Surgical management of BPH in patients on oral anticoagulation: transurethral bipolar plasma vaporization in saline versus transurethral monopolar resection of the prostate

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Introduction: To compare postoperative outcomes of patients on oral anticoagulation (OA) treated with transurethral plasma vaporization of the prostate in saline water (TUVis) and transurethral resection of the prostate (TURP).

Materials and methods: Between January and December 2009, 111 patients on OA therapy were treated with either TURP or TUV is in eight centers. Types of OA and perioperative management were collected. Postoperative outcomes were statistically compared between the two groups. Results: A total of 57 (51%) and 54 (49%) patients were treated with TURP and TUV is, respectively. Types of OA were not significantly different between the two groups,

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Address correspondence to Dr. Nicolas Barry Delongchamps, Department of Urology, Cochin Hospital, 27 rue du Faubourg Saint Jacques, 75014 Paris France but bladder catheterization prior to surgery was more frequently observed in the TUV is group. Before surgery, 28 patients were treated with warfarin alone, 74 with a platelet aggregation inhibitor (PAI) alone, and 9 with a combination of both. PAI was withdrawn preoperatively in 50 patients. All treatments with warfarin were switched for heparin. Comparison of the two groups showed significantly less hemorrhagic complications after TUVis. Patients treated with TUV is experienced less bladder washouts (2% versus 18%, p = 0.008), less late hematuria (4% versus 19%, p = 0.02), and lower decrease of serum hemoglobin (mean decrease of 0.66 versus 1.47 g/dL, p = 0.02). Postoperative bladder catheterization and hospital stay were significantly shorter, whereas the rate of urinary retention was significantly higher. Three months after surgery, functional results were not significantly different between the two groups. Conclusions: In patients on OA, TUV is led to significantly less bleeding, as well as shorter bladder catheterization and hospital stay than TURP.

Key Words: benign prostatic hyperplasia, plasma vaporization, TUVIS, TURP

Introduction

Transurethral resection of the prostate (TURP) is the gold standard for the endoscopic treatment of benign prostatic hyperplasia (BPH).¹ Nonetheless, Surgical management of BPH in patients on oral anticoagulation: transurethral bipolar plasma vaporization in saline versus transurethral monopolar resection of the prostate

it remains associated with significant morbidity, especially in terms of hemorrhage complications leading to delayed hospital discharge and possible blood transfusion.¹⁻³ The number of patients requiring oral anticoagulation (OA) with coumarin derivatives or platelet-aggregation inhibitors (PAI) is increasing steadily. Currently, approximately 30% of patients admitted for surgery have cardiovascular diseases and are treated with OA therapy.^{1,2} These patients are at increased risk of hemorrhagic complication, and represent therefore a challenging issue for urologists. Indeed, the hazards of altering chronic OA for surgery are vastly underestimated, and simple withdrawal of OA with no substitution has been shown to increase significantly the risk of thromboembolic events.⁴

To minimize per and postoperative bleeding, various minimally invasive alternatives have been introduced, including transurethral laser vaporization and more recently plasma vaporization of the prostate. A Cochrane systematic review published in 2004 concluded that laser techniques reduced the risk of transfusion and decreased the duration of hospitalization, as compared to classical TURP.⁵ Bipolar transurethral plasma vaporization of the prostate (transurethral plasma vaporization of the prostate (transurethral vaporization in saline: TUVis - Olympus) is a new technique which could also potentially decrease bleeding. However, these properties remain to be demonstrated. In this retrospective analysis, the objective was to compare per and postoperative outcomes between TUVis and TURP in patients under long term OA therapy.

Materials and methods

Patients' inclusion

In this multicentric observational study, we retrospectively collected data from patients with BPH treated with either TURP or TUVis between January and December 2009 in eight academic hospitals. A total of 111 patients were on OA therapy preoperatively, and were thus included for analysis.

Procedures and OA management

OA was managed by the anesthesiologist prior to surgery, and by both surgeons and anesthesiologists after the procedure. TUVis was performed using a bipolar highfrequency generator (Olympus UES-40 HF) and a 26-Fr continuous flow bipolar resectoscope (Olympus OES-Pro TURis). The procedure was performed following a classical TURP scheme, starting at the bladder neck and continuing onto the lateral and anterior lobes of the prostate. Isotonic 0.9% sodium chloride solution at 37°C was used as the irrigant and a continuous in-and-out flow was maintained during surgery.

Collected data and judgment criteria

Patients' preoperative characteristics included age, international prostate symptom score (IPSS), maximal urinary flow (Qmax), prostate-specific antigen level (PSA), postvoiding residual volume (PVR), prostate volume, preoperative bladder catheterization. For patients having a bladder catheter prior to surgery, the IPSS and Qmax were not assessed. Collected perioperative parameters included time of procedure, duration of hospital stay after surgery, duration of bladder catheterization after surgery, variation of serum hemoglobin (delta Hb (g/dL)) between day before and day after surgery, bladder clotting and blood transfusion. Collected postoperative complications included bladder clots occurring during hospitalization and requiring action of a physician (with or without surgical revision), blood transfusion, urinary retention, thrombo-embolic events (deep venous thrombosis or pulmonary embolism), TURP syndrome, late hematuria occurring after discharge from hospital, and urinary infection. Functional results were collected at 3 months postoperatively, and included IPSS, Qmax and PVR.

Statistical analyses

Statistical analyses were conducted using MedCalc software, version 11.0.0.0, with a p value < 0.05 considered as statistically significant. Preoperative and postoperative variables were compared between the two patient groups. The Student t test was performed for the comparison of quantitative variables, whereas the Fisher's exact test was applied for the comparison of binary variables.

Results

The demographical and clinical characteristics of the 111 patients included for analysis are summarized in Table 1. A total of 57 (51%) and 54 (49%) patients were treated with TURP and TUVis, respectively. Preoperative variables were not significantly different between the two groups, except for bladder catheterization prior to surgery, which was more frequently observed in patients treated with TUVis, Table 1.

Before surgery, 28 patients were treated with warfarin alone, 74 with PAI alone, and 9 with a combination of PAI and warfarin. PAI treatment indications were primary prevention of arterial disease, coronary disease and secondary prevention of arterial disease in 9, 56 and 18 patients, respectively. Warfarin treatment indications were the presence of a mechanical cardiac valvular prosthesis, a history of atrial fibrillation and a history of deep vein thrombosis in 6, 29 and 2 patients, respectively. A therapy received by patients prior to surgery was not significantly different between groups, Table 2.

	TURP (n = 57)	TUVIS (n = 54)	p value
Median age (yrs)	73 [62-90]	74.5 [56-90]	0.6
Median preoperative IPSS	18 [6-32]	20 [3-32]	0.8
Median preoperative Qmax (mL/s)	10 [3-27]	10 [4-17]	0.8
Median PVR (mL)	80 [0-620]	25 [0-500]	0.2
Mean prostate volume (cm ³)	48 [28-120]	47 [12-100]	0.9
Mean PSA (ng/mL)	4.24 [0.48-30]	3.14 [0.5-9]	0.8
No. of patients with bladder catheter prior to surgery	8 (14%)	25 (46%)	0.0003
Ranges are written in brackets. TURP = transurethral resection of	of the prostate; TUVIS	= transurethral vaporiz	ation in saline

TABLE 1.	Preoperative	characteristics	of the 111	patients	included	for a	analysis
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TABLE2. Typeoforal anticoagulation and perioperative management

	TURP (n = 57)	TUVIS (n = 54)
Aspirin alone	31	20
Withdrawal	26	11
Switch for heparin	0	1
Continuation	5	8
Clopidogrel alone	6	7
Withdrawal	6	6
Switch for heparin	0	0
Continuation	0	1
Warfarin alone	15	13
Withdrawal	2	1
Switch for heparin	13	12
Continuation	0	0
Clopidogrel and aspirin	4	6
Withdrawal of both	1	0
Withdrawal of clopidogrel	2	6
Withrawal of aspirin	1	0
Warfarin and clopidogrel	0	2
Switch of warfarin for heparin	0	2
and withdrawal of clopidogrel		
Warfarin and aspirin	1	6
Withdrawal of warfarin alone	1	0
Switch of warfarin for heparin and withdrawal of aspirin	0	4
Switch of warfarin for heparin and continuation of aspirin	0	2
TURP = transurethral resection of the TUVIS = transurethral vaporization in	prostate saline	

PAI was withdrawn preoperatively in 17 (51%) patients treated with TUVis. Comparatively, PAI was withdrawn in 33 (80%) patients treated with TURP (p = 0.01). In these patients, preventive doses of low molecular weight heparin were delivered during the perioperative period. Bleeding, postoperative bladder catheterization and hospital stay were not significantly different between patients who continued or stopped PAI. None of the patients experienced any thromboembolic event during follow up.

None of the treatments with warfarin (n = 37 patients) were continued during the perioperative period. Treatment was switched for curative doses of low molecular weight heparin in 33 (89%) patients. In the 4 remaining patients treated with warfarin preoperatively, treatment was withdrawn and they were given preventive doses of low molecular weight heparin.

Overall comparison of the two groups showed significantly less hemorrhagic complications in patients treated with TUVis, Table 3. They experienced less bladder washouts, less late hematuria, and lower decrease of serum hemoglobin. Postoperative bladder catheterization and hospital stay were significantly shorter in patients treated with TUVis, whereas the rate of urinary infection was significantly lower in patients treated with TURP.

Three months after surgery, functional results were not significantly different between the two groups, but there was a trend towards lower IPSS and higher Qmax in patients treated with TURP, Table 3.

Comparison between subgroups of patients treated only with curative doses of low molecular weight heparin and patients who continued their PAI showed also lower decrease in serum hemoglobin, as well as lower rate of bladder clots removal and late hematuria in patients treated with TUVis, Table 3. Postoperative bladder catheterization was significantly shorter after TUVis in all subgroups of patients. Surgical management of BPH in patients on oral anticoagulation: transurethral bipolar plasma vaporization in saline versus transurethral monopolar resection of the prostate

	Overall results			Heparin alone during perioperative period			PAI alone during perioperative period		
	TURP (n = 57)	TUVIS (n = 54)	p value	TURP (n = 13)	TUVIS (n = 19)	p value	TURP (n = 9)	TUVIS (n = 15)	p value
Mean operating time (min)	48 [15-75]	55 [15-120]	0.2	42 [30-60]	51 [15-85]	0.1	42 [15-60]	52 [20-90]	0.4
Mean duration of catheter drainage (hrs)	93 [24-192]	45 [14-240]	< 0.0001	96 [36-192]	54 [16-240]	0.05	130 [24-192]	40 [14-144]	0.0001
Mean duration of hospital stay (days)	4.1 [2-13]	3 [1-11]	< 0.0001	4 [3-7]	3.6 [1-11]	0.6	5.6 [3-13]	2.7 [1-7]	0.006
Median 3 mo.	7	9	0.3	8	9	0.4	5	10	0.3
IPSS	[3-16]	[1-25]		[5-16]	[1-20]		[3-15]	[0-23]	
Median 3 mo. postop Qmax (mL/s)	17.6 [7.5-27]	15.2 [6-36]	0.2	17.6 [7.5-27]	15 [6-27]	0.2	17 [8-20]	14 [9-17]	0.2
Median 3 mo. PVR (mL)	14 [0-60]	20 [0-170]	0.9	12 [0-35]	16 [0-70]	0.5	14 [0-60]	34 [0-170]	0.1
Mean delta Hb (g/dL)	-1.47 [-4.8;+0.1] [-0.66 -2.2;+1]	0.02	-1.06 [-2.1;-0.3]	-0.91 [-3.6;+0.9]	0.8	-1.68 [-4.8;+0.1]	-0.55 [-2.2;+0.6]	0.06
Bladder clots	10 (18%)	1 (2%)	0.008	3 (23%)	0 (0%)	0.05	4 (44%)	1 (7%)	0.05
Blood transfusion	0	0	1	0	0	1	0	0	1
Urinary retention	0	7 (13%)	0.005	0	3 (16%)	0.05	0	3 (20%)	0.3
Early reintervention for bladder clotti	0 ing	0	1	0	0	1	0	0	1
Late hematuria	11 (19%)	2 (4%)	0.02	3 (23%)	0 (0%)	0.05	4 (44%)	0	0.03
Infection	2 (3.5%)	5 (9%)	0.3	0 (0%)	2 (10%)	0.5	1 (11%)	2 (13%)	1

TABLE 3.	Postoperative	outcomes	and	comp	lications
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All 7 patients of the TUVIS group who experienced postoperative urinary retention had preoperative bladder catheterization. Three months after surgery, only 2 of these 7 patients still needed bladder catheterization.

TURP = transurethral resection of the prostate; TUVIS = transurethral vaporization in saline

Discussion

Surgical morbidity is a day-to-day concern for surgeons. Moreover, because the consequences of BPH are mainly functional, the issue is even more crucial. In patients on anticoagulation therapy, surgical benefit on LUTS has to be balanced with the risk of major bleeding and death.⁶⁹ On the other hand, anticoagulation withdrawal may lead to life threatening cardiovascular events, which does not make it a comfortable option either. Currently, there is no consensus in how to manage OA during the perioperative period. In patients treated with vitamin K antagonists, the most commonly used procedure is to switch the OA for heparin during the perioperative period.⁶ However, published data are sparse. The few reported series did not exceed 20 patients, and rate of blood transfusion and rehospitalization for hematuria after TURP were ranging between 20% and 30%.^{7,8} In patients treated with PAI, TURP may also lead to severe bleeding consequences,¹⁰ although one placebo-controlled study showed that low dose aspirin therapy (150 mg) was not associated with a significant increase of

transfusion rate, time to catheter removal, and hospital stay.¹¹ Additionally, whenever decision is taken to stop aspirin perioperatively, early reintroduction after 48 hours was shown to be safe enough. In a prospective randomized study, postoperative bleeding was not significantly different when aspirin was reintroduced 48 hours versus 3 weeks after TURP.¹² In our study, none of the patients treated with vitamin K antagonists continued their OA therapy during the perioperative period. All of them were treated with curative doses of low molecular weight heparin. Only a third of the patients treated with PAI preoperatively maintained their OA therapy, and these patients did not experience any significant increase of postoperative bleeding as compared to those who stopped PAI. However, most of these patients were treated with TUVis.

The challenging issues of operating patients on OA therapy may be brushed away by simply leaving patients on long term catheter drainage or using palliative procedures such as urethral implants. However, altered QOL of patients with bladder catheterization and reported morbidity of urethral implants have also to be taken into consideration, and may not be accepted by neither patients nor urologists. Additionally, one should also keep in mind that postponing surgery in these patients may increase even more bleeding risk, related to long term bladder catheterization and prostatic inflammation prior to TURP.

Various minimally invasive TURP alternatives have been reported to decrease postoperative bleeding.^{5,6,13,14,15} As suggested by a Cochrane systematic review,⁵ postoperative bleeding, blood transfusion and hospital stay seemed to be lower with laser techniques than with TURP. However, the authors noted also that small sample sizes and differences in study design limited any definitive conclusions regarding the preferred type of laser technique. Ruszat et al⁶ have reported their experience of photoselective laser vaporization of the prostate for the treatment of BPH. They compared 116 cases on OA to 92 control cases. OA was a coumarin derivative in 36 cases, aspirin in 71 patients and clopidogrel in 9. None of the OA therapies were stopped during the perioperative period. No case of persistent bleeding or blood transfusion was reported in any group, suggesting that laser vaporization may be safely used in patients on OA therapy. The same authors reported more recently the results of a prospective non randomized study comparing photoselective laser vaporization to TURP, with a follow up of 24 months.¹⁴ The rate of intraoperative bleeding (3% versus 11%), blood transfusions (0% versus 5.5%) and early postoperative clot retention (0.4% versus 3.9%) was

significantly lower after laser vaporization. Although improvement of peak urinary flow rate was higher after TURP, IPSS and PVR during follow up showed no significant difference.¹⁴

Holmium laser enucleation (HoLEP) has also been shown to decrease postoperative bleeding as compared to TURP.¹³ In patients on OA, however, no comparative study is available.

Elzayat et al¹⁵ reported their experience with HoLEP in a retrospective series of 81 patients on OA therapy. During the perioperative period, OA was continued in 14 patients, switched for low molecular weight heparin in 34, and withdrawn in 33. Only 7 patients (8%) required blood transfusion. Of them, 5 were on low molecular weight heparin, one was on PAI, and the last did not have any anticoagulation therapy.

Electrical vaporization of the prostate has been reported to reduce perioperative bleeding as compared to TURP. Monopolar vaporization of the prostate has been evaluated by a meta-analysis of 17 randomized clinical trials.¹³ The authors concluded that the technique reduced significantly bleeding risk and hospital stay, but increased the rate of urinary retention as compared to TURP. Bipolar vaporization of the prostate (Gyrus PlasmaKinetic vaporization) is of more recent development. Besides reducing bleeding, the potential advantage of this new technology, resides in the use of saline water instead of glycerine as irrigation fluid, which rules out the risk of "TURP syndrome" observed in 2%-10% of patients treated with monopolar TURP.¹⁶ Bipolar vaporization has been compared to TURP by two randomized prospective studies.^{3,17} None of them, however, demonstrated any advantage of bipolar vaporization in terms of bleeding.

TUVis is derived from Gyrus PlasmaKinetic vaporization, using the same principle but different loop shapes and generator settings. To our best knowledge, no studies to date have compared TURP to minimally invasive alternatives in selected, high risk patients under OA therapy. In this retrospective analysis, we found that TUVis significantly decreased postoperative bleeding, bladder catheterization time and hospital stay as compared to TURP, with similar functional outcomes at 3 months. Patients at highest risk of bleeding were those on PAI who maintained their treatment, and those on vitamin K antagonists who switched for curative doses of low molecular weight heparin. In these subgroups of patients, TUVis led also to significantly less bleeding complications than TURP. In patients on PAI, all bleeding parameters but one (delta Hb) were significantly less altered after TUVis, resulting in shorter bladder irrigation and catheterization, as well as shorter hospital stay, Table 3.

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In patients on curative doses of low molecular weight heparin, TUVis gendered also less bladder clots and hematuria, resulting in shorter bladder catheterization, but similar hospital stay, Table 3.

The improvement in bleeding observed after TUVis should however be balanced with the higher rate of urinary retention, unrelated to bladder clotting. Although this result may be explained by the higher rate of long term catheter drainage prior to surgery in patients treated with TUVis, it may also be due to the technique itself. Indeed, the meta-analysis of Lourenco¹³ showed a higher rate of urinary retention after monopolar vaporization of the prostate versus TURP, probably related to the higher levels of energy delivered. Although the energy is delivered differently with TUVis, consequences on prostatic tissue may be similar.

Our study has several limitations, the most obvious being the retrospective collection of the data, the absence of randomization, and a short follow up. Another limitation was the higher rate of patients with bladder catheter prior to surgery in the TUVis group. It was shown that the presence of preoperative indwelling catheter increased the risk of perioperative bleeding and urinary tract infection.¹⁶ Therefore, the lower risk of hemorrhagic complications we observed in the TUVis group might have been underestimated. Finally, we did not compare the cost of surgery between groups. Although TUVis is a more expensive procedure than TURP because of non-reusable electrodes, the global cost may be decreased by the lower hospital stay. Further prospective and randomized comparison is needed to investigate the advantage of TUVis over TURP in patients treated with OA.

Conclusions

In this retrospective study comparing TUVis to TURP in selected high risk patients on OA therapy, TUVis led to significantly less bleeding, as well as shorter bladder catheterization and hospital stay. These results have to be balanced with a higher rate of urinary retention unrelated to bladder clotting.

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