CHAPTER V

LASER-ASSISTED SURGICAL METHODS FOR PATIENTS WITH BENIGN PROSTATE HYPERPLASIA: HoLEP vs ThuLEP REVIEW ARTICLE

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1. Introduction

Lower urinary tract symptoms (LUTS) due to benign prostatic obstruction (BPO) are common in adult males (1). Transurethral resection of the prostate (TUR-P) is the gold standard surgical treatment in patients with prostate sizes less than 80 ml (2). Due to the limited applying of TUR-P in large prostate volumes and possible complications, alternative surgical methods have been improved. Holmium: YAG (Yttrium Aluminum Garnet) and Thulium: YAG are laser types for using in the surgical treatment of benign prostate hyperplasia (BPH) (3). Holmium Laser Enucleation of the Prostate (HoLEP) and Thulium Laser Enucleation of the Prostate (ThuLEP) are surgical methods independent of prostate size. HoLEP and ThuLEP have become an alternative to TUR-P in patients with a prostate volume less than 80 mL and alternative to open prostatectomy for prostate volumes greater than 80 mL (5).

In this study, comparing of Holmium and Thulium lasers in minimally invasive surgical treatment of BPH was investigated by literature.

2. Material And Method

A comprehensive search of PubMed/Medline and Embase database from 01 January 2008 to 31 December 2020. Inclusion criteria: full text publications in English language were included in the study. Exclusion criteria: case reports, letters, publications with editorial comments were excluded from the study.

3. Results

3.1. Holmium Laser

Holmium laser has a wavelength of 2140 nm. Holmium laser beams are strongly absorbed by water and fluids of cell (3). During the use of holmium laser, energy is released in short pulses. Holmium laser has 0.4

mm tissue penetration in prostate tissue (4). Holmium and thulium laser use normal saline to avoid hyponatraemia. Since the prostate tissue contains high water, it enables to perform coagulation and tissue ablation (3). The incision and dissection of the prostate tissue is performed by the tissue ablation and coagulation effect of Holmium laser (5).

In 1998, Gilling et al. described HoLEP operation (8). HoLEP can be applied regardless of prostate size. HoLEP is an alternative surgical method to TUR P and open prostatectomy in terms of efficacy, safety and complications (3).

3.2. Thulium Laser

The wavelength of the Thulium laser is 2013 nm. Energy is provided by continuous waves. Thulium laser has 0.25 mm tissue penetration in prostate tissue. (3). Because of short penetration depth, high energy density occurs. Effective vaporization and hemostasis provides image clarity during operation (6). Thulium laser can be used for laser vaporization, resection or enucleation.

In 2010, Hermann et al. described ThuLEP operation (12). Thulium laser is used effectively and safely in the surgical treatment of BPH like Holmium laser (5, 6).

3.3. Functional Results Of HoLEP And ThuLEP

Open prostatectomy is applied for LUTS caused by prostate sizes greater than 80-100 mL (7). HoLEP and ThuLEP are minimally invasive surgical methods that can be applied regardless of prostate size (8). Bach et al. followed up 90 BPH patients with a volume greater than 80 mL for 12 months after ThuLEP surgery. There was a significant improvement in International Prostate Symptom Score (IPSS), Quality of Life (QoL), maximum urine flow (Qmax) and post voiding residual volume (PVR) compared to the preoperative period. In the peroperative period, superficial ureteral orifice injury during enucleation was observed in 1 (1.11%) patient due to the enlarged median lobe. Stress urinary incontinence (SUI) was observed in 10 patients (11.11%) in the postoperative period. SUI improvement was observed in 8 of these patients within 1 to 6 months (9).

Morozov et al. performed a retrospective analysis of patients who had undergone one of three forms of endoscopic enucleation of prostate (EEP): HoLEP, ThuLEP or monopolar enucleation of the prostate (MEP). They compared intraoperative, early postoperative and 3rd-6th months follow-up complications. A total of 1413 patients were included in this study; 509 (36%) patients underwent HoLEP, 812 (57.5%) patients underwent ThuLEP and 92(6.5%) patients in MEP group. Clavien-Dindo grade 1 complication was ureteral orifice injury in 0.5% of the cases; 3 cases in HoLEP, 4 cases in ThuLEP, and none in MEP. The Clavien-Dindo

grade 2 complication in the early postoperative period was a fever of >38°C in 2.76% of patients; 2.95% cases after HoLEP, 2.46% cases after ThuLEP, 4.3% cases after MEP, p=0.56). In patients with prostate volumes <80 mL, fever was found in 3% of the patients after any type of enucleation. In patients with larger than 80 mL prostate volumes, fever was revealed 2.5% of the patients. Statistical differences were insignificant between the groups (p=0.3). Another common grade 2 complication was the necessity to delay morcellation due to intraoperative hemorrhage and consequent unsatisfactory visualization. This complication was found in 1.4% of cases; 2% in HoLEP, 1.2% in ThuLEP and 2.2% in MEP, p=0.27). This complication was found 1% cases of patients with prostate volume <80mL 1% in and 1.8% cases of patients with larger glands (p=0.09). It was observed that prostate volume did not produce any significant effect on complication frequency. The most frequently observed Clavien-Dindo grade 3 complication was bladder tamponade. The complication frequency of bladder tamponades was 2.2% after HoLEP, 2% after ThuLEP, and 4.3% after MEP (p=0.267). The tamponade frequency in the patients with prostate volumes <80mL and >80mL was 2% and 2.9%, respectively (p=0.4). Stress urinary incontinence was found in 3.9% of patients at 3 months and in only 1.4% of patients at 6 months after the operation. Urethral stricture at 6 months after the surgery was observed in 1.4% of patients. Bladder neck sclerosis was observed in only 0.9% of these cases. No significant difference was observed between these complication frequencies (10).

Gazel et al. in their randomized prospective study, HoLEP operation was performed on 119 patients with BPH whose prostate volume was greater or less than 80 mL. Enucleation time, morcellation time and total operation time were found to be significantly longer in the prostate volume greater than 80 ml group (p=0.001). It was observed that the tissue weight and total laser energy enucleated were significantly higher in the group with prostate volume greater than 80 ml (p=0.001). Enucleation efficiency and rate, morcellation and laser efficiency were observed similarly in the two groups. There was no statistically significant difference between the two groups in terms of Qmax, PVR, IPSS, and QoL score. In the group with greater than 80 ml volume, catheter removal time, hospitalization time and maximum voiding time were found to be significantly longer (p=0.005, p=0.01, p=0.002, respectively) (11).

Zhang et al. in a randomized controlled study, total of 116 consecutive patients with large prostate volume (>80 cc) were be treated surgically with either HoLEP (n= 58) or ThuLEP (n= 58). Follow-up was assessed at 1, 3, 6, 12 and 18 months after surgery. Enucleation and total operation time were significantly shorter in the ThuLEP group (p <0.001). There was no statistically significant difference between morcellation time,

removed tissue weight, decrease in hemoglobin, catheterization time and hospitalization time ($p > 0.05$). At the end of 18 months of follow-up, there was no significant difference between the two groups in terms of IPSS, PVR, QoL, and Qmax values. Postoperative hematuria was seen in 3 patients (5.2%) in the HoLEP group, 1 patient (1.7%) in the ThuLEP group; transient incontinence was seen 5 patients (8.6%) in the HoLEP group and 2 patients (3.4%) in the ThuLEP group; bladder mucosal injury was observed in 4 patients (6.9%) in the HoLEP group and 1 patient (1.7%) in the ThuLEP group ($p > 0.05$). No significant difference was observed between the two groups in terms of bladder neck contracture and urethral stricture at 12 and 18 months of follow-up (12).

Studies show that HoLEP and ThuLEP are an effective treatment method in patients with prostate volumes greater than 80 mL. HoLEP and ThuLEP are minimally invasive prostate surgeries that can be an alternative to open prostatectomy.

3.4. Effects Of HoLEP And ThuLEP On Continence

After HoLEP surgery, the prevalence of SUI is between 4.9-12.5% (13). SUI complaint resolves within 6 to 12 months in most patients (14). Saitta et al. reported the SUI rates after HoLEP surgery at the 1, 3 and 6 months follow-up as 5.8%, 1.5% and 0.7%, respectively (15). Minagawa et al. reported the incidence of SUI as 3% at the 3 month after HoLEP (16). Krambeck et al. reported the incidence of incontinence as less than 5% in their 1000 cases of HoLEP series (17). Alkan et al. in their retrospective study, postoperative SUI after HoLEP was reported as 1% (18).

Elmansy et al. in their retrospective study, they included 949 patients by scanning 10-year data. They found that prostate volume greater than 81 gm, operation time more than 96 minutes, PSA value decrease of more than 84% and the presence of diabetes mellitus were significantly associated with the development of SUI in patients undergoing HoLEP ($p < 0.02$, $p < 0.01$ and $p < 0.001$, respectively) (19). In a multi-center, prospective and randomized study, functional and complication results of HoLEP and TUR-P compared. Transient urge incontinence was similar between the two groups; dysuria was found to be more common in the HoLEP group ($p = 0.0002$) (20). In the early postoperative period, SUI was observed at similar rates in patients who underwent HoLEP, TUR-P, and open prostatectomy (2%) (6, 20, 21).

Transient urinary incontinence after ThuLEP was reported as 0.5-6.7% (3). Iacono et al. reported temporary urge incontinence rate as 6.7% after ThuLEP in 148 patients (22). Yuan et al. reported the late period SUI rate as 0.5% in 188 patients who underwent ThuLEP (23). Sun et al. in a multicenter prospective study involving 2216 patients, SIU was reported as 0.1% after thulium laser prostate resection (24). Xia et al. compared

ThuLEP and TUR-P in a randomized prospective study and there was no significant difference between the two groups in terms of stress incontinence (p = 0.48) (32).

Studies showed that after HoLEP and ThuLEP surgery incontinence rates decrease in follow-up.

3.5. Effects Of HoLEP And ThuLEP On Sexual Functions

The association of erectile dysfunction (ED) and BPH is common in patients with LUTS (25). Kim et al. in a prospective study involving 60 patients who were sexually active with a median age of 68.5 years. They investigated the sexual functions of patients who underwent HoLEP for BPH by using the Male Sexual Health Questionnaire (MSHQ). There was no significant difference in erection, ejaculation, anxiety and sexual desire at the 6th month after the operation (p> 0.05). Decrease of sexual satisfaction score due to retrograde ejaculation was observed in 38 patients (63.3%) (26). Pushkar et al. in their prospective study compared HoLEP and TUR-P in terms of postoperative erectile functions by using the International Index of Erectile Function (IIEF-15) score. The groups are divided into two groups as younger than 55 years old and older age group. In HoLEP group patients IIEF-15 score was normalized at the 6th postoperative month, but remained significantly lower in older age groups. In TUR-P group, the IIEF-15 score was found to be significantly lower in all age groups. Patients greater than age of 55 who underwent HoLEP or TUR-P, the IIEF-15 score changing at 3rd and 6th months were not statistically significant (p> 0.05) (27). Alkan et al. reported that there was no change in postoperative IIEF-5 scores in long-term follow-up after HoLEP (18). Capogrosso et al. in their study mean follow-up period was 152.1 months and they included 135 patients. They observed decrease in the average IIEF multidimensional score in the long-term patients who were applied HoLEP (28).

In a prospective study, investigated the effects of ThuLEP on erectile and ejaculatory functions. There was no significant difference in IIEF-5 scores at postoperatively 4th and 8th months compared to preoperative values (p=0.195 and p=0.26, respectively). Ejaculatory function assessed by Male Sexual Health Questionnaire-Ejaculatory Disease (MSHQ-EjD) and a significant reduction in ejaculation was observed (p <0.0001) (29). Enikeev et al. compared ThuLEP and TUR-P in terms of erectile function. Included 469 patients data were analyzed and it was shown that there was no significant difference between preoperative and postoperative IIEF-5 scores in the ThuLEP group (p= 0.08). Mean IIEF-5 score was shown significant increase in the ThuLEP group (0.72) and comparing to decrease in TUR-P patients (0.24) (p <0.001) (30). Carmignani et al. in a prospective study involving 110 patients with mean

age of 67.83 years. There was no significant difference in the preoperative and postoperative erectile functions of the patients at the 3rd and 6th months after ThuLEP. Postoperative ejaculatory functions were evaluated with MSHQ-EjD, and preservation of ejaculatory function was demonstrated in 58 patients (52.7%) after ThuLEP. Painful ejaculation was observed in 7 (12.1%) of 58 patients (31). Xia et al. They found that retrograde ejaculation was seen in 55% after ThuLEP and 65% after TUR-P (p=0.42) (32).

3.6. HoLEP And ThuLEP On Anticoagulant-Antiplatelet Drug Use

Anticoagulant (AC) or antiplatelet (AP) use is common in patients with BPH. With the use of laser in BPH surgery, the amount of bleeding and blood transfusion rate were expected to decrease. Agarwal et al. performed a retrospective review of HoLEP patients on AP and AC therapy compared to none. There were no differences in morcellation time, enucleation time, total operation time and amount of laser energy. There were no difference in postoperative trial passage and hemoglobin drop. Postoperatively, there was a higher complication rate in AP and AC groups in 90 days (p=0.035), but there was not an increase in Emergency Department visits (p=0.557) or Clavien 3 complications (p=0.16). (33). Yuk et al. investigated the efficacy and complication rate in HoLEP surgery due to discontinuation of antithrombotics. There were 248 (25.96%) patients in antithrombotic drugs use group and 707 (74.04%) patients in non-antithrombotic group. Seventy-five (66.5%) and 70 patients (28.2%) discontinued the antithrombotic therapy 5–7 days and <1 week preoperatively, respectively. Three patients (1.21%) were switched to low-molecular-weight heparin therapy, and 10 (4.03%) continued antithrombotic therapy. There were no significant differences in the incidence rates of postoperative transfusion (p=0.894), thrombosis (p=0.946), haemorrhage requiring bladder irrigation (p=0.959), complications from antithrombotic use, transurethral coagulation (p=0.894), cardiovascular events (p=0.845) and cerebrovascular events (p=0.848). Efficacy and complications related to the short-term antithrombotic withdrawal before and no significant differences also showed after HoLEP (34). Tayeb et al. compared 116 patients who required AC / AP treatment and 1558 patients who did not required. Significant differences were observed in enucleation times (51 min vs 65 min, respectively, p <0.001) and morcellation rate (5 g / min vs 4.5 g / min, respectively, p = 0.02) in patients AC / AP using and not using. Hospitalization time (27.8 hours vs 24 hours, p <0.001) and the continuous bladder irrigation time (15 hours vs 13.5 hours, p <0.001) were observed significantly longer in patients using medication. There was no significant difference in postoperative transfusion rate (3.5% and 1.6%, p = 0.128).

They reported that the use of intermittent or continuous anticoagulant therapy did not adversely affect outcomes of HoLEP (35).

Becker et al. compared the results of patients who used oral anticoagulants (n=94) or vitamin K antagonists (n=151) and those who did not use any anticoagulants. They observed the mean hemoglobin decrease significantly more in anticoagulants or vitamin K antagonists using group. The mean catheterization time and hospitalization time were significantly longer in drug users than in non-users ($p < 0.001$). Blood transfusion was performed in 1 patient (1.3%) in the oral anticoagulant group, 3 patients (2.2%) in the vitamin K antagonist group and 4 patients (0.2%) in the control group. Statistical differences were found to be significant compared to the control group ($p < 0.001$) (36). In a meta-analysis published by Zheng et al, a lower rate of blood transfusion and bladder tamponade was found in who did not use antithrombotics ($p<0.0001$ and $p=0.004$, respectively). Shorter operation time was observed in the not using group ($p<0.00001$). Hemoglobin decrease and hospitalization time were similar between the two groups ($p= 0.63$ and $p= 0.90$, respectively) (37).

More studies are needed on the efficacy and safety of ThuLEP in patients using AC / AP.

3.7. HoLEP And ThuLEP On Elderly Patients

BPH patients may be at high risk in the presence of significant comorbidities and with increasing age. Piao et al. investigated the effectiveness of HoLEP in patients with different age groups. It was found that age group over 80 years old (n = 38) had significantly longer enucleation time, morcellation time, and total operation time compared to the lower age groups ($p = 0.002$, $p = 0.010$ and $p < 0.01$, respectively). In patients over 80 years old, significant decrease was observed in the maximum micturition rate on the uroflowmeter at postoperative 2nd week and 3rd month ($p < 0.01$ and $p = 0.004$, respectively). A significant difference was observed in terms of IPSS between the groups at postoperative 6th month ($p < 0.05$) (38). In a study involving 412 patients comparing the ThuLEP results in over and below 75 years of age. There was no significant difference between the two groups in terms of IPSS, Qmax, QoL, reoperation rate, median operation time, catheterization time and hospitaization time at 1-year follow-up (39).

Morozov et al. performed a retrospective analysis of patients who had undergone HoLEP, ThuLEP or MEP. They compared complication rates in two groups: 626 (44.3%) patients aged 65 years or younger and 787 (55.7%) patients older than 65. Stress urinary incontinence after 3

months was found 3.4% of patients aged 65 years or youngers and 4.3% of patients older than 65 (p=0.2). Urethral stricture was found 1.4% both of the groups (p=0.5). Bladder neck sclerosis was found 1.1% of patients aged 65 years or youngers and 0.8% of patients older than 65 (p=0.2) (10).

4. Conclusion

When HoLEP and ThuLEP are compared with other minimally invasive BPH surgeries and open prostatectomy, their functional outcomes and complications are comparable. HoLEP or ThuLEP operation can be applied safely in patients with large prostate volume by minimally invasive surgery and can be applied safely in patients using anticoagulants.

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