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.

KEY MESSAGES

- Nocturia is a serious cause of morbidity and mortality, especially in elderly patients.
- New treatments are needed due to the limited effects of existing treatments in elderly patients and the side effects of these options.
- Radiofrequency thermotherapy has a more acceptable effect on obstructive complaints in comparison to transurethral resection of the prostate and could be more effective on nocturia and associated quality of life.
- With its minimal side-effect profile and its effects on nocturia and related quality of life, transurethral bipolar radiofrequency ablation therapy may be an appropriate treatment method in this patient group.

Introduction

Nocturia is defined as the need to wake at night once or multiple times to urinate. The higher the frequency of nocturia, the higher its effects on quality of life (QoL) and the greater the emergence of associated issues.[1] 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.[2]

Nocturia is considered among the most distressing and treatment-resistant lower urinary tract symptoms (LUTS). It has been stated that it occurs at a higher than 50% rate in men of advanced age, and in this patient group, nocturia is mostly related to benign prostate obstruction (BPO).[3] Due to bladder outlet resistance, increased amounts of residue urine, and changes in the detrusor muscle observed in BPO, nocturia is the most frequently observed complaint after both medical and surgical treatments.[4]

Medical treatments for nocturia remain inadequate, and a reduction in the frequency of nocturia is more noticeable after surgical treatments. In comparison to alpha-blockers and other medical treatments, transurethral resection of the prostate (TURP) is seen as a superior treatment in terms of

response;[5] however, it is thought that the reduction in nocturia frequency achieved with TURP is still not sufficient.[6] Therefore, for BPO-related nocturia, there is a need for new treatment options.

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.[7] Studies conducted with BPO patients have shown that it is not as effective as TURP in the removal of the obstruction; however, it was reported that it is more effective on storage complaints due to its denervation effect, which distinguishes it from TURP.[8] Regarding its effects on nocturia, data are still in the literature.

Currently, there are not enough studies in the elderly patient group on treatment options for BPO-related nocturia, particularly on the effects of minimally invasive methods. The purpose of this study was to investigate the outcomes of the TURP and transurethral bipolar RF thermotherapy in patients who have received at least four weeks of alpha-blocker treatment but continue to have persistent nocturia complaints, and to compare their three-month results in terms of nocturia frequency and nocturia-related QoL.

Methods

Study cohort

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 TURP procedures were prospectively recorded and retrospectively examined. The study was performed according to the Declaration of Helsinki and approved by local ethics committee of the Ordu University, Turkey (No. 2022/31).

All participants provided written informed consent before participating in the study. Before the procedures, the patients were given detailed information about TURP and RF thermotherapy procedures, and the groups were planned accordingly. The uroflowmetry results, prostate volumes, postvoid residual (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. Patients were called to followup at the third month after the procedures and all measurements were taken by the same physician.

The study included patients who had received alpha-blocker treatment due to BPO for at least one month but required surgical treatment, had persistent nocturia (≥2 voids/night) and wanted to be treated for this complaint, 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.

Exclusion criteria included 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, or a history of radiotherapy in the pelvic region.

Procedures

RF thermotherapy was performed with the TEMPRO direx transurethral thermotherapy RF 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 three different sensors for different parts of the prostate was inserted into the patient's urethra. The transurethral bipolar RF ablation treatment was performed on each patient with the middle model gradient method at 55°C for one hour. After the TURP and RF thermotherapy procedures, the patients used Foley catheters for five days.

Measuring tools

The IPSS form is a questionnaire used to examine lower urinary tract complaints. It is a fast and validated test that questions QoL index values while also questioning the obstructive voiding complaints and nocturia frequencies of patients.

Consisting of 13 items, the 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.

Statistical analysis

Statistical analyses used SPSS 21.0 (IBM, Chicago, IL, U.S.). The one simple Kolmogorov-Smirnov test was used to determine the fit of variables to normal data. Variables with normal distribution are shown 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 için 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

There were 102 patients who received bipolar RF thermotherapy and 102 patients who received TURP. The mean age of the RF thermotherapy group was 75.81±11.34 (66–93) years, and the mean age of the TURP group was 72.68±12.51 (65–88) years (p=0.514). The mean body mass index values were found to be 26.63±3.47 (18.4–31.7) kg/m^2 in the RF thermotherapy group and 23.56±4.84 (18.5–30.2) kg/m^2 in the TURP group (p=0.31). The median American Society of Anesthesiologists (ASA) score of both groups was similarly calculated as 3.0±1.0 (p=0.72) (Table 1).

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 cm^3 and after the procedure as 45.4±21.3 cm^3 (p=0.79); however, PVR value, measured as 84.5±36.2 ml before the procedure, was measured significantly lower at 58.9±33.5 ml after the procedure (p=0.046). The mean total IPSS value of the patients in the RF thermotherapy arm significantly fell from 17.5±6.3 to 11.8±4.1 (p<0.001). Within the IPSS values, the mean score of the second 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 fourth question about difficulty in postponing urination (p=0.854) (Table 2).

In the TURP 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 — significantly higher (p<0.001). There was a significant decrease in PVR values after the procedure (p=0.014). There was also a significant reduction in prostate volume of the patients in the TURP group vs. the those in the RF thermotherapy group (p=0.02). The mean total IPPS of 21.7±6.1 before the procedure in the TURP group significantly decreased to 8.7±4.3 (p<0.001) after the procedure. While there was also a significant decrease in the mean score of the second 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 fourth question (Table 3).

Table 1. Distribution of demographic characteristics

Characteristics	Groups		
	RF thermotherapy (n=102)	TURP (n=102)	p
Age (years)	75.81±11.34	72.68±12.51	0.514
Body mass index	26.63±3.47	23.56±4.84	0.31
ASA score	3.0±1.0	3.0±1.0	0.72

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

	Before	3-month	p
Prostate volume (cm^3)	53.8±26.6	45.4±21.3	0.79
PVR (ml)	84.5±36.2	58.9±33.5	0.046*
Qmax (ml/sec)	9.3±3.1	14.2±3.2	0.034*
IPSS			
Q2	2.61±1.5	1.92±1.1	0.028*
Q4	2.68±1.4	2.53±1.6	0.854
Total	17.5±6.3	11.8±4.1	0.000**
QoL	4.1±1.7	2.6±1.5	0.031*
Nocturia frequency	4.5±1.6	2.3±1.4	0.002*

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

The mean frequency of nocturia in the RF thermotherapy group before the procedure was 4.5±1.6 times, whereas this number dropped to 2.3±1.4 times after the procedure (p=0.002). There was also a significant decrease in the mean frequency of nocturia in the TURP 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 TURP group (p=0.005).

In general, there were significant improvements in the quality of life of the patients in both groups (Figure 1).

In the N-QoL form, while next-day complaints such as difficulty concentrating, need for sleep, and reduced energy and productivity were seen "most days" in the RF group before the procedure, they significantly decreased to the level of "rarely" (p<0.001) afterwards. The improvement in these complaints was significantly higher in the RF thermotherapy group than the TURP group (p<0.001) (Figure 2).

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

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

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

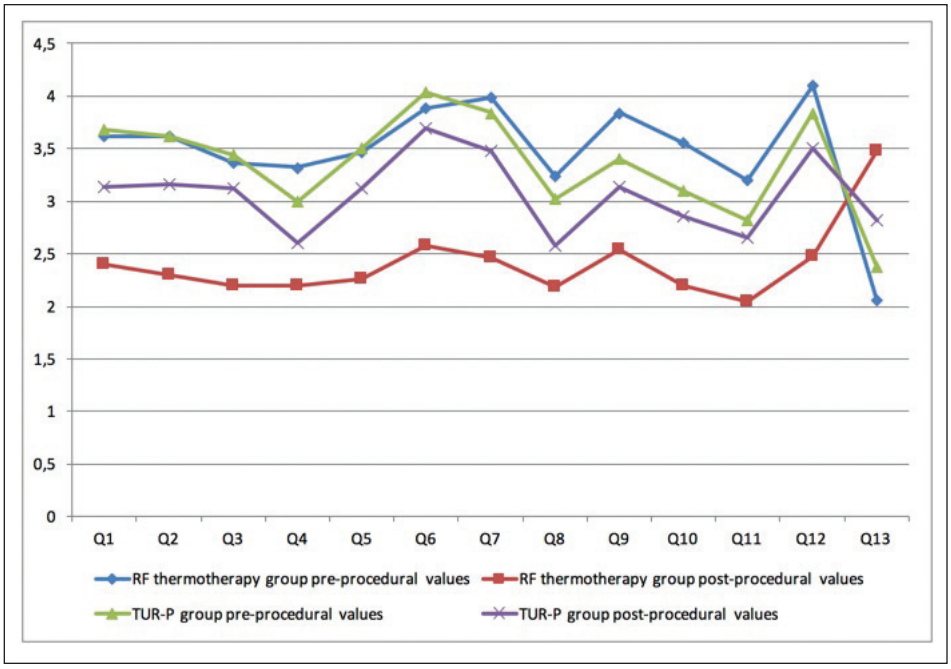

Figure 1. Quality of life (QoL) improved for patients in both the RF thermotherapy and TURP arms of the study, as shown in the QoL score before and after each procedure. RF: radiofrequency thermotherapy; TURP: transurethral resection of the prostate.

While there were evident reductions in these complaints in the TURP group, the responses after the procedure were most frequently "some days" (p=0.04). The changes in the improvement rates in terms of "lowered productivity" the next day were not significantly different between the groups (p=0.57); however, the increase in the patients being able to participate in the activities they like and the reduction of their concerns about when and how much they consumed fluids were more pronounced in the RF thermotherapy group compared to the TURP group (p<0.001).

In comparison to the TURP 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 others due to their 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 QoL were significantly more noticeable in the RF thermotherapy group than in the TUR-P group (p<0.001).

Discussion

Although both RF thermotherapy and TURP were effective in reducing the frequencies of nocturia among the patients in our cohort, the former procedure was significantly more effective (p<0.005). While similar results were seen in the effects of these procedures on the nocturia-related QoL of the patients, more noticeable improvements were found in most of the nocturia-related next-day complaints, as well as in patients' nocturia-related concerns, in the RF thermotherapy group in comparison to the TURP group.

Among lower urinary system complaints in elderly men, nocturia is one of the most frequently observed and most distressing symptoms. It is noted to be the most treatment-resistant urinary symptom with the existing treatment armamentorium.[9] In epidemiological studies, the prevalence of nocturia is calculated as 49%, and this prevalence increases with age.[10] This rate can be as high as 72% in men over the age of 60, and it becomes a serious health problem that disrupts the patient's quality of life.[11]

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.[12] 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 treatment groups. Nonetheless, it was thought that the improvements in the QoL 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 IPPS form (i.e., the section concerned with voiding frequency).

Nocturia has a multifactorial etiology, but the most significant causes of nocturia in men at advanced age are BPO

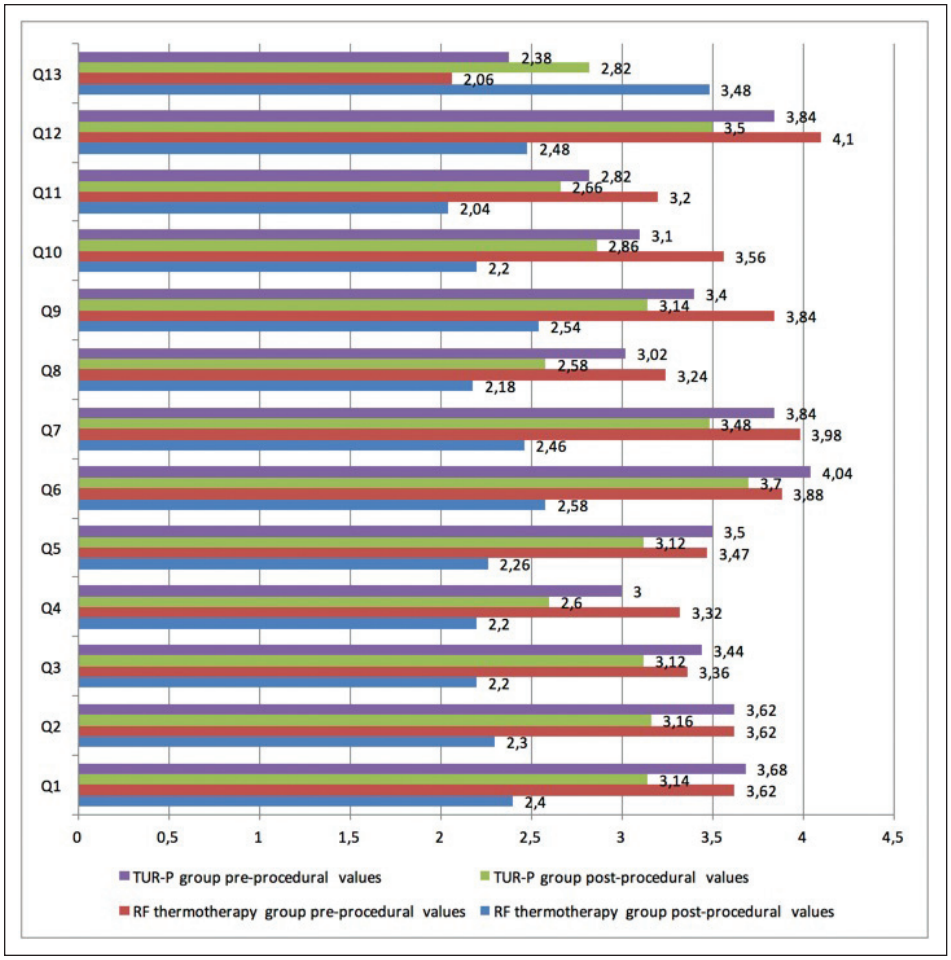

Figure 2. Rates of nocturia-related next-day complaints in patients before and after RF thermotherapy and TURP treatment. RF: radiofrequency thermotherapy; TURP: transurethral resection of the prostate.

and BPO-related LUTS.[13] Studies about bladder outlet resistance developing with BPO have reported hypertrophy in the detrusor muscle and increased extracellular matrix and collagen synthesis levels.[14] Moreover, hypertrophy develops in the afferent and efferent nerve fibers in the detrusor muscle and the urethra.[15]

Along with these changes, which result in disruptions in the spinal voiding reflex, new reflex pathways and reactions develop with C fibers.[16] 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.[17] 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.[18]

In addition, the increasingly higher rate of urine formation at night compared to daytime that occurs 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.[19] For these reasons, eliminating the obstruction in these patients is a significant intervention for reducing nocturia but it is not sufficient in and of itself.[20]

In our study, there was a higher degree of increase in the Qmax values of the TURP group in comparison to the RF thermotherapy group, but no statistically significant difference was found (p=0.11). Similarly, the PVR change in both groups was found to be at a similar rate (p=0.08). The improvement in the IPSS values of the TURP group was more pronounced (p<0.001); however, considering the effects of the two procedures on nocturia response and nocturia-related QoL after the procedures, we showed that the RF thermotherapy procedure was significantly more effective than TURP. Previous studies have shown that nocturia response following TURP in BPO patients is better compared to medical treatments involving agents such as alpha-blockers, anticholinergics, and desmopressin;[21] however, despite better outcomes than medical treatments, the nocturia response to TURP is still inadequate.[22,23]

It has been reported that while nocturia improvements have been seen in patients who undego prostatectomy for

BPO, similar to TURP, the effects are limited.[24] While the obstructive complaints of patients decreases significantly after surgery, nocturia is not sufficiently resolved due to the permanent detrusor overactivity developing with obstruction.[25] Therefore, in the treatment of nocturia, there is a need for a modality that not only removes obstruction but also has an inhibitory effect on bladder functions like that of an anticholinergic agent.[26]

The transurethral bipolar RF thermotherapy method shows an inhibitory effect on muscle tissue due to 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.[27] Studies have reported that in addition to RF thermotherapy's effect on bladder outlet dysfunction, it may also be effective against nocturia because of afferent and efferent neuron damage seen in these regions.[28] Although our study showed 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.

The RF thermotherapy method may be considered an important treatment modality in BPO patents experiencing nocturia, as it does not have the potential side effects of medical agents, it does not require anesthesia (as TURP does), and it is a procedure that can be performed in outpatient clinic.[29,30]

This study had some limitations, including its single-center setting and short-term (three months) followup. Broader and multicenter studies are needed to see the long-term effects of RF thermotherapy on nocturia.

Conclusions

Nocturia is a highly prevalent and 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 treatment option to eliminate the obstruction and have effects on storage symptoms. In our study, this method had acceptable effects on obstructive complaints compared to TURP and it was more effective in decreasing nocturia frequency and improving nocturia-related QoL. RF ablation treatment may be an appropriate option for treating nocturia symptoms in eligible patients.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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