Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2023.50.008008

Cardiovascular and Thromboembolic Risk of Aspirin and Warfarin Interruption at Transurethral Resection of Prostate

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ARTICLE INFO

Received: May 26, 2023

Published: June 02, 2023

Citation: Sameh Hijazi and Pavlo Synoverskyy. Cardiovascular and Thromboembolic Risk of Aspirin and Warfarin Interruption at Transurethral Resection of Prostate. Biomed J Sci & Tech Res 50(5)-2023. BJSTR. MS.ID.008008.

ABSTRACT

Introduction: To evaluate cardiovascular, thromboembolic and bleeding risk of aspirin and warfarin interruption for transurethral resection of prostrate (TURP).

Methods: A total of 508 patients who underwent TURP were divided into 3 groups: group without anticoagulant or antiplatelet (AC/AP) (n=347), aspirin (100mg) group (n=130), and warfarin group (n=31). Cardiovascular, thromboembolic and bleeding complications were analyzed and compared. Aspirin and warfarin intake were interrupted seven days before procedure.

Results: Warfarin and aspirin groups had a significantly higher perioperative cardiovascular complication rate compared to without AC/AP group (9.7% vs 0.6%, p = <0,001 and 3.9% vs 0.6%, p = 0.008, respectively). The Aspirin group had a significantly higher thromboembolic complication rate compared to without AC/AP group (1.6% vs 0.6%, p = 0.031, respectively). The postoperative blood loss did not significantly differ amongst the three groups. Nevertheless, the blood transfusion rate was significantly higher in warfarin and aspirin groups compared to the without AC/AP group (12.9% vs 1.2%, p = 0.001, and 6.2% vs 1.2 %, p = 0.001, respectively). The operative revision rate due to bleeding or bladder tamponade was significantly higher in the warfarin group compared to the without AC/AP group (22.6% vs 8.4%, p = 0.01, respectively). The bleeding rate was not significantly higher in the aspirin group compared to the without AC/AP group (10% vs 8.4%, p = 0.41).

Conclusion: Warfarin patients had a significantly higher risk for cardiovascular complications and bleeding following TURP. Perioperative interruption of aspirin increases the risk for thromboembolic events. Currently, to default the cessation of aspirin periprocedural is not appropriate.

Keywords: TURP; Aspirin; Warfarin; Antiplatelet; Anticoagulation

Abbreviations: BPH: Benign Prostate Hyperplasia; TURP: Transurethral Prostatectomy; AC: Oral Anticoagulant; AP: Oral Antiplatelet; TRUS: Transrectal Ultrasound; PSA: Prostate-Specific Antigen; SPSS: Statistical Package for the Social Sciences; ASA: American Society of Anesthesiologists

Introduction

Benign prostate hyperplasia (BPH) associated with lower urinary tract symptoms is a very common disease in elderly men. Transurethral prostatectomy (TURP) is still considered the gold standard of operative therapy for BPH with prostates of < 80 ml volume compared to other transurethral procedures in terms of urodynamic outcomes [1-3]. In our continuously aging population, increasing amounts of older und multimorbid men managed by oral anticoagulant (AC) and oral antiplatelet (AP) drugs are having TURP performed. Approximately 25% of men over the age of 65 are taking aspirin [4]. Men taking AC or AP can have an elevated risk of complications under TURP. Periprocedural, AC and AP are often

interrupted due to possible bleeding complication [5]. Previous studies have reported an increased risk of bleeding under AC [6-9]. On the other hand, discontinuing of AC or AP for treatment increases the risk of cardiovascular and cerebrovascular events [4,10]. The objective of our study was to evaluate the thromboembolic, cardiovascular and bleeding events of aspirin and warfarin interruption for TURP compared to patients not receiving AC/AP. The interruption of oral AC and oral AP can increase the risk of cardiovascular and cerebrovascular complications. Despite the preoperative interrupting of AC and AP intake, bleeding complications can be increased.

Materials and Methods

Patient Population

We evaluated a total of 508 patients undergoing TURP, retrospectively. Patients were divided into three groups: without AC/AP group included 347 patients, aspirin (100mg) group included 130 patients, and warfarin group included 31 patients. The indication for aspirin was as prophylaxis for coronary heart disease. Warfarin and aspirin were ceased seven days before procedure. Follow-up was 30 days after TURP. The study was approved by the local Ethics Committee (2017-604-b-S). Inclusion criteria were the performance of TURP by low-pressure monopolar resection and by the two surgeons with long-term experience in transurethral interventions. Excluding criteria were the history of prostate cancer, recurrent prostate adenoma, and the intake of many AC or AP. Perioperative diagnostics included urine analysis, urine culture, prostate volume determined by transrectal ultrasound (TRUS), prostate-specific antigen (PSA), uroflowmetry (Qmax), nephrosonography and residual urine volume. We studied the following characteristics: length of hospital stay, operating time, catheterization time, postoperative hemorrhage, blood transfusion, bladder tamponade, operative revision, cardiovascular and thromboembolic events. Blood counts controls were performed on the first and forth day postoperatively. As in most other studies, the operation duration was recorded for the entire procedure and not merely the resection time. The minimal quick value for the patients to have surgery was 70%. The preoperative morbidity was determined using the ASA-classification (American Society of Anesthesiologists) and the postoperative complications using the Clavien-classification. Postoperatively, patients without AC/AP and aspirin patients were administered nadroparin 0.3 ml subcutaneous once daily. Warfarin patients were bridged using body weight adjusted low molecular heparin derivatives. AC/AP was resumed as soon as possible after the intervention.

Statistical Analysis

Data was analysed using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL) programme. We used a T-test for continuous data and Chi square test for dichotomous data. The Significance level was set at a P value of less than 0.05.

Results

Patient's characteristics and urodynamic outcomes are showed in Table 1. The postoperative cardiovascular complication rate was significantly higher in the warfarin and aspirin groups compared to the without AC/AP group (9.7% vs 0.6%, p = <0.001 and 3.9% vs 0.6%, p = 0.008, respectively). Two patients (6.5%) of the warfarin group had cardiac decompensation and one patient (3.2%) had a hypertensive crisis postoperatively. The Aspirin group had a higher thromboembolic complication rate compared to the without AC/AP group (1.6% vs 0.6%, p = 0.031, respectively). Postoperatively, two patients of the aspirin group (1.5%) had deep vein thrombosis and one patient (0.8%) had a pulmonary embolism. In the group without AC/AP two cases of deep vein thrombosis occurred. In the aspirin group one patient (0.8%) had an acute coronary syndrome, one patient (0.8%) experienced cardiac decompensation, and one patient (=.(%) had a hypertensive crisis. Intensive care treatment was required in two patients (1.5%) of the aspirin group. Perioperative blood loss is described in Table 2. Hemoglobin and hematocrit were determined on postoperative day 1 and 4 in 94.5%, 92.3%, and 94.8% of without AC/AP, aspirin, and warfarin groups respectively. Postoperatively, there were no significant differences in blood loss amongst the three groups. Nevertheless, the blood transfusion rate was significantly higher in the warfarin and aspirin groups compared to the without AC/AP group (12.9% vs 1.2%, p = 0.001 and 6.2% vs 1.2 %, p = 0.001, respectively). Table 3 describes the postoperative complications classified by the Clavien system. Despite the preoperative interruption of warfarin intake, the operative revision rate due to bleeding or bladder tamponade was significantly higher in the warfarin group compared to the without AC/AP group (22.6% vs 8.4%, p = 0.01, respectively). The bleeding rate was not significantly higher in the aspirin group compared to the without AC/AP group (10% vs 8.4%, p = 0.41).

Table 1: Patient's characteristics and urodynamic outcomes.

	Gr without AC/AP(n=347)	Aspirin (n=130)	Warfarin (n=31)	p-value without AC/AP vs aspirin	p-value without AC/AP vs warfarin
Age (years)	68±7.6	72±8.5	74±6	n.s.	n.s.
ASA classification:					
I (%)	39	1.5	0	0.001	0.002
II (%)	51	86.5	55	0.02	n.s.
III (%)	10	13	45	n.s.	0.0005
PSA (ng/ml)	3.3±21	4.6±6	3.7±7	0.002	n.s.
Quick (%)	105±11	102±14	78±12	0.0016	n.s.
Prostate volume (ml)	40±23	40±24	40±18	n.s.	n.s.
Stay time (d) (mean ± range)	8±4.4	10±7.5	14±11.3	0.03	0.0005
Catheterization time (d) (mean ± range)	2±1	2.1±1.2	3±5.2	n.s.	0.003
Postoperative Qmax (ml/sec) (mean ± range)	21±9	22±10	17±11	n.s.	n.s.
Postoperative residual urine (ml) (mean ± range)	20±44	23±41	25±96	n.s.	n.s.
Operating time (min) (mean ± range)	40±20	45±21	40±20	n.s.	n.s.
Resection weight (g) (mean ± range)	24±20.9	25.5±24	22±15.4	0.008	0.003
Prostate cancer rate at histology of TURP (%)	6.6	5.4	6.5	n.s.	n.s.

Note: AC anticoagulation, PSA prostate specific antigen, Qmax maximal flow rate. n.s. not significant, d day.

Table 2: Postoperative blood less.

	without AC/AP (n=347) n(%)	Aspirin (n=130) n(%)	Warfarin (n=31) n(%)	p-value without AC/AP vs aspirin	p-value without AC/AP vs warfarin
Hb loss (1st postoperative day; g/dl)	1.3±5.7	1.3±1.1	1±0.8	n.s.	n.s.
Hb loss (4th postoperative day; g/dl)	1.2±1.3	1.3±1	1.2±0.9	n.s.	n.s.
Ht loss (1st postoperative day;%)	2±3.4	3±3	2±2.7	n.s.	n.s.
Ht loss (4th postoperative day;%)	3±3.7	3.3± 3.1	3±3.3	n.s.	n.s.

Note: AC Anticoagulation, Hb Hemoglobin, Ht Hematocrit, n.s. not significant.

Table 3: Peri- and postoperative complications.

	without AC/AP (n=347) n (%)	Aspirin (n=130) n (%)	Warfarin (n=31) n (%)	p-value without AC/AP vs aspirin	p-value without AC/AP vs warfarin
Clavien I-Complications	42(12.1)	20 (15.3)	4 (12.9)	n.s.	n.s.
Capsule perforation	1 (0.3)	0	0	n.s	n.s.
Bladder tamponde/evacuation through catheter	5 (1.4)	5 (3.8)	0	n.s.	n.s.
Postoperative urinary retention	24 (6.9)	12 (9.2)	4 (12.9)	n.s.	n.s.
Stress urinary incontinence	12 (3.5)	3 (2.3)	0	n.s	n.s.
Clavien II-Complications:	123 (34.8)	60 (40.1)	17 (54.8)	0.022	0.013
Urinary tract infections	72 (20.7)	23 (17.7)	8 (25.8)	n.s.	n.s.

Hematuria	31 (8.8)	13 (10)	3 (9.7)	n.s.	n.s.
Epididymitis	7 (2)	3 (2.3)	0	n.s.	n.s.
TUR-Syndrome	4 (1.2)	2 (1.5)	1 (3.2)	n.s.	n.s.
Blood transfusions	3 (1.2)	8 (6.2)	4 (12.9)	0.001	<0.001
1-2 RCC	3 (1.2)	4 (3.1)	2 (6.4)	n.s.	0.009
2-4 RCC	0	4 (3.1)	0	0.01	n.s.
> 5 RCC	0	0	2 (6.4	n.s.	<0.001
Decompensated glucose metabolism	0	1 (0.8)	0	n.s.	n.s.
TIA	1 (0.3)	1 (0.8)	1 (3.2)	n.s.	0.031
Thrombosis	2 (0.6)	1 (0.8)	0	n.s.	n.s.
Clavien IIIb-Complications:	68 (19.7)	17 (13.1)	10 (32.2)	n.s.	n.s.
Bladder tamponade/operative revision	29 (8.4)	13 (10)	7 (22.6)	n.s.	0,01
apical follow-up resection	10 (2.9)	2 (1.5)	1 (3.2)	n.s.	n.s.
Bladder neck obstruction	8 (2.3)	1 (0.8)	1 (3.2)	n.s.	n.s
Urethral stricture	21 (6.1)	1 (0.8)	1 (3.2)	0.014	n.s.
Clavien IVa-Complications	2 (0.6)	5 (3.9)	3 (9.7)	0.008	<0.001
Intensive care	1 (0.3)	2 (1.5)	0	n.s	n.s
Hypertensive crisis	1 (0.3)	1 (0.8)	1 (3.2)	n.s	0.031
Cardiac decompensation	0	1 (0.8)	2 (6.5)	n.s.	<0.001
Acute coronary syndrome	0	1 (0.8)	0	n.s.	n.s.
Clavien V-Complications	0	1 (0.8)	0	n.s	n.s
Mortality	0	1 (0.8)	0	n.s.	n.s.

Note: AC Anticoagulation, RCC Red cell concentrate, n.s. not significant, TIA transient ischemic attack.

Discussion

Frequently, the urologist is presented with multimorbid men suffering BPH managed by oral AC and oral AP drugs. TURP is still considered first line treatment for BPH with small and medium sized prostate adenomas. Disadvantages of TURP are the high perioperative morbidity and the risk of bleeding events. In our study, cardiovascular complications were significantly higher in patients who discontinued warfarin and aspirin intake compared to patients without AC/AP. The most occurred cardiovascular events were perioperative cardiac and hypertensive decompensation. Major thromboembolic events occurred in patients who interrupted aspirin intake. Tayler et al reported in their study an elevated cardio- and cerebrovascular complication rate (9%) in patients who ceased aspirin intake before TURP [11]. The elevated rate of complications in our aspirin and warfarin groups is explained by the cardiovascular morbidity and discontinuation of AC. A recent retrospective study showed no significant difference in cardiovascular events between patients undergoing TURP that ceased aspirin intake preoperatively and AC/AP naïve patients [12]. In our study, the cardiopulmonary complication rate in the without AC/AP group was comparable to other TURP studies without AC/AP (0.1%) 7. One patient who ceased aspirin died due to pulmonary embolism. The overall mortality rate (0.2%) in our study was not significantly higher than rates described in literature (0.1%) 7. Although blood loss didn't significantly differ between all three groups in our study, the warfarin group did have the highest postoperative bleeding, bladder tamponade, operative revision, and blood transfusion rate. Interestingly, all bleeding cases in the warfarin group were major and required surgical revision despite the perioperative interruption of warfarin intake and normal coagulation values. In our study, bleeding complications in the aspirin group were not significantly increased compared to the without AC/AP group. A Danish randomized prospective study double blindly compared TURP on patients taking 150 mg of aspirin a day and a placebo group. This study showed a significantly higher bleeding rate in the patients on aspirin compared to the placebos (median 284 ml vs 144 ml) [13]. However, this did not lead to a higher transfusion rate. Finnish authors didn't show in their study a significant difference in intraoperative blood loss in patients on aspirin and those without AP (250 mg/day) [14]. However, they did report that 8% of patients taking aspirin had postoperative hemorrhage and bladder tamponade while no postoperative bleeding needing treatment occurred in the patients not taking AC/AP. Taylor et al. retrospectively compared patients undergoing TURP without AC/AP, with preoperative

cessation of AC/AP and patients taking AC/AP [11]. They found out in their study a significantly higher (p = 0.01) postoperative hemorrhage rate in the group of patients that paused AC/AP (20%) and continued AC/AP (86%) compared to the group not taking AC/AP (9.9%). Rühle et al. highlight in their study that patients with AP therapy undergoing TURP don't have increased bleeding after surgery [15]. However patients under AC with warfarin have an increased blood transfusion rate (9%), bleeding, and longer stay time in hospital after TURP. The explanations for the significantly higher transfusion rate in aspirin and warfarin patients in our study are the significantly higher cardiovascular comorbidity and wider anesthesiological indication for blood transfusions. Literature describes a TURP transfusion rate of up to 20% [16,17]. In our study, catheterization time was significantly longer in the warfarin group than the without AC/AP group (p = 0.003). The responsible factor for this was prolonged hematuria. The warfarin group had the longest average postoperative length of stay time in hospital due to preoperative cardiovascular diagnostic evaluation, low Quick values, and long duration until catheter removal, postoperative hemorrhage, and cardiovascular complications. Wenders et al. reported in their study a significantly shorter hospital stay in the group without AC compared to the group with aspirin in men undergoing TURP [18]. Our study is limited by its retrospective nature. However, a randomised controlled trial can shed more light.

Conclusion

Patients on warfarin undergoing TURP have a higher bleeding and cardiovascular risk. Perioperative cessation of aspirin intake is associated with a higher risk in cardiovascular and thromboembolic events. Before TURP the cease of aspirin is not required and is not recommended.

Author Disclosure Statement

The authors declare no conflict of interest.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.50.008008

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