Original Article

Secondary hemorrhage after bipolar transurethral resection and vaporization of prostate

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Abstract

Introduction: We evaluated the factors associated with secondary hemorrhage after bipolar transurethral resection of prostate (TURP) and vaporization of prostate.

Materials and Methods: The perioperative data of patients undergoing endoscopic surgery for benign prostatic hyperplasia (BPH) were prospectively collected. Procedures involved included bipolar TURP, bipolar vaporization of prostate, and hybrid bipolar TURP/vaporization of prostate. Secondary hemorrhage was defined as bleeding between 48 h and 30 days postsurgery requiring hospital attendance with or without admission. Risk factors for secondary hemorrhage were analyzed.

Results: From 2010 to 2013, 316 patients underwent bipolar surgery for BPH. Bipolar TURP accounted for 48.1% of the procedures, bipolar vaporization accounted for 20.3% of the procedures, and the rest were hybrid TURP/vaporization of prostate. Among this cohort of patients, fifty patients had secondary hemorrhage with hospital attendance. Consumption of platelet aggregation inhibitors (PAIs) was found to be associated with secondary hemorrhage ($P < 0.0005$). Age, prostate volume, operation type, the use of 5-alpha reductase inhibitors, and being with a urethral catheter before operation were not found to be statistically significant risk factors for secondary hemorrhage.

Conclusions: Secondary hemorrhage after bipolar surgery for BPH is a common event. Consumption of PAI is a risk factor for such complication.

Key Words: Benign prostatic hyperplasia, hemorrhage, transurethral resection of prostate

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INTRODUCTION

Lower urinary tract symptoms (LUTS) are common.[1,2] Currently, monopolar transurethral resection of the prostate (TURP) is considered the surgical standard for the management of symptomatic benign prostatic enlargement in prostates between 30 and 80 ml.[3] However, monopolar TURP has some drawbacks which include a higher risk of TURP syndrome.

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Bipolar TURP is one of the major advances that have tried to address the flaws of monopolar TURP. Bipolar TURP systems use an active and return pole incorporated at the electrode design. While there are several systems that have been developed to apply the bipolar principle, all share the common feature to perform in normal saline. This decreases the risk of TURP syndrome. When comparing the outcome of monopolar and bipolar TURP, a systemic review concluded that both monopolar TURP and bipolar TURP shared a similar short-term efficacy.[4] A modification of the bipolar TURP technique is transurethral resection in saline (TURis) bipolar electrovaporization. The employment of a "button" electrode instead of a resection-based technique has been reported to reduce the bleeding rate.[5] A randomized controlled trial showed that a hybrid bipolar vaporization and resection technique reduced catheterization time when compared with bipolar resection alone.[6]

Secondary hemorrhage following monopolar TURP is common. Early literature reported a rate of its happening ranging from 1% to 15%.[7,8] In the comparison between monopolar TURP and bipolar TURP, some studies have reported a lower intraoperative bleeding tendency in favor of the bipolar modality.[9,10] However, data concerning delayed postoperative bleeding in bipolar surgery for benign prostatic hyperplasia (BPH) are scarce although this can be a distressing problem for both patients and surgeons. In this study, we investigated the frequency of secondary hemorrhage after bipolar transurethral resection and vaporization of prostate, as well as the risk factors associated with its occurrence.

MATERIALS AND METHODS

This was an observational study with prospectively planned data collection involving two centers. Demographic characteristics of the participants were documented. Preoperative assessment with the International Prostate Symptom Score (IPSS), quality of life (QoL) score, digital rectal examination (DRE), uroflowmetry, and prostate-specific antigen (PSA) was performed. Transrectal ultrasonography (TRUS) was used for prostate size assessment. Patients included in the study had LUTS or retention of urine related to BPH requiring surgical intervention. Indications for surgery were moderate to severe LUTS (IPSS ≥ 8), maximum urinary flow rate (Q_{max}) < 10 ml/s, previous medical therapy failure, or urodynamic obstruction without detrusor dysfunction. If there was an elevated PSA level or abnormal DRE, TRUS-guided prostate biopsies were taken to exclude prostate cancer. General medical history and medication history, including the use of 5-alpha reductase inhibitors (5-ARIs), anticoagulants, and platelet aggregation inhibitors (PAIs), were acquired. Patients on anticoagulants would be bridged with heparin infusion or low-molecular heparin injection in the perioperative period. Patients on PAI would be asked to stop the medication 5 days before operation if it was not contraindicated according to the advice of physicians. PAI would be resumed upon discharge from the hospital.

Secondary hemorrhage was defined as bleeding between 48 h and 30 days postsurgery requiring hospital attendance with or without admission. This included accident and emergency department attendance without admission into the general urological ward. Postoperatively, the patients were assessed on IPSS and uroflowmetry at 6 months.

Surgical procedures under study included TURis bipolar vaporization of the prostate, TURis bipolar resection of the prostate, and TURis bipolar hybrid procedure (vaporization plus resection). All procedures employed the Olympus SurgMaster UES-40 Bipolar Generator (Olympus, Tokyo, Japan). A "button" type vaporization electroe was used in the TURis vaporization technique. Vaporization and coagulation were set at 280 and 100 W , respectively. For hybrid surgery, the resection mode and the vaporization mode were used interchangeably (with changes of electrodes). In most instances, the lateral and median lobes were removed with the vaporization loop, and the final resection of tissue tags and apical tissue around the verumontanum was performed with the resection loop, which also enabled tissue extraction for histopathologic examination. Additional hemostasis was achieved using the "button" electrode where deemed necessary. All operations were performed under general or spinal anesthesia by surgeons who have passed their learning curve in TURP, with at least 50 cases a year. A three-way indwelling 22- or 24-F Foley catheter was inserted into the bladder at the end of the procedure in all patients. Postoperative bladder irrigation lasted for 6 h unless hematuria was significant according to a standardized color chart. If so, bladder irrigation was continued until the urine was sufficiently clear. The catheter was removed, and the patient was discharged to go home when found to be clinically fit, which was at the discretion of the managing clinicians. All patients received an intravenous antibiotic upon induction of prostate surgery, and two extra doses were given after the operation.

Descriptive statistics were used to characterize the clinical characteristics of the study cohort. One-way ANOVA test was used for continuous data. Fisher's exact test was applied for categorical data. $P < 0.05$ was considered statistically significant. SPSS software package version 21 (SPSS Inc, Chicago, IL, USA) was used for all calculations.

RESULTS

From May 2010 to December 2013, 316 patients underwent bipolar surgery for the management of BPH. Mean age was

71.6 ± 8.8 years and mean prostate volume was 62.5 ± 32.5 cc. Three forms of bipolar surgery were performed, namely, bipolar TURP, bipolar vaporization of prostate, and bipolar hybrid surgery [Table 1]. Bipolar resection accounted for the majority of the procedures, which was 48.1% of the whole cohort. Bipolar vaporization accounted for 20.3% of the procedures, and the rest were hybrid resection/vaporization of the prostate. The mean hospital stay was 2.6 days and the mean catheter time was 2.0 days. Almost half of the patients in the study were on Foley catheter before their prostate surgery.

Among this cohort of patients, fifty patients had secondary hemorrhage with hospital attendance. Twenty-five patients in the end required hospital admission. None of the patients required another operation for clot evacuation and hemostasis. No Grade III or above complication according to the Clavien Classification of Surgical Complications System was documented. Hematuria resolved spontaneously soon after admission with or without bladder irrigation. Factors of age, PSA, preoperative prostate volume, preoperative status of Foley catheter, operation type, the use of 5-ARIs, and the use of PAI were analyzed to study if there is any correlation with the risk of secondary hemorrhage [Table 2]. Upon analysis, the only factor associated with secondary hemorrhage was the consumption of PAI ($P < 0.0005$). Multivariate analysis also confirms such finding [odds ratio 5.573, 95% confidence interval: 2.309–13.451, $P < 0.0005$, Table 3].

Operative outcome of the patients was summarized in Table 4. The cohort experienced statistically significant improvement in IPSS, QoL, Q_{max}, and postvoid residual after bipolar endoscopic surgery for BPH at 6 months.

DISCUSSION

While much has been studied to minimize intraoperative bleeding and perioperative hemorrhage concerning monopolar TURP, relatively little effort has been observed in the literature which addressed the issue of secondary hemorrhage. In the limited data of monopolar TURP concerning postoperative secondary hemorrhage, the reported risk of its occurrence has been variable. In the study by Harvey *et al*., they reported an overall risk of secondary hemorrhage in their series being 25%.[11] Ehrlich *et al*. observed the rate of secondary hemorrhage to be 10.8% in their cohort.[12] Such difference was in part due to a different definition in secondary hemorrhage. Harvey *et al*. defined secondary hemorrhage to be the occurrence of bloodstained urine after a period of at least 24 h with clear urine, and Ehrlich *et al*. defined late hematuria as hematuria happening after catheter removal which necessitates bladder catheter drainage, restoration of bladder irrigation, or cessation of aspirin treatment. While these two different definitions would explain a higher rate of secondary hemorrhage in the series of Harvey *et al*., a spectrum of secondary hemorrhage could be observed. This would provide us with a general idea

Table 1: Demographics and characteristics of the study cohort

Parameters	Number
Total number	316
Age (mean, years)	71.6±8.8
PSA (mean, ng/mL)	8.97±11.98
Prostate volume (mean, cc)	62.5±32.5
On Foley catheter preoperative, *n* (%)	156 (49.4)
Procedures, *n* (%)	
Bipolar TURP	152 (48.1)
Bipolar hybrid	100 (31.6)
Bipolar vaporization	64 (20.3)

PSA: Prostate specific antigen, TURP: Transurethral resection of prostate

Table 2: Analysis for risk of secondary hemorrhage

	Without secondary hemorrhage (*n*=266)	With secondary hemorrhage (*n*=50)	*P*
Age (mean, years)	71.7±8.7	70.9±9.5	0.557
PSA (mean, ng/mL)	8.47±9.05	11.74±21.92	0.564
Prostate volume (mean, cc)	61.6±30.3	66.8±42.0	0.895
Procedures, *n* (%)			
Bipolar TURP	130 (48.9)	22 (44.0)	0.573
Bipolar hybrid	81 (30.5)	19 (38.0)	
Bipolar vaporization	55 (20.7)	9 (18.0)	
Use of 5-ARI (%)	24 (9.0)	5 (10.0)	0.826
Use of PAI (%)	36 (13.5)	20 (40.0)	<0.0005
Preoperative with catheter (%)	129 (48.5)	27 (54.0)	0.475

PSA: Prostate specific antigen, TURP: Transurethral resection of prostate, 5-ARI: 5-alpha reductase inhibitor, PAI: Platelet aggregation inhibitor

Table 3: Multivariate analysis for risk of secondary hemorrhage

	OR	95% CI	*P*
Preoperative PSA level	0.996	0.976-1.016	0.693
Prostate volume (mean, cc)	0.722	0.991-1.013	0.722
Procedures			
Bipolar TURP	1.457	0.530-4.005	0.466
Bipolar hybrid	1.768	0.672-4.653	0.249
Bipolar vaporization	-	-	0.514
Use of 5-ARI	0.804	0.239-2.697	0.723
Use of PAI	5.573	2.309-13.451	<0.0005
Preoperative with catheter	0.950	0.447-2.019	0.894

PSA: Prostate specific antigen, TURP: Transurethral resection of prostate, 5-ARI; 5-alpha reductase inhibitor, PAI: Platelet aggregation inhibitor, OR: Odds ratio, CI: Confidence interval

Table 4: Operative outcome

	Preoperative	6 months postoperative	*P*
Mean IPSS score±SD	21.4±7.0	9.2±6.8	<0.0005
Mean QoL score±SD	3.7±1.2	1.6±1.2	<0.0005
Mean Q_{max}, mL/s±SD	8.3±3.4	15.1±8.2	<0.0005
Mean PVR, mL±SD	134.3±136.0	49.5±68.7	<0.0005

SD: Standard deviation, IPSS: International Prostate Symptoms Score, QoL: Quality of life, Q_{max}: Maximal flow rate, PVR: Postvoid residuals

to understand the presentation of this complication and to estimate its incidence.

Bipolar prostate surgery has emerged to be a promising alternative to monopolar TURP in recent years. Its inherent safety advantage is evident by a much reduced risk of dilutional hyponatremia and fluid absorption overload, giving the credit to the use of saline irrigation instead of glycine irrigation.[13] However, controversial results have been observed concerning its hemostatic property. In a cohort of patients older than 75-year-old, Yang *et al*. reported that bipolar TURP exhibited less intraoperative bleeding and a shorter irrigation time when compared with monopolar TURP ($P < 0.001$).[9] However, in a recent *post hoc* analysis of a European Multicenter Randomized Controlled Trial, both bipolar TURP and monopolar TURP demonstrated a similar clot retention risk (B-TURP 1.4% vs. M-TURP 1.8% $P = 1.000$) and blood transfusion risk (B-TURP 2.9% vs. M-TURP 1.8% $P = 1.000$).[13] A similar result was echoed by Stucki *et al*., who showed that there were no significant perioperative differences in blood loss or rates of blood transfusion.[14] Our study addressed the issue of secondary hemorrhage concerning bipolar prostate surgery. We reported a secondary hemorrhage rate of 15.8%. If only late hematuria necessitating hospitalization is taken into account, such rate would be 7.9%. These rates of secondary hemorrhage were in general lower than that of monopolar TURP. One postulation for such observation would be a more secured hemostatic effect by bipolar energy. In an *in vivo* study by Maddox *et al*., prostatic specimens from 12 patients after bipolar surgery were examined.[15] The mean depth of thermal injury was found to be 2.4 mm, a much greater depth of penetration than that reported by Akgül *et al*. in monopolar TURP, which was 1.52 mm.[16] As a result, the advantage in hemostasis by bipolar energy may be subtle when we study its intraoperative and early perioperative outcome, but its advantage concerning hemostasis security becomes more obvious when we study the risk of secondary hemorrhage.

The modality of bipolar surgery might also affect postoperative hemostatic performance. As a matter of fact, the *in vivo* study by Maddox *et al*. employed mostly bipolar vaporization cases.[15] The depth of thermal injury reported by them was greater than previous studies of bipolar TURP.[17] As our current cohort consisted of bipolar vaporization of prostate, this might be one of the reasons accounting for a lower rehospitalization rate in our series when compared with the series of bipolar TURP by Stucki *et al*., which was 11.4%.[14] It is worthwhile to note that surgical modality, i.e. resection versus vaporization versus hybrid, was not found to be correlated with the risk of secondary hemorrhage in our study. As the difference in hemostatic property between bipolar resection and bipolar vaporization is small, it is possible that a bigger cohort is needed to demonstrate the advantage of vaporization concerning secondary hemorrhage prevention.

In the literature, only a few studies were performed to investigate possible strategies for minimizing the risk of secondary hemorrhage in monopolar TURP, and none was reported on the risk analysis of bipolar prostate surgery secondary hemorrhage. Since the early development of monopolar TURP, urinary tract infection was postulated to be a trigger of secondary hemorrhage. Harvey *et al*. attempted to use a 2-week course of co-trimoxazole to decrease the risk of secondary hemorrhage without success.[11] In their randomized controlled trial, while there was a significant correlation between the incidence of secondary hemorrhage and urine infection at catheter removal, no difference in the incidence of bleeding was found in the two treatment arms. No more studies on urinary tract infection and secondary hemorrhage after TURP had been published ever since. On the other hand, Heer *et al*. investigated the relationship between urinary tract infection and secondary hemorrhage after transurethral resection of bladder tumor (TURBT) years later.[18] Their retrospective review of 2830 patients concluded that only 14% of the cases of secondary hemorrhage yielded significant bacteriuria on urine culture. Furthermore, there was no significant difference in the clinical parameters supportive of infection between patients with bacteriuria and sterile urine.

Our current study revealed PAI as a risk factor predisposing bipolar prostatectomy patients to secondary hemorrhage. The observation of a relationship between aspirin use and hemorrhagic complication was suggested by Watson *et al*. in their retrospective case–control study of patients undergoing monopolar prostatectomy.[19] Unfortunately, in their study, the timing of hemorrhage was not mentioned, and the perioperative aspirin regimen was not clarified. Thus, it was not possible to ascertain if the issue of secondary hemorrhage was being addressed by them. The most common PAI, nowadays, is aspirin, which is also true for our cohort. Aspirin irreversibly inhibits cyclooxygenase-1 (COX-1), leading to decreased production of thromboxane-A2. However, there are some relatively newer forms of PAI in the market which are also gaining popularity due to the use of drug-eluting coronary stents. One example is clopidogrel, which accounted for a few cases in our study population. Our study did not separately look at the risk of aspirin and clopidogrel with respect to secondary hemorrhage. However, with a general belief that clopidogrel being a more potent anticoagulant than aspirin, we would not be surprised to find that both aspirin and clopidogrel would contribute to a higher risk of secondary hemorrhage on its own.

In our study, patients were asked to resume PAI upon discharge. The timing of resuming aspirin with respect to secondary

hemorrhage was studied by Ehrlich *et al*.[12] In their cohort, monopolar TURP, open prostatectomy, and TURBT patients were all grouped together for investigation. All patients withheld aspirin treatment at least 5 days before surgery, and they were randomized into either resuming aspirin 24 h after the completion of bladder irrigation, or 3 weeks after the surgery. The results of their study showed that early aspirin resumption after surgery did not carry an increased risk of secondary hemorrhage. Together with the results of our study, it may suggest that the risk of secondary hemorrhage lies in the history of PAI consumption, rather than just the resumption of PAI. In other words, the effect of PAI on coagulation and bleeding may last longer than one expects, even after its withdrawal before surgery. Despite having a plasma half-life of only 15–20 min, the platelet inhibitory effect of aspirin remains for the lifespan of the platelet which is 7–10 days. This is explained by the irreversible effect on COX-1.[20] Such effect may explain the higher risk of secondary hemorrhage in the group of patients taking aspirin.

Finasteride was investigated for its role in preventing secondary hemorrhage in monopolar TURP. Hagerty *et al*. compared the postoperative outcome in a group of patients pretreated with finasteride for 2–4 months before TURP, with those patients without finasteride pretreatment.[21] Finasteride pretreatment group demonstrated a secondary hemorrhage risk of 8.3%, and the group without pretreatment demonstrated a secondary hemorrhage risk of 36.8%. However, such an impact from 5-ARIs on secondary hemorrhage was not observed in our cohort of bipolar prostate surgery. Up to this moment, the only available randomized controlled trials investigating the effect of 5-ARIs on prostate surgery were performed on monopolar TURP. Furthermore, the only available randomized controlled trials investigating the relationship between 5-ARIs and secondary hemorrhage yielded negative results.[22-24] Together with the results from our study, the role of 5-ARIs in secondary hemorrhage is yet to be confirmed.

CONCLUSIONS

Secondary hemorrhage after bipolar surgery for BPH is a common event. The risk of its occurrence appears to be smaller when compared with its monopolar counterpart. Consumption of PAI is positively correlated with such complication. Consumption of 5-ARIs was not found to be useful in minimizing the risk of its happening.

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Conflicts of interest
There are no conflicts of interest.

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