Prostate volume reduction following pure transurethral bipolar plasma vaporization and conventional transurethral resection of the prostate: a prospective investigation using transrectal 3D ultrasound volumetry

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Abstract: PURPOSE To evaluate and compare postoperative changes in prostate volume and clinical outcome after bipolar plasma vaporization (BPV) and conventional transurethral resection of the prostate (TURP). PATIENTS AND METHODS Consecutive series of patients undergoing BPV or TURP were included in this prospective, nonrandomized study. Planimetric volumetry after transrectal three-dimensional ultrasound of the prostate was performed preoperatively and postoperatively after 6 weeks, 6 months and 12 months. Additionally, changes in clinical outcome parameters were assessed and compared between the groups. The reduction ratio and analysis of covariance were used to compare volume changes between BPV and TURP. Multiple regression analysis was performed to assess a possible interaction between preoperative prostate volume and effect of therapy. RESULTS A total of 157 patients were included (BPV: n = 68, TURP: n = 89). Median preoperative prostate volume was 43.1 ml in the BPV group and 45.9 ml in the TURP group (p = 0.43). Postoperatively, the prostate volumes decreased significantly in both groups. After catheter removal, the relative residual prostate volume was significantly higher in the BPV group (66.6 vs. 60.8 %; p = 0.02). Thereafter, significant differences were not detectable anymore (12 months: 46.6 vs. 47.1 %; p = 0.82). Regression analysis revealed that tissue ablation after BPV was superior to TURP in prostates <45 ml but inferior in prostates >45 ml. All clinical outcome parameters improved significantly and were not significantly different between the groups. CONCLUSIONS Volume reduction and short-term clinical outcome following pure BPV was excellent and comparable to conventional TURP. However, volume reduction seems to be limited in patients with larger prostates.

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Prostate volume reduction following pure transurethral bipolar plasma vaporization and conventional transurethral resection of the prostate: A prospective investigation using transrectal 3D-ultrasound volumetry

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ABSTRACT

Purpose: To evaluate and compare post-operative changes in prostate volume and clinical outcome after bipolar plasma vaporization (BPV) and conventional transurethral resection of the prostate (TURP).

Patients and Methods: Consecutive series of patients undergoing BPV or TURP were included in this prospective, non-randomized study. Planimetric volumetry after transrectal three-dimensional ultrasound of the prostate was performed pre- and post-operatively after six weeks, six months and twelve months. Additionally, changes in clinical outcome parameters were assessed and compared between the groups. The reduction ratio and analysis of covariance were used to compare volume changes between BPV and TURP. Multiple regression analysis was performed to assess a possible interaction between pre-operative prostate volume and effect of therapy.

Results: A total of 157 patients were included (BPV: n=68, TURP: n=89). Median preoperative prostate volume was 43.1ml in the BPV group and 45.9ml in the TURP group ($p=0.43$). Postoperatively, the prostate volumes decreased significantly in both groups. After catheter removal the relative residual prostate volume was significantly higher in the BPV group (66.6% vs. 60.8%; $p=0.02$). Thereafter significant differences were not detectable anymore (twelve months: 46.6% vs. 47.1%; $p=0.82$). Regression analysis revealed that tissue ablation after BPV was superior to TURP in prostates <45ml but inferior in prostates >45ml. All clinical outcome parameters improved significantly and were not significantly different between the groups.

Conclusions: Volume reduction and short-term clinical outcome following pure BPV was excellent and comparable to conventional TURP. However, volume reduction seems to be limited in patients with larger prostates.
Keywords: benign prostatic hyperplasia, transurethral electrovaporization of prostate, transurethral resection of prostate, ultrasound of the prostate, 3D imaging
Introduction

Transurethral bipolar plasma vaporization of the prostate (BPV) has been introduced as a minimally invasive treatment option for patients with lower urinary tract symptoms caused by prostatic bladder outlet obstruction [1]. It combines the benefits of bipolar electro-surgery (excellent hemostasis, irrigation with isotonic saline and use of a conventional bipolar TUR generator) with the advantages of tissue vaporization to reduce bleeding complications during and after the procedure [2]. A plasma corona on the surface of the spherical vaporization electrode is moved over the surface of the prostate to vaporize the tissue with simultaneous coagulation of deeper tissue layers.

It has been shown that BPV is a low morbidity procedure with functional short- to mid-term results comparable or even superior to conventional transurethral resection of the prostate (TURP) [3-9]. However, long-term results following BPV, which are needed to prove the durability of symptom improvement and eventually non-inferiority compared to conventional TURP are lacking.

The extent of prostate tissue ablation is known to have an impact on the long-term effectiveness of a transurethral procedure [10,11]. After tissue resection the extent of tissue removal can be estimated by the weight of the resected tissue. However, after tissue vaporization, it has to be assessed differently. Conventional biplane transrectal prostate volume measurements by ultrasound are not accurate enough due to the central defect in the prostate after transurethral surgery. Planimetric volumetry following transrectal three-dimensional (3D) ultrasound of the prostate is a valid technique to reliably measure volume changes following transurethral surgery of the prostate [12,13].

Using this technique we have previously shown that volume reduction after greenlight laser vaporization is less extensive than after conventional TURP, particularly in larger prostates.
[12]. The aim of the present investigation was to assess volume changes following BPV and compare them to volume changes after conventional TURP.
Patients and methods

This prospective study was performed in a tertiary care academic center with consecutive series of patients who underwent either routine BPV or conventional TURP for prostatic bladder outlet obstruction. In general, patients undergoing platelet aggregation inhibition therapy with acetylsalicylic acid or patients with particular interest in a minimally invasive technique were offered to undergo BPV. Patients without platelet aggregation inhibitors were offered to undergo TURP. Exclusion criteria for both techniques were dual anti-platelet aggregation therapy or medication with oral anticoagulants. Further exclusion criteria were medication with 5-alpha-reductase inhibitors or known prostate cancer at the time of surgery. Patients were also excluded from further analysis, if prostate cancer was detected histologically on the TURP specimens, because the different growth characteristics of prostate cancer tissue compared to benign prostate tissue might affect the volumetry results of this study. The local ethics committee approved the study protocol and all included patients provided written informed consent.

The pre-operative patient assessment included a uroflow study with measurements of the maximum urinary flow rate (Qmax) and post-void residual volume (PVR), the International Prostate Symptom Score (IPSS) with Quality of Life (QoL) assessment, a prostate specific antigen (PSA) test, a urinalysis and a urine culture. In case of an elevated PSA test or a suspicious digital rectal examination, a transrectal prostate biopsy was performed. Furthermore, transrectal 3D-ultrasound of the prostate was performed using a ProFocus 2202 ultrasound scanner and a UA0513 magnetic wheel probe mover (both BK Medical, Herlev, Denmark).

All procedures were performed either under general or spinal anesthesia using a SurgMaster UES-40 generator (Olympus Winter & Ibe GmbH, Hamburg, Germany) for BPV and a 160W ICC 350 generator (Erbe, Tübingen, Germany) for TURP. The procedures were performed as
described earlier [14,15]. The total operative time and the weight of the resected prostate tissue (after TURP) were recorded.

Postoperatively, the catheter was usually removed after three days recording to institutional guidelines. Following catheter removal, transrectal 3D-ultrasound, uroflowmetry and PVR measurements were performed.

Follow-up visits took place six weeks, six months and twelve months after the procedures. At every visit clinical outcome parameters (IPSS and QoL, Qmax, PVR and PSA) were assessed and patients were asked whether they had any symptoms of dysuria. Furthermore, transrectal 3D-ultrasound of the prostate was performed.

Planimetric volumetry of the prostate was performed on the generated 3D-images using the BK-3D view software (BK Medical) as described earlier [12]. Two investigators (BK and OG) performed the measurements without knowing the patients’ identities and their respective treatment modalities. All measurements were controlled and approved by the principal investigator (TH) prior to the final analysis.

SPSS Statistics Software version 21 (IBM, Armonk, USA) and R version 2.15.3 (R Foundation for Statistical Computing, Vienna, A) were used for statistical analyses. Fisher’s exact test and Mann-Whitney U-test were used to compare nominal and continuous variables between the two treatment arms. Based on residual analysis, prostate volume was log-transformed in order to obtain homoscedastic residuals. To compare volume changes between BPV and TURP at the different follow-up times the raw reduction ratio was calculated (residual prostate volume relative to preoperative prostate volume (BPV) / residual prostate volume relative to preoperative prostate volume (TURP)). Additionally, analysis of covariance (ANCOVA) was performed to adjust post-operative prostate volume changes for pre-operative volume is smaller for BPV (BPV is superior) and above 1 that the relative post-operative volume is higher for BPV (TURP is superior). To assess whether the initial prostate
volume has an impact on the relative volume reduction and whether there is a difference between BPV and TURP, the relative postoperative prostate volumes 12 months after BPV and TURP were plotted against the initial prostate volume. A regression analysis was performed to compute the crossing point of the two graphs. All p-values <0.05 were considered statistically significant.
Results

Of 157 included men 68 (43.3%) underwent BPV and 89 (56.7%) TURP. Baseline parameters of the two groups are displayed in Table 1a. Patients in the BPV group were more often under medication with platelet aggregation inhibitors. Furthermore, positive pre-operative urine cultures were more frequent in the BPV group, particularly in men with an indwelling Foley catheter. All other baseline parameters were not significantly different between the two groups. The pre-operative prostate volumes were also not significantly different between the BPV group (43.1ml) and the TURP group (45.9ml, \( p=0.43 \); Table1a).

Table 1b summarizes intra- and peri-operative data of the two groups. Statistically significant differences were not detectable. In the TURP group the median resection weight was 16.3g (range: 5.0-67.4g). Major intra- or peri-operative complications did not occur and blood transfusions were not necessary in either group.

Median duration of postoperative catheterization was 3 days in both groups (BPV: 2-13 days, TURP: 2-22 days). Two men in the BPV group (2.9%) and five men in the TURP group (5.6%) were discharged with an indwelling catheter (\( p=0.7 \)). The median post-operative hospital-stay was 4 days (2-8 days) after BPV and 4 days (2-18 days) after TURP (\( p=0.3 \)).

Six weeks after the operation the number of men who reported persisting dysuria was rather high in both groups (Table 1c). At this time, patients in the BPV group had a significantly higher rate of urinary tract infections (17.6% vs. 2.2%; \( p<0.001 \)). Subsequently, the rate of patient reported dysuria declined and remained low in both groups (Table 1c).

All patients completed the pre-operative, post-operative and six week assessment. A total of 136 patients (86.6%) and 128 patients (81.5%) were followed up for six months and twelve months, respectively (Online Resource 1).
Post-operative changes in prostate volumes and differences between BPV and TURP are illustrated in Table 2. At the time of catheter removal the residual prostate volume was 66.6% of the initial volume after BPV. Subsequently, the residual prostate volume continued to decrease (six weeks: 52.4%, six months: 48.2%) resulting in a relative residual prostate volume of 46.6% after twelve months. A comparable decrease was found in the TURP group with a relative residual prostate volume of 60.8% after catheter removal, 53.7% after six weeks, 49% after six months and 47.1% after twelve months. A significant difference between BPV and TURP was only found after catheter removal (raw reduction ratio: 1.10, \( p=0.019 \); adjusted reduction ratio: 1.08, \( p=0.03 \)). Thereafter, volume reduction was in favor of TURP but differences between the groups were statistically non-significant (Table 2).

Changes in relative volume reduction in relation to the initial prostate volume were calculated after 12 months. With increasing initial prostate volumes the residual prostate volume remained almost stable around 45 to 50% after BPV. After TURP the residual prostate volume decreased with increasing initial prostate volumes (around 50% for a 40ml prostate and 40% for a 80ml prostate). Regression analysis revealed a crossing point of the two graphs at an initial prostate volume of 45ml (95% confidence interval=34-58ml). This indicates that prostate volume reduction is better after BPV if the initial prostate volume is below 45ml and better after TURP if the volume is above 45ml (Online Resource 2).

Table 1d summarizes the changes in clinical outcome parameters. After catheter removal all parameters improved significantly in both groups. A further improvement was detectable up to the six months follow-up examination. Subsequently the results remained stable. Significant differences in clinical outcome between the two groups were only transient and were not detectable anymore after twelve months.
Postoperatively, three patients in either group developed a urethral stricture (Table 1c), which were all treated by internal urethrotomy. Re-operations due to residual adenoma or bladder neck sclerosis were not necessary (Table 1c).
Discussion

Our prospective investigation of post-operative changes in prostate volume revealed that BPV is an effective minimally invasive treatment option for patients suffering from prostatic bladder outlet obstruction. A prostate volume reduction of more than 50% of the initial prostate volume was accompanied by a statistically significant and clinically meaningful improvement of all investigated outcome parameters. Compared to conventional TURP there was no overall difference in volume reduction and improvement of clinical outcome. However, prostate volume reduction was different between the two procedures depending on the initial prostate volume. Our analysis revealed that in smaller prostates (<45ml) BPV is superior and in larger prostates (>45 ml) TURP is more efficient.

It is known that extensive volume reduction of the prostate is not necessary to achieve good functional short-term results after transurethral prostate surgery [14]. In the past, numerous procedures showed excellent initial outcome but were subsequently abandoned due to high retreatment rates caused by residual adenoma tissue [15]. There is evidence that volume reduction has an impact on the durability of a procedure but it is not exactly known how much tissue needs to be removed to achieve long lasting symptom improvement [10,11]. Retreatments are almost inexistent for enucleation procedures where the entire adenoma is removed (e.g. open, holmium or thulium laser enucleation) [16]. In contrast, rather high reoperation rates have been reported after prostate vaporization using the first generation 80W greenlight laser. It is assumed that insufficient tissue ablation due to the low power output of this model is responsible for retreatment rates of up to 25% after five years [16]. It remains to be seen whether the increased output power of the two successor models will translate into lower retreatment rates. The reported reoperation rates after 120W laser vaporization were already 11% after a follow up of three years [17]. We have recently shown that volume reduction after 120W laser vaporization was significantly lower than after conventional
TURP [12]. The maximum power output of the laser was recently increased to 180W but mid-term outcome is not yet available.

Whether the maximum power of the applied energy or the type of energy itself (laser energy versus bipolar electro energy) or even the type of energy deposition (resection versus vaporization) determines the effectiveness of a procedure is unknown. Our results indicate that there are no significant differences in volume reduction and clinical outcome between electro-vaporization and electro-resection.

However, looking further into the details of our results, we identified important differences in the effectiveness of tissue ablation between BPV and TURP. The percentage of adenoma volume increases with growing overall prostate volume [18]. Thus one would expect that after efficient ablation of the adenoma, the relative residual prostate volume decreases with increasing initial prostate volume. In fact, the relative residual volume after TURP decreased constantly with increasing initial prostate volumes. In the BPV group, however, the relative residual prostate volume remained almost stable around 50%. The reason for this difference remains unclear. A potential explanation would be that significant abrasion of the vaporization electrode occurs during the procedure resulting in a continuous shrinkage of the electrode (Online Resource 3). This, in turn, makes tissue ablation slower and less efficient with increasing operative time and thus, might be responsible for the less extensive tissue ablation in larger prostates. Reduced tissue ablation in larger prostates compared to TURP was also found after 120W greenlight laser vaporization [12]. Similar to the changes observed at the vaporization electrode, degradation of the laser fiber occurred during the procedure and was associated with a significant decrease in power output [19]. It seems that extensive tissue removal in large prostates might be a limitation for vaporization techniques. Probably, more efficient enucleation procedures should be favored in these patients. Replacement of altered
BPV vaporization electrodes might be another simple, but also costly way to improve tissue ablation in larger prostates.

Changes in clinical outcome after twelve months were not significantly different to those after TURP and comparable to the results reported by others [4,6,20-22]. However, we were not able to identify superiority of BPV compared to TURP [5,23]. Significant changes in prostate volume and clinical outcome parameters were not detectable anymore after six months. Thus, either for clinical evaluation or for research purposes the final assessment of the clinical outcome and volume changes after transurethral surgery should only be made after completion of the six months follow-up. Our data furthermore indicates that the change in serum PSA is not a reliable surrogate marker for volume changes after transurethral surgery. Although volume changes were not significantly different after BPV and TURP the relative PSA reduction was about 50% after BPV but almost 70% after TURP. Urinary tract infections but also differences in PSA secretion of different prostate zones might be responsible for the insufficient correlation of prostate volume and serum PSA [24]. The rate of postoperative urethral strictures after BPV was comparable with the rate reported by Geavlete and colleagues but reoperation rates were lower in the present investigation [7].

The non-randomized study design is a limitation of our study. Particularly differences in platelet aggregation inhibitor medication might have an impact on differences in volume reduction between the two groups. It is possible that awareness of anti-platelet aggregation medication led to more cautious tissue removal in the BPV group. However, the comparable overall volume reduction and the even higher reduction after BPV in the group of smaller prostates make a relevant bias rather unlikely. The overall dropout rate of 18.5% after twelve months is another limitation. However dropout rates around 20% in this elderly patient population are common even in studies without unpleasant transrectal ultrasound examinations [25]. Furthermore, dropout rates were similar in the BPV and TURP group.
Conclusions

Volume reduction and short-term clinical outcome following pure BPV was excellent and comparable to conventional TURP. Volume reduction after BPV was superior to TURP in prostates <45 ml but limited in patients with larger prostates. The use of a second vaporization electrode or alternative procedures should be taken into consideration in these patients to lower the risk of retreatments with longer follow-up.
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References


Legends to Online Resources (Supplementary Material)

**Online Resource 1:** Study profile

**Online Resource 2:** Changes in relative volume reduction (in %; y-axis) in relation to the initial prostate volume (ml; x-axis) 12 months after BPV (red line) and TURP (green line)

**Online Resource 3:** The spherical vaporization electrode before the procedure (A) and after BPV of a 50ml prostate (B)