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ORIGINAL ARTICLE

Longitudinal changes in erectile function after thulium:YAG prostatectomy for the treatment of benign prostatic obstruction: a 1-year follow-up study

Jae Seung Chung[1] · Sang Hyun Park[1] · Cheol Kyu Oh[1] · Seong Cheol Kim[1] · Taek Sang Kim[2] · Pil Moon Kang[2] · Won Ik Seo[3] · Wan Seok Kim[3] · Jang Ho Yoon[3] · Dong Il Kang[3] · Kweon Sik Min[3] · Jae Il Chung[3]

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Abstract This study aimed to evaluate the impact of thulium:yttrium-aluminum-garnet (Tm:YAG) (RevoLix®) laser prostatectomy for the treatment of benign prostatic obstructions on erectile function (EF). A total of 208 patients who underwent Tm:YAG laser prostatectomies participated in this study. All cases were evaluated preoperatively and at 3, 6, and 12 months postoperatively using the International Prostate Symptom Score (IPSS), quality of life (QoL) score, and the International Index of Erectile Function (IIEF-5) questionnaires. Patients were divided into groups A (severe erectile dysfunction [ED]), B (moderate ED), and C (mild-to-normal ED), according to their IIEF-5 scores. The median patient ages were 69, 65, and 62 years in groups A, B, and C, respectively. Significant improvements occurred in the IPSS and QoL score within the groups during the 12-month follow-up period. The IIEF-5 scores at 3 months postoperatively were lower than the preoperative scores in groups B and C. The IIEF-5 scores subsequently improved during the 12-month follow-up period. The slope of the relationship between the IIEF-5 score and the time since Tm:YAG laser prostatectomy had a β value of 0.2210 (95% confidence interval 0.103 to 0.338, $p = 0.0003$); hence, each postoperative month was associated with an increase of 0.2210 in the IIEF-5 score. The IIEF-5 scores gradually increased and reached the preoperative levels by the 12-month follow-up assessment. Although the IIEF-5 score dropped significantly during the first 3 months postoperatively, it improved over the following 12 months. Tm:YAG laser prostatectomy did not impact on EF ultimately.

Keywords Laser therapy · Prostatatic hyperplasia · Thulium · Erectile dysfunction · International Index of Erectile Function · Prostatectomy

Introduction

As the population ages, lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) are becomingly increasingly prevalent, and they can cause sexual dysfunction, which has negative effects on the quality of the lives of aged men [1, 2]. To alleviate LUTS caused by BPH, many surgical techniques, including transurethral resection of the prostate (TURP) and minimally invasive laser treatments, have been performed; however, these surgical treatments can depress sexual function and cause retrograde ejaculation [3–5]. The different surgical techniques impact upon erectile function (EF) to different extents, and this depends on the surgical components used and the level of damage that occurs to the nerves around the prostate. While it is important for surgeons to be informed about the rapid advances associated with minimally invasive treatments, gaining therapeutic effects from these tools is much more important. Numerous studies have evaluated the effects of the different surgical treatments for LUTS caused by BPH, including TURP, potassium-titanyl-phosphate (KTP) laser vaporization of the prostate, holmium laser enucleation of the prostate (HoLEP), on sexual function,

Jae Seung Chung and Sang Hyun Park contributed equally to the work.

✉ Jae Il Chung
prosdoc@hanmail.net

[1] Department of Urology, Haeundae Paik Hospital, Inje University, Busan, South Korea

[2] Department of Urology, Kosin Gospel Hospital, Kosin University, Busan, South Korea

[3] Department of Urology, Busan Paik Hospital, College of Medicine, Inje University, 75 Bokji-ro, Busanjin-gu, Busan 614-735, South Korea

and they have generated conflicting results that range from improvements in outcomes to deteriorating outcomes [3, 4].

Thulium:yttrium-aluminum-garnet laser prostatectomy (Tm:YAG prostatectomy) is a relatively new laser treatment that has gained traction [6–10]. The impact of Tm:YAG prostatectomy on sexual function differs from the impacts of photoselective vaporization of the prostate (PVP) or HoLEP on sexual function, because it uses a different type of energy. At present, data on EF after Tm:YAG prostatectomy are insufficient to enable definitive conclusions to be drawn. In addition, detailed investigations into the longitudinal effects of Tm:YAG prostatectomy on EF have not been undertaken. This study aimed to evaluate the impact of Tm:YAG prostatectomy for the treatment of LUTS caused by BPH on EF.

Materials and methods

Patients

Between March 2010 and July 2014, 475 patients underwent Tm:YAG prostatectomy for LUTS caused by BPH that was refractory to medical therapy with alpha blockers. Of these patients, 208 patients for whom 1-year follow-up data relating to the International Index of Erectile Function-5 (IIEF-5) questionnaire were available were included in the study. Patients who were taking alpha blockers for LUTS caused by BPH before surgery were included in this study. The study's exclusion criteria were the presence of prostate cancer or a neurogenic bladder, previous prostate or urethral surgery, or the presence of a urethral stricture. Patients were also excluded from the study if they used phosphodiesterase type 5 inhibitors, but patients were not excluded if they had received 5-alpha-reductase inhibitors before surgery.

Patients completed self-administered questionnaires regarding their LUTS and EF before and at 3, 6, and 12 months after Tm:YAG laser prostatectomy. LUTS were evaluated using the International Prostate Symptom Score (IPSS) and quality of life (QoL) score questionnaires. A Korean version of the IIEF-5 questionnaire [11] was administered to assess EF. The questionnaires were completed by the patients themselves or with the assistance of the clinical research coordinator, if required. All patients gave their informed consent prior to their surgery. The patients were stratified into three categories based on the severity of their erectile dysfunction (ED) that was determined from the IIEF-5 scores, as follows: group A, IIEF-5 $\leq$7, n = 69 (severe ED); group B, 8$\leq$ IIEF-5 $\leq$16, n = 98 (moderate ED); group C, IIEF-5 $\leq$17, n = 41 (mild-to-normal ED). We obtained approval from the institutional review boards at Haeunde Paik Hospital and Busan Paik Hospital.

Surgical methods

Tm:YAG prostatectomies (Revolix®; LISA Laser Products OHG, Katlenburg-Lindau, Germany) were carried out as described in detail previously [12]. The laser energy was transmitted through 550-μm end-firing fibers to the prostate at an energy setting of 60 W. All surgical procedures were performed under spinal or general anesthesia using normal saline as the irrigation fluid. Briefly, the first step involved removing the median lobe by making incisions at the 5- and 7-o'clock positions around the verumontanum. Then, the lateral lobes of the prostate were vaporesected or vapoenucleated until the prostate capsule was identified [12]. At the end of surgery, a 22-French three-way Foley catheter was placed into all patients to maintain continuous bladder irrigation using a 30-cm^3 balloon that contained saline.

Statistical analyses

Descriptive statistics were used to analyze the patients' baseline characteristics. The independent t test was used to analyze the continuous variables, and the χ^2 test was used to evaluate differences in the proportions among the three groups in relation to the categorical variables. Longitudinal changes in EF were determined by comparing the preoperative total IIEF-5 scores with the scores generated at each postoperative follow-up assessment using the paired t test. We used linear mixed models to assess the changes in the IIEF-5 scores and the slopes describing the changes in EF over time after Tm:YAG prostatectomy, which allowed for associations among the repeated measurements of the outcome within the patients and accounted for any missing data. The slopes were expressed as regression coefficients with the 95% confidence intervals (CI). Furthermore, we produced separate regression lines with time slopes and calculated the average lines of best fit from the pooled data to enable comparisons of the differences in the slopes of the IIEF-5 changes among the groups that had been stratified according to the IIEF-5 scores. The statistical analyses were performed using Statistical Analysis System software, version 9.1.3 (SAS Institute Inc., Cary, NC), and they were based on a two-sided significance level of $p < 0.05$.

Results

The patients' baseline characteristics and the variables are presented in Table 1. The median ages of the patients in groups A, B, and C were 69, 65, and 62 years, respectively. All of the enrolled patients had taken alpha blockers, and 83 (39.9%) patients had been administered 5-alpha-reductase inhibitors before surgery. Nine (4.3%) cases had capsular perforations and five (2.4%) cases had bladder mucosal injuries. Three patients required blood transfusions.

Table 1 Baseline description of patients who underwent thulium laser prostatectomy

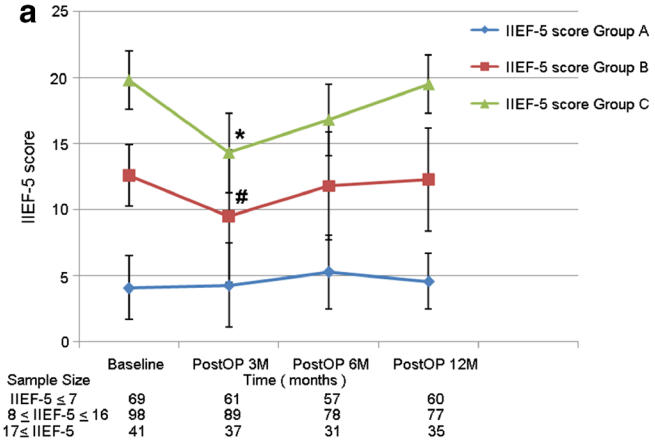
	Group A IIEF-5 ≤7	Group B 8≤ IIEF-5 ≤16	Group C 17≤ IIEF-5	*p* value
No. of patients	69	98	41	
Age, mean (median, range), years	70.4 ± 6.3 (69, 59–84)	66.4 ± 5.8 (65, 54–79)	62.6 ± 5.5 (62, 47–75)	<0.001
Diabetes (%)				
No	43 (62)	67 (68)	31 (76)	0.348
Yes	26 (38)	31 (32)	10 (24)	
Hypertension (%)				
No	34 (49)	42 (43)	23 (56)	0.342
Yes	35 (51)	56 (57)	18 (44)	
PSA, mean (median, range), ng/ml	6.4 ± 18.3 (5.3, 0.4–151.0)	5.3 ± 5.4 (4.5, 0.4–24.2)	3.8 ± 3.5 (4.2, 0.3–7.4)	0.508
Pre-prostate size, mean (median, range), mL	57.2 ± 22.5 (56, 23–112)	55.0 ± 23.4 (54, 21–127)	54.5 ± 24.6 (53, 28–155)	0.650
Post-prostate size, mean (median, range), mL	28.2 ± 8.6 (27, 17–52)	27.6 ± 9.2 (28, 12–53)	26.2 ± 9.1 (25, 15–54)	0.683
Total OP time, mean (median, range), min	64.2 ± 29.8 (63, 13–145)	61.6 ± 26.4 (60, 20–200)	63.5 ± 27.7 (62, 25–135)	0.391
Laser time, mean (median, range), min	22.3 ± 14.3 (22, 6–68)	23.6 ± 16.3 (23, 8–68)	27.1 ± 12.3 (26, 9–65)	0.379
Total laser energy, mean (median, range), J	58,960 ± 22,581 (61,514, 22,516–109,298)	57,683 ± 22,785 (57,821, 24,685–136,552)	54,985 ± 21,779 (73,271, 25,997–120,098)	0.699
Catheterization time, mean (median, range), days	2.4 ± 0.8 (2, 1–5)	2.6 ± 0.9 (2, 1–6)	2.5 ± 1.0 (2, 1–6)	0.576
Capsular perforation (%)	3 (4.3)	5 (5.1)	1 (2.4)	0.781
Bladder mucosal injury (%)	2 (2.9)	3 (3.1)	0 (0.0)	0.532
Blood transfusion (%)	1 (1.4)	2 (2.0)	0 (0.0)	0.655

No. number, *OP* operation

There were no significant differences among the groups with respect to the total operation time. The preoperative prostate sizes in groups A, B, and C were 56, 54, and 53 cm^3, respectively. Significant prostate size reductions occurred in all groups. The estimated postoperative prostate sizes in groups A, B, and C were 27, 28, and 25 cm^3, respectively. Significant improvements in the IPSS and QoL score were observed within the three groups during the 12-month follow-up period (Fig. 3).

With regard to changes in EF, the IIEF-5 scores at 3 months postoperatively were lower than the preoperative IIEF-5 scores in groups B and C (group A: 4.1 vs. 4.4; group B: 12.4 vs. 9.6; group C: 19.7 vs. 14.4), and transient but significant declines in the IIEF-5 scores were observed in the early postoperative period. The IIEF-5 scores subsequently improved during the 12-month follow-up period (Fig. 1a). The slope of the relationship between the IIEF-5 score and the time since Tm:YAG laser surgery had a β value of 0.2210 (95% CI 0.103 to 0.338, $p = 0.0003$), indicating that each month after surgery was associated with an increase of 0.2210 in the IIEF-5 score (Fig. 1b). The IIEF-5 scores gradually increased and reached the preoperative levels by 12 months postoperatively (group A 4.5; group B 12.5; group C 19.5).

When we analyzed the changes in EF according to ED severity, which was determined from the IIEF-5 scores, the trends in EF recovery differed among the groups. The IIEF-5 scores were restored postoperatively in patients with preoperative IIEF-5 scores of ≥8, whereas patients with preoperative IIEF-5 scores of ≤7 remained at a particular level without any changes. For patients in group A with preoperative IIEF-5 scores of ≤7, the associations between increases in the IIEF-5 scores and the time after surgery were unclear (Fig. 2a). Group B showed a significant increase in the IIEF-5 score during the follow-up period (Fig. 2b). Group C also showed a significant increase in its IIEF-5 score after 3 months had elapsed following surgery (Fig. 2c), with the IIEF-5 score increasing by 0.4755 (95% CI 0.130 to 0.820, $p = 0.0078$). Therefore, patients with higher IIEF-5 scores were more likely to experience aggravations in relation to their EF during the early postoperative period. In contrast, those with severe ED were not likely to be affected by Tm:YAG prostatectomy. Table 2 shows the effect of multiple alternative laser prostate surgical approaches on postoperative EF. Significant improvements in the IPSS and QoL score were observed within the three groups during the 12-month follow-up period (Fig. 3)



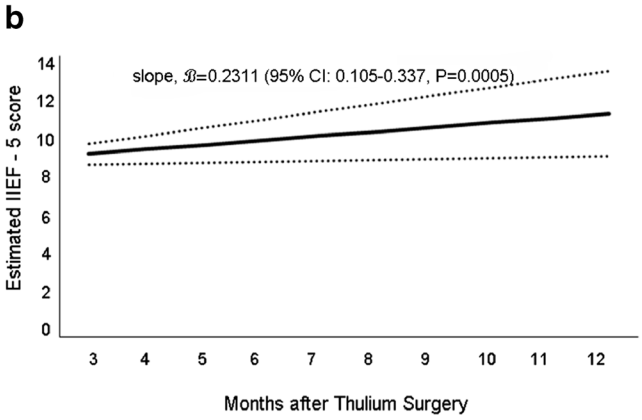


Fig. 1 **a** Longitudinal changes in the International Index of Erectile Function-5 (*IIEF-5*) score after thulium:yttrium-aluminum-garnet (*Tm:YAG*) laser prostatectomy. *, #$p < 0.05$ for the mean IIEF-5 score versus the preoperative IIEF-5 score. **b** The IIEF-5 score according to time since Tm:YAG laser prostatectomy in all patients without distinction among the subgroups. The slopes are based on regression coefficients derived from the linear mixed models. The *solid line* indicates the regression line, and the *dotted line* represents the 95% confidence interval. *IIEF-5* International Index of Erectile Function-5; *PostOP* postoperative; *CI* confidence interval

Discussion

A considerable amount of information has been published about sexual function after laser treatment for LUTS caused by BPH [3, 4]. However, there have been many disagreements about sexual function after surgery. It is important to recognize that the pattern of postoperative sexual function will differ according to surgical components used. We can assume that the impact of Tm:YAG prostatectomy on EF will differ from the impacts of other laser therapies on EF, because it has its own unique wavelength and penetration depth. To date, several attempts have been made to determine the effects of Tm:YAG prostatectomy on EF. Recent studies have reported marginal nonsignificant improvements in EF 12 months after Tm:YAG prostatectomy [6, 22, 23]. However, Yee et al. showed that Tm:YAG prostatectomy was associated with a 20% overall risk for worsening EF and that 6% of the patients noticed improvements [24]. Therefore, the impact of Tm:YAG prostatectomy on EF is ambiguous and the available evidence is contradictory. Moreover, we cannot determine the changes in EF over time because most studies assessed postoperative EF at one time point. Hence, it is difficult to draw definitive conclusions about the effect of Tm:YAG prostatectomy on EF.

In this study, Tm:YAG prostatectomy negatively influenced EF during the early postoperative period, and the IIEF-5 scores declined in the two groups of patients whose EF was relatively normal preoperatively. The negative impact of this procedure on EF is more pronounced in patients who have normal preoperative EF. There are several mechanisms that might explain why EF declines during the early postoperative period following laser surgery, which include neuropraxia caused by the direct thermal injury of the erectile nerves [15, 25], α-adrenergic overstimulation caused by the psychological stress associated with surgery [13, 26], and the high incidence of postoperative dysuria may induce a decline in EF. However, it is noteworthy that the IIEF-5 score subsequently improved and returned to the baseline score over time. The IIEF-5 score gradually increased and reached the preoperative levels by 12 months postoperatively. However, there is no tangible body of evidence that can be used to explain the favorable recovery of EF over time. Improvements in LUTS, including painful voiding, as a consequence of successful laser surgery, may improve EF. The discontinuation of 5-alpha-reductase inhibitors also favors better EF. The ED that is a consequence of the neuropraxia caused by thermal injury may be temporary, and this might have contributed to the recovery of EF.

We assumed that psychogenic factors, including the fear associated with surgery and pain, rather than thermal injuries caused the initial reduction in EF. EF is thought to recover to its preoperative level as a patient's psychological status stabilizes over time. When nerve damage occurs as a result of thermal injury, the endothelial cells of the corpus cavernosum become damaged, and irreversible fibrosis of the corpus cavernosum tissues occurs that accompanies changes in behavior [27]; consequently, EF will not improve despite the surgery improving the LUTS. However, as seen from the results, EF recovered over time, and the role of thermal injuries was not remarkable. Therefore, we thought that psychogenic factors may also contribute to the initial reduction in EF postoperatively. We always instruct patients to not sit down for a long time and to avoid pressure on their belly to prevent postoperative bleeding. Thus, we cannot exclude the possibility that such instructions affect the patient's initial sexual life. Even in the presence of thermal injury, it is highly probable that the peripheral nervous tissues are slightly affected, leading to temporary damage.

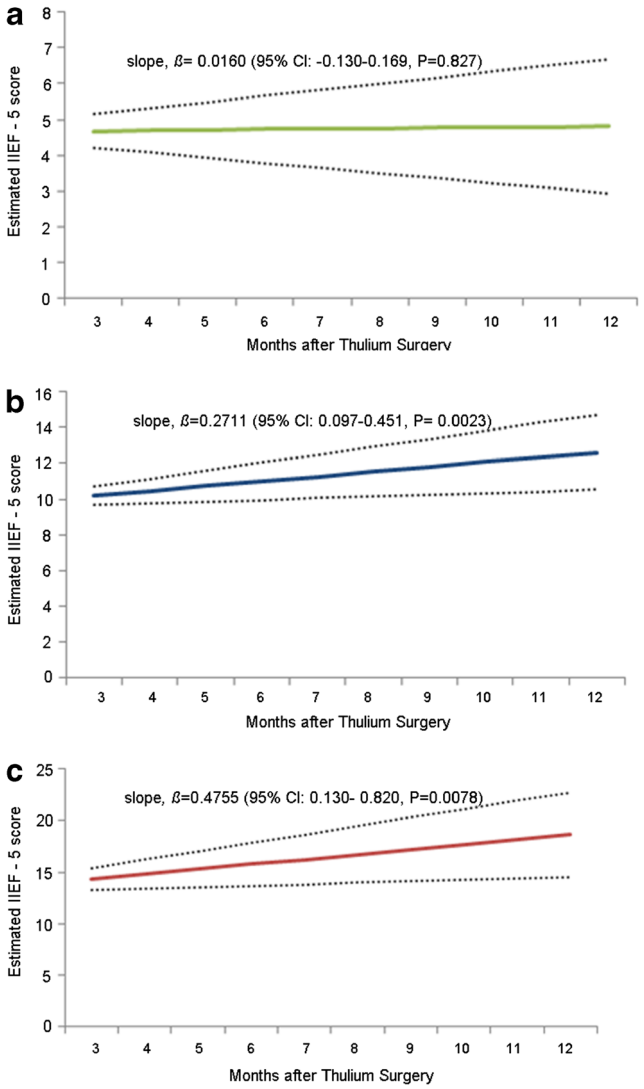


Fig. 2 Changes in the International Index of Erectile Function-5 (*IIEF-5*) score over time after thulium:yttrium-aluminum-garnet laser prostatectomy in the subgroups of patients. **a** Group A, IIEF-5 ≤7. **b** Group B, 8≤ IIEF-5 ≤16. **c** Group C, IIEF-5 ≤17. The slopes are based on the regression coefficients derived from the linear mixed models. The *solid line* indicates the regression line, and the *dotted line* represents the 95% confidence interval. *IIEF-5* International Index of Erectile Function-5; *CI* confidence interval

Importantly, the interpretation of our findings should not be oversimplified by stating that Tm:YAG prostatectomy is not associated with worsening EF after surgery on the basis of comparisons between the preoperative IIEF-5 scores and the IIEF-5 scores at 12 months postoperatively. Indeed, significant drops in the IIEF-5 scores occurred during the early postoperative period, and the IIEF-5 scores subsequently showed continuous improvements over the next 12 months in the sexually active men in groups B and C. This observation is completely different from the fact that Tm:YAG prostatectomy has just no significant impact on EF after surgery. However, there was no change in EF before and after operation in group A. The patients in group A were older than those in group B. Moreover, although there was no statistical difference, the proportion of diabetes in group A was the highest among the three groups. Thus, these basal conditions of patients in group A may negatively affect postoperative EF recovery.

Many studies have been conducted that have evaluated the effects of surgical treatment for BPH on sexual function. These studies have shown that TURP, which is the gold standard for the surgical treatment of LUTS caused by BPH, has generated conflicting outcomes in association with sexual function after surgery that range from improvements in sexual function to an absence of notable outcomes to detrimental effects on sexual function [13–15, 25, 26, 28]. Furthermore, the effect of PVP on sexual function remains controversial [16, 17, 29–31]. However, it is generally accepted that HoLEP has no significant impact on sexual function [20, 21, 32, 33]. Briganti et al. reported that TURP and HoLEP treatment of BPH had similar effects on EF [19].

The wavelengths of the KTP, holmium, and thulium lasers are 532, 2100, and 2013 nm, respectively, and their penetration and coagulation depths are 0.8, 0.4, 0.2 mm, respectively, [18, 34]. Although the thermal impacts of lasers depend on their specific properties, the conflicting results described previously may, in part, be associated with not accounting for the dynamic changes in EF over time. Hence, if the IIEF-5 is determined immediately after surgery, for example, within 6 months of surgery, many patients might have reductions in their EF. However, EF assessed after a longer period of time following surgery may be the same as the preoperative EF.

Our study has attributes that distinguish it from other studies that have investigated the impact of surgical treatment for BPH on EF. To date, very few studies have evaluated the natural course of postoperative EF after laser treatment for BPH. Previous cross-sectional studies have examined EF preoperatively and at one time point after surgery, and most of these studies simply presented ratios of improvement or impairment in EF in patients, or ratios that showed no changes in EF. An important distinguishing feature of this study is that we measured EF more than three times postoperatively and observed changes in EF at each time point. Hence, although the present study showed the same results as previous studies on the twelfth postoperative month, it demonstrated that the dynamic changes in EF in the intervening period can also be investigated. The results from this study add to the current body of knowledge about EF after laser treatment for BPH.

This study has several limitations. First, this study was not a prospective randomized clinical trial, and several cases were not accounted for because their IIEF-5 score data were not available for the follow-up period. Second, in addition to EF, ejaculation should have been described in relation to sexual function. However, the ejaculation data could not be presented because ejaculation was investigated in a small number of the patients only. Third, to accurately evaluate the direct effect of Tm:YAG

Table 2 The effect of multiple alternative approaches on postoperative erectile function

Author (study year)	Type of surgery	Control	No. of patients (*N*)	Validated questionnaire	Follow-up (months)	EF outcome
Tscholl et al. (1995) [13]	TURP	None	98	None	3	EF (8.3% ↓)
Muntener et al. (2007) [14]	TURP	None	988	DANPSS	60	No change
Mamoulakis et al. (2013) [15]	TURP	Bipolar TURP	149	IIEF-15	12	No change
Paick et al. (2007) [16]	PVP	None	45	IIEF	6	EF domain (slight EF ↑)
Bruyere et al. (2010) [17]	PVP	None	149	IIEF-5	24	EF reduction in patients with IIEF ≥19
Bouchier et al. (2010) [18]	PVP	TURP	60	BSFQ	12	No change
Briganti et al. (2006) [19]	Holmium	TURP	32	IIEF	24	EF (1.7% ↑)
Jeong et al. (2012) [20]	Holmium	None	38	IIEF	12	No change
Klett et al. (2014) [21]	Holmium	None	393	IIEF-5	36	No change
Xia et al. (2008) [6]	Thulium	TURP	52	IIEF-5	12	No change
Tiburtius et al. (2014) [22]	Thulium	None	72	IIEF	12	No change

BSFQ Baseline Sexual Function Questionnaire, *DANPSS* Danish Prostatic Symptom Score, *EF* erectile function, *IIEF* International Index of Erectile Function, *TURP* transurethral resection of the prostate, *PVP* photoselective vaporization of the prostate, *no.* number, ↓ Decrease in erectile function, ↑ Increase in erectile function

prostatectomy on EF, changes in EF should have been analyzed according to the patients' ages, the presence or absence of underlying diseases, for example, diabetes and cardiovascular disease, and the duration of 5-alpha-reductase inhibitor therapy. Fourth, although two surgical methods that used Tm:YAG laser treatment were combined in the present study, it is thought that their effects on EF would not have differed because the characteristics of the laser were the same despite the methods of excision being slightly different. However, it would be better if we could separate the group according to the technique used. Hence, this study was limited by its lack of detailed analyses which was associated with the small number of study participants.

In this study, we observed changes in EF until 1 year after surgery. It remains unclear whether EF changes significantly beyond 1 year postoperatively. Theoretically, sexual function could improve after the operation because of the amelioration of the LUTS. Thus, it would be very beneficial to determine whether EF continuously improves in long-term follow-up studies. Our data will be valuable when counseling patients regarding their EF expectations after Tm:YAG laser prostatectomy.

Although patients with higher IIEF-5 scores were more likely to experience aggravations in their EF during the early postoperative period after Tm:YAG laser prostatectomy, the IIEF-5 scores were restored over the course of the 12-month follow-up period. In contrast, the EF of those with severe ED was not likely to be affected by Tm:YAG laser prostatectomy. Overall, Tm:YAG laser prostatectomy did not impact on EF.

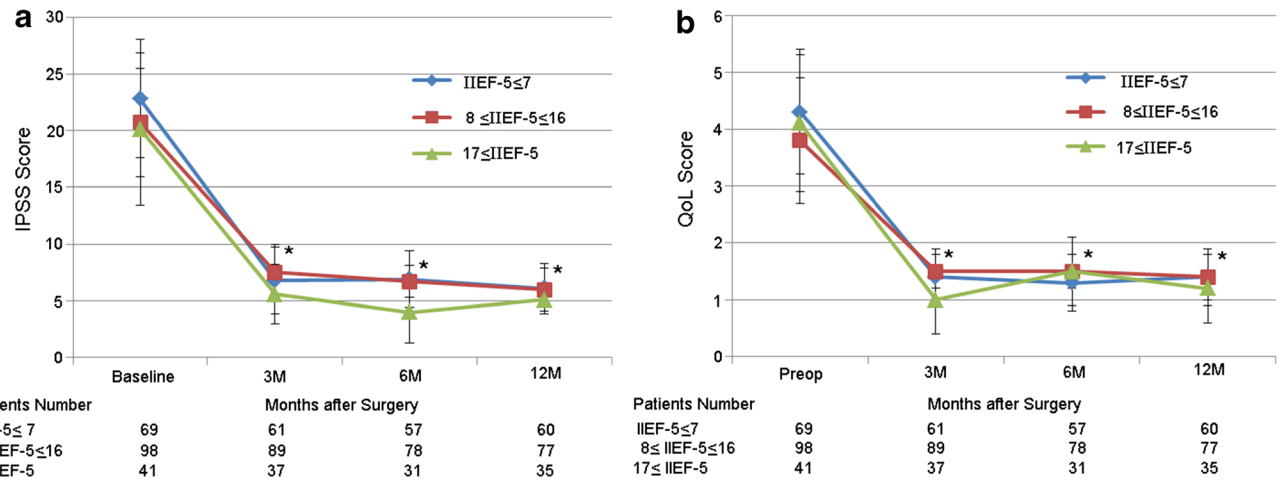


Fig. 3 Preoperative and follow-up functional outcomes. **a** International Prostate Symptom Score. **b** Quality of life score. *$p < 0.05$ for the mean International Index of Erectile Function-5 (*IIEF-5*) score versus the preoperative IIEF-5 score in all three groups. *IPSS* International Prostate Symptom Score; *QoL* quality of life; *IIEF-5* International Index of Erectile Function-5

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Compliance with ethical standards We obtained approval from the institutional review boards at Haeunde Paik Hospital and Busan Paik Hospital.

Conflict of interest The authors declare that they have no conflict of interest.

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