure (p=0.002), while the frequency of nocturia in the TUR-P group decreased from 5.1±2.42 times to 3.9±2.1 times (p=0.044). Although both procedures were significantly effective in reducing the frequencies of nocturia among the patients, the RF thermotherapy procedure was significantly more effective than TUR-P (p<0.005). Similar results were seen in the effects of these procedures on the nocturia-related quality of life of the patients. More noticeable improvements were found in most of the nocturia-related next-day complaints of the patients in the RF thermotherapy group, as well as their nocturia-related concerns, in comparison to the TUR-P group. In general, there were significant improvements in the quality of life of the patients (Figure 2).

Among lower urinary system complaints in elderly men, nocturia is one of the most frequently observed and most distressing symptoms. It is still stated to be the most treatment-resistant urinary symptom with the existing treatment methods. In epidemiological studies, the prevalence of nocturia is stated as 49%, and this prevalence increases with age. It is seen
that this rate reaches 72% in men over the age of 60, and it becomes a serious health problem
that disrupts the patient’s quality of life. In the elderly who wake up more than twice at
night to urinate, clear increases are seen in the risk of falls, limb fractures, diurnal and
hormonal problems, sleep disorders, and mood disorders, resulting in severe risk of morbidity
and mortality. In our study, there were significant reductions in complaints such as limited
participation in social activities, low energy and concentration difficulties, which are nocturia-
related next-day symptoms, in both groups. Nonetheless, it was thought that the
improvements in the quality of life of the patients in the RF thermotherapy group were more
evident because there was a higher degree of decrease in the frequency of nocturia, as well as
a higher level of reduction in their scores in the second question of the IPSS form that is
concerned with voiding frequency (p<0.001).

Nocturia has a multifactorial etiology, but the most significant causes of nocturia in
men at advanced ages are stated as BPO and BPO-related LUTS. Studies about bladder
outlet resistance developing with BPO have reported hypertrophy in the detrusor muscle and
increased extracellular matrix and collagen synthesis levels. Moreover, hypertrophy
develops in the afferent and efferent nerve fibers in the detrusor muscle and the urethra.

Along with these changes, which result in disruptions in the spinal voiding reflex, new
reflex pathways and reactions develop with C fibers. Through all these muscarinic and
purinergic receptor expression changes, deterioration is observed in the contraction strength
of the detrusor muscle and the storage function of the bladder. Both the reduction in storage
function and the loss in contraction strength with bladder outlet obstruction cause severe
decreases in the functional capacity of the bladder.

In addition to these changes, the increasingly higher rate of urine formation at night
compared to daytime along with aging results in a higher load on the bladder at night, and it
strains the bladder that already has a deteriorated storage function even further in relation to
nocturia. For these reasons, eliminating the obstruction in these patients is a significant
intervention for reducing nocturia, but it is not sufficient by itself.

In our study, there was a higher degree of increase in the Qmax values of the TUR-P
group in comparison to the RF thermotherapy group, but no statistically significant difference
was found (p=0.11). Similarly, the PVR changes in both groups was found at a similar rate
(p=0.08). While the improvement in the IPSS values of the TUR-P group was more
pronounced (p<0.001). However, considering the effects of the two procedures on nocturia
response and nocturia-related quality of life after the procedures, it was seen that the RF
thermotherapy procedure was significantly more effective than TUR-P (p=0.005, p<0.001).
Previous studies have shown that nocturia response following TUR-P in BPO patients is
better compared to medical treatments involving agents such as alpha-blockers,
anticholinergics, and desmopressin. However, it has been shown that despite its better
outcomes than medical treatments, its nocturia response is inadequate.

It was reported that while improvements were seen in nocturia in patients who
underwent prostatectomy, similar to TUR-P, the effects were limited. It was found that the
obstructive complaints of patients decreased significantly after surgery, but symptoms like
nocturia were not sufficiently resolved due to the permanent detrusor overactivity developing
with obstruction.\textsuperscript{25} Therefore, in the treatment of nocturia, there is a need for a treatment modality that not only removes obstruction but also has an inhibitory effect on bladder functions like that of an anticholinergic agent.\textsuperscript{26} The transurethral bipolar RF thermotherapy method shows an inhibitory effect on muscle tissue with the vascular thrombosis and coagulative necrosis it causes in prostate tissue and regions close to the urethra and trigone, as well as its axon loss and denervation effects.\textsuperscript{27} Studies have reported that in addition to the effect of this method regarding the elimination of bladder outlet dysfunction, it may also be effective against nocturia because of afferent and efferent neuron damage seen in these regions.\textsuperscript{28}

It is accepted that the feature of RF thermotherapy that can make a difference in this patient group compared to the TURP procedure may be due to its denervation effect. Although there was an improvement in obstructive complaints as a result of both procedures, it is thought that the denervation effect is behind the higher rate of improvement in nocturia frequency in the RF thermotherapy group. For this reason, although the decrease in prostate volumes after the procedure was significantly higher in the TUR-P group than in the RF thermotherapy group (p<0.001), different results can be obtained compared to tissue resection due to the denervation effect.

In our study, while a significant reduction was seen in the frequency of nocturia from 4.5±1.6 to 2.3±1.4 times per day after the RF thermotherapy procedure (p=0.002), the procedure also provided satisfactory results, albeit not as satisfactory as the results of the TUR-P procedure. In the N-QOL form, there was a significantly higher degree of regression in next-day symptoms, sleep difficulties and nocturia-related concerns in the RF thermotherapy group compared to the TUR-P group.

As other nocturia-related symptoms, there was no significant difference between the two groups only in terms of next-day productivity and causing discomfort in others due to waking up at night because of nocturia. A possible reason for this may be the fact that our patients were over the age of 65, and they could have held different perspectives in their responses to these questions. The RF thermotherapy method may be considered as an important treatment modality as it does not have the potential side effects of medical agents used to treat nocturia in patients over the age of 65, it does not require anesthesia as the TUR-P procedure does, and it is a procedure that can be performed in outpatient clinic conditions.\textsuperscript{29,30}

This study had some limitations. While it was conducted at a single center, the patients were analyzed based on their 3-month outcomes. Broader and multi-center studies are needed to see the long-term effects of RF thermotherapy on nocturia.

Conclusions
Nocturia is seen as a highly prevalent and the most distressing urinary symptom in elderly male patients. The most frequently encountered cause of nocturia in this age group is BPO, and the transurethral bipolar RF thermotherapy method can be an appropriate option in its treatment for both eliminating the obstruction and showing effects on storage symptoms. In our study, it was seen that this method had acceptable effects on obstructive complaints.
compared to TUR-P, and it could be more effective on nocturia frequency and nocturia-related quality of life. RF ablation treatment may be an appropriate option for treating nocturia symptoms in eligible patients.
Radiofrequency thermotherapy vs. TURP for nocturia

References

Figures and Tables

Figure 1. RF: radiofrequency thermotherapy; TURP: transurethral resection of the prostate.
Figure 2. RF: radiofrequency thermotherapy; TURP: transurethral resection of the prostate.

Table 1. Distribution of demographic characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Groups</th>
<th>TURP (n=102)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>RF thermotherapy (n=102)</td>
<td>75.81±11.34</td>
<td>0.514</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>72.68±12.51</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>RF thermotherapy (n=102)</td>
<td>26.63±3.47</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>23.56±4.84</td>
<td></td>
</tr>
<tr>
<td>ASA score</td>
<td>RF thermotherapy (n=102)</td>
<td>3.0±1.0</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>3.0±1.0</td>
<td></td>
</tr>
</tbody>
</table>

ASA: American Society of Anesthesiology; RF: radiofrequency thermotherapy; TURP: transurethral resection of the prostate.
Table 2. Preprocedural and 3rd-month postprocedural values of patients who underwent RF thermotherapy

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>3-month</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.vol (cm³)</td>
<td>53.8±26.6</td>
<td>45.4±21.3</td>
<td>0.79</td>
</tr>
<tr>
<td>PVR (ml)</td>
<td>84.5±36.2</td>
<td>58.9±33.5</td>
<td>0.046+</td>
</tr>
<tr>
<td>Qmax (ml/sec)</td>
<td>9.3±3.1</td>
<td>14.2±3.2</td>
<td>0.034+</td>
</tr>
<tr>
<td>IPSS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>2.61±1.5</td>
<td>1.92±1.1</td>
<td>0.028+</td>
</tr>
<tr>
<td>Q4</td>
<td>2.68±1.4</td>
<td>2.53±1.6</td>
<td>0.854</td>
</tr>
<tr>
<td>Total</td>
<td>17.5±6.3</td>
<td>11.8±4.1</td>
<td>0.000**</td>
</tr>
<tr>
<td>QoL</td>
<td>4.1±1.7</td>
<td>2.6±1.5</td>
<td>0.031+</td>
</tr>
<tr>
<td>Nocturia frequency</td>
<td>4.5±1.6</td>
<td>2.3±1.4</td>
<td>0.002+</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.001. IPSS: International Prostate Symptom Score; PVR: postvoid residual; RF: radiofrequency thermotherapy; QoL: quality of life; Qmax: maximal flow rate.

Table 3. Preprocedural and 3rd-month postprocedural values of patients who underwent TUR-P

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>3-month</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.vol (cm³)</td>
<td>56.9±17.6</td>
<td>21.2±15.5</td>
<td>0.02*</td>
</tr>
<tr>
<td>PVR (ml)</td>
<td>82.6±27.7</td>
<td>43.9±26.2</td>
<td>0.014+</td>
</tr>
<tr>
<td>Qmax (ml/sec)</td>
<td>8.6±2.5</td>
<td>19.6±5.4</td>
<td>0.000**</td>
</tr>
<tr>
<td>IPSS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>3.12±1.9</td>
<td>2.83±1.6</td>
<td>0.045+</td>
</tr>
<tr>
<td>Q4</td>
<td>2.78±1.2</td>
<td>2.52±1.3</td>
<td>0.732</td>
</tr>
<tr>
<td>Total</td>
<td>21.7±6.1</td>
<td>8.7±4.3</td>
<td>0.000**</td>
</tr>
<tr>
<td>QoL</td>
<td>3.9±2.1</td>
<td>2.3±1.4</td>
<td>0.02*</td>
</tr>
<tr>
<td>Nocturia frequency</td>
<td>5.1±2.4</td>
<td>3.9±2.1</td>
<td>0.044+</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.001. IPSS: International Prostate Symptom Score; PVR: postvoid residual; RF: radiofrequency thermotherapy; QoL: quality of life; Qmax: maximal flow rate.