BMC Urology

RESEARCH

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Impact of oral antithrombotic agents on urinary continence recovery following robot-assisted radical prostatectomy: a retrospective cohort study

Masashi Oshima[1*], Satoshi Washino[1], Kai Yazaki[1], Shozaburo Mayumi[1], Yuhki Nakamura[1], Tsuzumi Konishi[1], Kimitoshi Saito[1] and Tomoaki Miyagawa[1]

Abstract

Background Robot-assisted radical prostatectomy (RARP) is a preferred minimally invasive surgical treatment for prostate cancer. The number of elderly patients and those with cardiovascular and/or cerebrovascular issues undergoing surgery is increasing, and many of them are taking antithrombotic (AT) agents. However, the effect of AT agents on postoperative urinary recovery has not been adequately studied. In this study, we analyzed the differences in the postoperative recovery of urinary continence and oncological outcomes in patients undergoing RARP for localized prostate cancer between AT agent adherents and non-adherents.

Methods A total of 394 patients who underwent conventional anterior RARP between February 2015 and February 2021 were categorized into two groups: those taking oral AT agents (AT group) and the control group. Urinary continence recovery, complications, and oncological outcomes were compared between the groups. A Cox proportional hazards analysis was performed to identify clinical factors that affect urinary continence recovery.

Results The background data and bleeding complications did not differ significantly between the groups. The recovery of continence was significantly poorer in the AT group in terms of complete pad free (HR: 0.53 [95% CI: 0.39–0.71]) and use of ≤ 1 safety pad (HR: 0.74 [95% CI: 0.59–0.94]). The rate of anastomotic leakage on cystography was significantly higher in the AT group (20.9% vs. 6.7%). A univariate analysis revealed that taking antithrombotic agents, higher prostate-specific antigen levels, and a more advanced clinical stage were associated with a poor urinary continence recovery; a multivariate analysis showed that taking AT agents was an independent factor negatively associated with urinary continence recovery. There was no significant difference between the groups in the positive surgical margin rate (19.0% vs. 23.8%) or the biochemical-recurrence-free rate.

Conclusion Taking oral AT agents may be associated with poor urinary continence recovery after RARP.

Keywords Antithrombotic agents, Prostate cancer, Robotic surgical procedures, Surgical oncology, Urinary incontinence

*Correspondence:
Masashi Oshima
m_ohshima@jichi.ac.jp
[1]Department of Urology, Jichi Medical University Saitama Medical Center, 1-847, Amanuma-cho, Omiya-ku, Saitama-shi, Saitama 330-8503, Japan

Introduction

Prostate cancer (Pca) is the most commonly diagnosed cancer in men worldwide, and its incidence has been increasing over the past decade [1]. With the widespread use of PSA screening, more patients are being diagnosed with this type of cancer, and radical prostatectomy has become a prevalent treatment option for localized or locally advanced Pca. Robot-assisted laparoscopic radical prostatectomy (RARP) has gained popularity for the management of nonmetastatic Pca in recent years [2]. Furthermore, RARP has been reported as a cytoreductive therapy for oligometastatic Pca, which has led to an expansion of its indications [3]. Because of the less-invasive nature of RARP, it has been increasingly performed in elderly patients and those with various comorbidities, including cardiovascular and/or cerebrovascular diseases, most of whom may take antithrombotic (AT) agents [4, 5]. In patients taking AT agents, interrupting these agents during the perioperative period increases the risk of thromboembolism, whereas surgeries performed under continued AT agents may have an increased rate of bleeding events. In turn, it has been reported that RARP can be safely performed in patients taking AT agents [6, 7].

Functional loss associated with treatment is a significant concern for patients with Pca, especially regarding postoperative urinary incontinence, which can have a negative impact on their quality of life. AT agents are associated with prolonged wound healing [8], which could be true for the anastomotic junction between the bladder and the urethra and may result in poor postoperative recovery of urinary continence. However, the association between oral AT agents and postoperative urinary continence recovery has not been examined to date. Therefore, we investigated how AT agents affected urinary continence recovery following RARP.

Materials and methods

Study design and inclusion/exclusion criteria

In this retrospective study, we collected data for patients with Pca who underwent conventional anterior RARP between May 2015 and February 2021 at a single medical center. This study was approved by the Institutional Review Board and Ethics Committee of Jichi Medical University Saitama Medical Center (RinS20-058) and carried out according to the Declaration of Helsinki and its amendments. All data were retrospectively collected from the electronic medical records.

Among a total of 564 patients who underwent RARP, the 441 patients who received conventional anterior RARP were included in the present study, whereas patients who underwent Retzius-sparing RARP (RS-RARP) [9, 10] or RARP using the Hood technique [11], both of which aim to improve urinary continence recovery, were not included in this analysis. After the exclusion of 47 patients for the reasons listed in Supplementary Table 1, a total of 394 patients were assessed. Patients were divided into the AT group with taking AT agents (n=84) and the control group (n=310). The AT group was further categorized into three subgroups based on the type of antithrombotic agent: oral antiplatelet (AP) agents (n=66), oral anticoagulant (AC) agents (n=14), and those taking both types of agents (AP+AC) (n=4) (Fig. 1). All patients underwent a comprehensive preoperative clinical staging workup, including a digital rectal exam, measurement of serum prostate-specific antigen (PSA), a multiparametric magnetic resonance imaging (MRI) scan of the prostate, a transperineal or transrectal ultrasound-guided prostate biopsy, a thoracoabdominal CT scan, and a whole-body bone scan.

A total of 564 patients who underwent robotic-assisted radical prostatectomy (RARP) between May 2015 and February 2021 were included in the present study. Of these patients, 123 who underwent Retzius-sparing RARP or Hood-RARP to improve continence were excluded from the analysis, resulting in a cohort of 441 patients who underwent conventional backward RARP. Further exclusions were carried out based on specific criteria, thus eliminating 47 patients for reasons such as a history of preoperative hormone therapy (n=20), insufficient abstinence data (n=9), advanced cancer stages (such as cT4, N1, or M1) (n=6), treatment with active surveillance (n=5), or other factors (n=7). The final cohort for analysis consisted of 391 patients. These patients were stratified into control, AP, AC, and AP+AC groups according to antithrombotic use and specific medication type.

Surgical procedure

All surgeries were conducted via a standard transperitoneal approach using the da Vinci Si® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). A total of nine surgeons performed RARP. The details of the surgical procedure are provided in our previous report [10]. Briefly, a posterior approach was used first, followed by the development of the Retzius space via an anterior approach. A nerve-sparing procedure was carried out in patients with preserved preoperative sexual function; this was performed when no tumor was detected in the posterior lesion on preoperative MRI and no Gleason score of 8 or higher on prostate biopsy was detected for the relevant side. Pelvic lymph node dissection (PLND) was performed only in cases in which MRI or CT scans indicated lymph node swelling in the pelvis.

Perioperative data collection

The background data, including age, body mass index (BMI), serum PSA levels, clinical stage, National

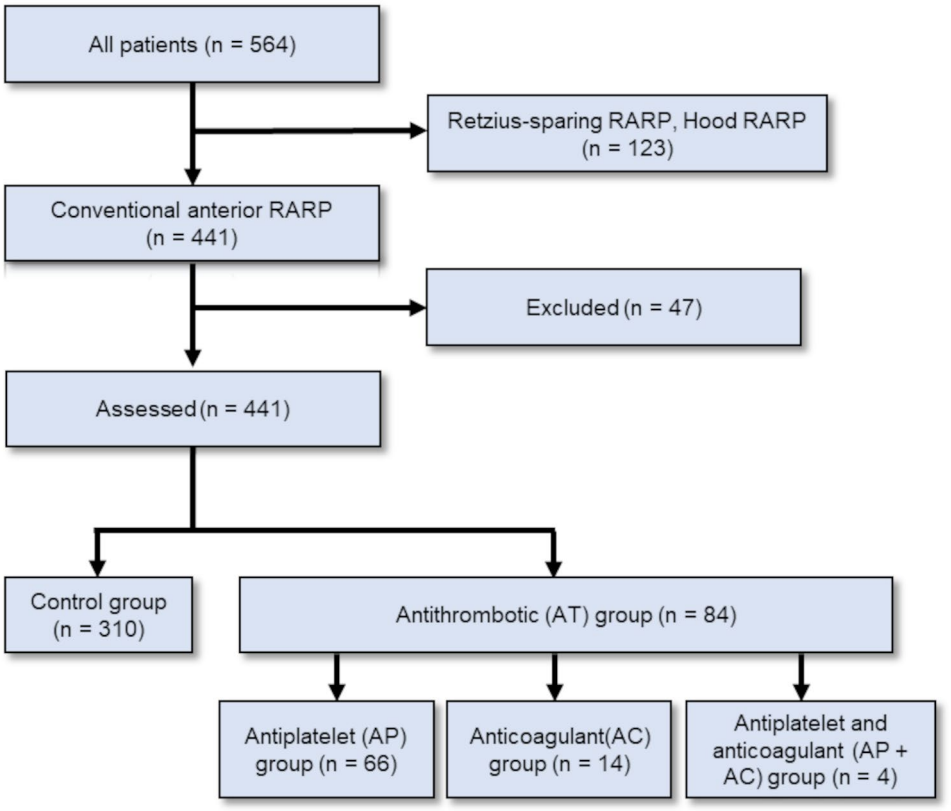

Fig. 1 Enrollment criteria used in this study

Comprehensive Cancer Network (NCCN) risk classification, and MRI-determined prostate volume, of the patients were collected. Operation time, console time, and estimated blood loss during surgery were recorded. We also assessed blood transfusion during and after surgery, and the incidence of overall and hemorrhagic complications. The complications were graded according to the Clavien–Dindo classification. All patients underwent cystography to evaluate for anastomotic leakage on postoperative day 6.

Assessment of the recovery of urinary continence

Urinary continence was assessed at 1, 3, 6, 9, and 12 months after RARP and every 12 months thereafter. Two levels of postoperative urinary incontinence were defined: completely pad-free level (0 pad) and ≤1 safety pad level (0–1 pad).

Study endpoints

The primary objective of the present study was to compare the urinary continence recovery following RARP between the AT and control groups. We also assessed the effect of the number and types of AT agents and of the perioperative management of these agents on urinary continence recovery. Furthermore, oncological outcomes, including the positive surgical margin (PSM) rate, biochemical recurrence (BCR)-free survival, and overall survival, were compared between the two groups. BCR was defined as PSA≥0.2 or the initiation of salvage therapy after RARP.

Statistical analysis

Variables were compared using Student's t-test, Fisher's exact test, the Mann–Whitney U test, or the χ^2 test. Urinary continence recovery and survival were assessed using the Kaplan–Meier method and compared using a log-rank (Mantel–Cox) test. Univariate and multivariate analyses were performed using Cox's proportional hazard model. All data are presented as the mean with standard deviation unless otherwise indicated. All statistical analyses were performed using the GraphPad Prism software, version 9.0 (GraphPad Software, La Jolla, CA, USA). Significance was set at $P<0.05$.

Results

Patient characteristics

There were no significant differences in patient characteristics between the control and AT groups, including age (68.9±5.9 vs. 70.2±5.0 years, $P=0.07$), BMI (23.7±2.7 vs. 24.1±3.2, $P=0.23$), clinical stage ($P=0.11$), biopsy International Society of Urological Pathology grade ($P=0.73$), NCCN risk ($P=0.93$), prostate volume (42.4±18.0 vs.

46.0±20.5 cm^3, P=0.12), and medication for benign prostate hyperplasia (BPH) (P=0.16) or diabetes mellitus (DM) (P=0.07), except for the serum PSA levels, which were higher in the AT group (13.0±15.6 vs. 10.1±8.7 ng/ml, P=0.03) (Table 1).

Details and management of the antithrombotic agents

Among the 66 patients in the AP group, 58 were taking a single AP, 7 were taking dual APs, and 1 was taking triple APs whereas all 14 patients in the AC group were on a single AC agent (Table 2). The AP agents were prescribed for the following reasons. AP: ischemic heart disease (n=38), primary prevention (n=13), stroke (n=9), and spinal canal stenosis (n=6); and all AC agents were prescribed for the management of chronic atrial fibrillation (n=14).

The details of the management of AP and/or AC agents are shown in Table 3. Basically, at least a single AP agent was continued during RARP, except for those prescribed for primary prevention, whereas AC agents were either interrupted or bridged to heparin, and resumed as soon as possible once the bleeding issues were cleared.

Intra- and postoperative findings and complications

The console time (176.9±54.5 vs. 182.9±56.6 min, P=0.37) or estimated blood loss (87.3±98.9 vs. 98.5±112.0 ml, P=0.37) did not differ significantly between the control and AT groups. Nerve-sparing and PLND were performed in 59 (19.0%) and 26 (8.4%) patients in the control group and in seven (8.4%) and five (6.0%) patients in the AT group, respectively.

There were no significant differences in the frequency of blood transfusion (0.3% vs. 0%, P>0.99), bleeding complications (4.8% vs. 8.5%, P=0.29), and overall complications (P=0.12) between the groups. Conversely, the frequency of anastomotic leakage was significantly higher in the AT group compared with the control (20.9% vs. 6.7%, P<0.001) (Table 4). Finally, the hospitalization days (7.5±2.2 vs. 7.1±0.6, P=0.17) were comparable between the groups.

Urinary continence recovery

Compared with the control group, the AT group exhibited a poorer urinary continence recovery (0 pad: HR: 0.53 [95% CI: 0.39–0.71], P=0.0003; 0–1 pad: HR: 0.74 [95% CI: 0.59–0.94], P=0.02) (Fig. 2A–B). Moreover, taking AP and AC was associated with a poor urinary continence recovery compared with the control, respectively (AP group: 0 pad: HR: 0.49 [95% CI: 0.35–0.68], P=0.0017; 0–1 pad: HR: 0.70 [95% CI: 0.55–0.91], P=0.018; AC group: 0 pad: HR: 0.56 [95% CI: 0.31–0.99], P=0.049; 0–1 pad: HR: 0.77 [95% CI: 0.47–1.27], P=0.15) (Fig. 2C–D). The number of AP agents or whether AP was continued or interrupted during the perioperative

Table 1 Patient characteristics

Variables	Control (n=310)	AT (n=84)	P-value
Age, mean±SD	68.9±5.9	70.2±5.0	0.07
BMI (kg/m^2), mean±SD	23.7±2.7	24.1±3.2	0.23
Serum PSA (ng/mL), mean±SD	10.1±8.7	13.0±15.6	0.03
Clinical stage, n (%)			
cT1-T2	270(87.1%)	67(79.8%)	0.11
cT3-T4	40(12.9%)	17(20.2%)	
Biopsy ISUP grade, n (%)			
1	25(8.1%)	10(11.9%)	0.73
2	134(43.2%)	39(46.4%)	
3	60(19.4%)	13(15.5%)	
4	35(11.2%)	8(9.5%)	
5	56(18.1%)	14(16.7%)	
NCCN Risk classification			0.93
Low	15(4.8%)	5(6.0%)	
Favorable intermediate	142(45.8%)	38(45.2%)	
Unfavorable intermediate	37(11.9%)	12(14.3%)	
High	89(28.7%)	21(25.0%)	
Very High	27(8.7%)	8(9.5%)	
MRI Prostate volume (cm^3) mean±SD	42.4±18.0	46.0±20.5	0.12
Medication for BPH, n (%)	63(20.3%)	11(13.1%)	0.16
Medication for DM, n (%)	46(14.8%)	20(23.8%)	0.07

n: number; SD: standard deviation; BMI: body mass index; PSA: prostate specific antigen; ISUP: International Society of Urological Pathologists; NCCN: National Comprehensive Cancer Research; MRI: magnetic resonance imaging; BPH: benign prostate hyperplasia; DM: diabetes mellitus

Table 2 Details of antithrombotic agents

Details of AP medication (*n* = 66)			***n***
single AP	Aspirin		38
(*n* = 58)	Clopidogrel		8
	Ethyl icosapentate		4
	Limaprost		4
	Cilostazol		3
	Dipyridamole		1
double APs	Aspirin + Clopidogrel		3
(*n* = 7)	Aspirin + Prasugrel		2
	Cilostazol + Limaprost		1
	Ethyl icosapentate + Limaprost		1
triple APs	Aspirin + Clopidogrel + Ethyl icosapentate		1
(*n* = 1)			
Details of AC medication (*n* = 14)			***n***
single AC	Warfarin		4
	DOAC	Dabigatran	4
		Apixaban	2
		Edoxaban	2
		Rivaroxaban	2
Details of AP + AC medication (*n* = 4)			***n***
AP + AC	Aspirin + Warfarin		1
	Aspirin + Apixaban		1
	Aspirin + Dabigatran		1
	Ethyl icosapentate + Rivaroxaban		1

AP: antiplatelet; n: number; AC: anticoagulant; DOAC: direct oral anticoagulant

Table 3 Perioperative AP/AC management

	Management	***n***
Single AP	Interruption	16
(*n* = 58)	Continuation	42
Dual APs	One AP continuation	6
(*n* = 7)	Both APs continuation	1
Triple APs	One AP continuation	1
(*n* = 1)		
Single AC	Interruption	6
(*n* = 14)	Heparinization	8
AP + AC	AP interruption AC interruption	1
(*n* = 4)	AP continuation AC interruption	1
	AP continuation AC heparinization	2

AP: antiplatelet; AC: anticoagulant; n: number

period was not associated with urinary continence recovery (number of AP agents: 0 pad: P=0.77, 0–1 pad: P=0.40; Handling of AP agents: 0 pad: P=0.39, 0–1 pad: P=0.67); moreover, whether AC was interrupted or switched to heparin was not associated with urinary continence recovery (0 pad: P=0.13, 0–1 pad: P=0.43) (Fig. 3A–F).

Oncological outcomes

There was no significant difference in the PSM rate between the groups (19.0% in the control group vs. 23.8% in the AT group, P=0.33). The BCR-free survival or overall survival did not differ significantly between the groups (BCR-free survival: HR: 0.77 [95% CI: 0.44–1.38], P=0.42; overall survival: HR: 3.30 [95% CI: 0.32–34.34], P=0.16) (Fig. 4A–B).

Clinical factors that affect urinary continence recovery

To identify the clinical factors that affect urinary continence recovery, we performed a Cox proportional hazards analysis using clinical variables to achieve 0 pad use following RARP. In the univariate analysis, serum PSA levels (HR, 0.98 (95% CI 0.97–1.00), P=0.048), advanced clinical T stage (≥T3a) (HR, 0.64; 95% CI (0.42–0.94), P=0.03), and taking AT agents (HR, 0.53 (95% CI, 0.36–0.74, P=0.0004) were associated with a poor urinary continence recovery. In the multivariate analysis, taking AT agents was the only independent factor for 0 pad use (HR, 0.55 (95% CI, 0.38–0.78), P=0.001) (Table 5).

Discussion

This study demonstrated that taking AT agents was associated with a poor urinary continence recovery and identified it as an independent factor for 0 pad use following RARP.

As cardiovascular diseases were prevalent among patients with Pca and most of them take AT agents, the prevalence of patients with Pca taking AT agents has also increased recently, some of whom would undergo RARP. We reported previously that RARP can be safely performed in patients with Pca taking AT agents [10];

Table 4 Perioperative findings

Variables	Control (*n* = 310)	Antithrombotic (*n* = 84)	*P*-value
Perioperative findings			
Operation time (minutes), mean ± SD	218.3 ± 59.4	225.3 ± 65.6	0.35
Console time (minutes), mean ± SD	176.9 ± 54.5	182.9 ± 56.6	0.37
Estimated blood loss (ml), mean ± SD	87.3 ± 98.9	98.5 ± 112.0	0.37
Blood transfusion during surgery, n (%)	0(0%)	0(0%)	N/A
Nerve-sparing, n (%)			
None	251(81.0%)	77(91.7%)	0.06
One side	42(13.5%)	4(4.8%)	
Both sides	17(5.5%)	3(3.6%)	
Lymph node dissection, n (%)	26(8.4%)	5(6.0%)	0.65
Postoperative findings			
Blood transfusion after surgery, n (%)	1(0.3%)	0(0%)	> 0.99
Bleeding complications*, n (%)			
Yes (CTCAE ver5.0 Gd1 or more)	15(4.8%)	7(8.5%)	0.20
No	295(95.2%)	75(91.5%)	
Complications* during 90 days after surgery, n (%)			
Gd0	262(84.5%)	64(78.0%)	0.12
Gd1	26(8.4%)	9(11.0%)	
Gd2	16(5.2%)	9(11.0%)	
Gd3-5	6(1.9%)	0(0%)	
POD7 cystography leakage, n (%)			
Yes	17(6.7%)	14(20.9%)	< 0.001
No	235(93.3%)	53(79.1%)	
Hospitalization (days), mean ± SD	7.7 ± 2.1	7.9 ± 2.4	0.83

n: number; SD: standard deviation; POD: post operative day; Gd: grade; NA: not assessed

* Complications according to Common Terminology Criteria for Adverse Events (CTCAE) version5.0

however, multiple treatment options are available for nonmetastatic Pca, including radiotherapy and active surveillance in addition to prostatectomy. The advantages and disadvantages of each of these modalities in terms of oncological aspects and health-related quality of life should be thoroughly discussed with the patients.

Urinary incontinence is a significant burden for patients after RARP and can dramatically impact their quality of life (QOL) [12]. In a randomized controlled trial assessing the effects of various treatments for Pca on the patients' QOL, RARP was associated with a greater deterioration in terms of urinary incontinence and sexual function compared with active surveillance and radiotherapy. Although some recovery was observed over time, these outcomes remained worse in the RARP group throughout the entire duration of the 6-year trial [13].

Multiple clinical studies have been carried out to identify the factors that affect post-RARP urinary continence recovery; these include patient-specific factors, such as age [14, 15], prostate volume [16], presence of preoperative lower-urinary-tract symptoms [17], a high Charlson comorbidity index [15], preoperative erectile dysfunction [18], smoking [16], and a history of Transurethral Resection of the Prostate [19]; as well as intraoperative factors, including the length of the surgical time [14].

Several surgical advancements have been proposed to improve urinary continence recovery after RARP. Techniques such as bladder neck-sparing [20], Retzius-sparing technique [21], maximal urethral length preservation [22], posterior reconstruction (Rocco stitch) [23], and anterior retropubic suspension (Patel stitch) [24] have yielded promising results regarding the improvement of postoperative continence.

Although it remains unestablished how AT agents are related to a poor urinary continence recovery, this association may be attributed to the prolonged wound-healing process observed in patients taking these agents. During the wound-healing process, a thrombus first forms at the wound surface [25]. Thrombi are mainly composed of fibrin and platelets, which stabilize the thrombus. Thrombus formation proceeds most efficiently when the coagulation system is fully functional [25, 26]. Properly synthesized thrombi induce the production of various cytokines involved in the inflammatory phase, which is the next critical step in wound healing. Thus, incorrect thrombus formation may lead to inadequate wound healing because of the prolonged hemostasis and inflammatory phases of the wound [27]. AP agents that directly inhibit platelet action and AC agents that inhibit the formation of thrombi have been suggested to have an

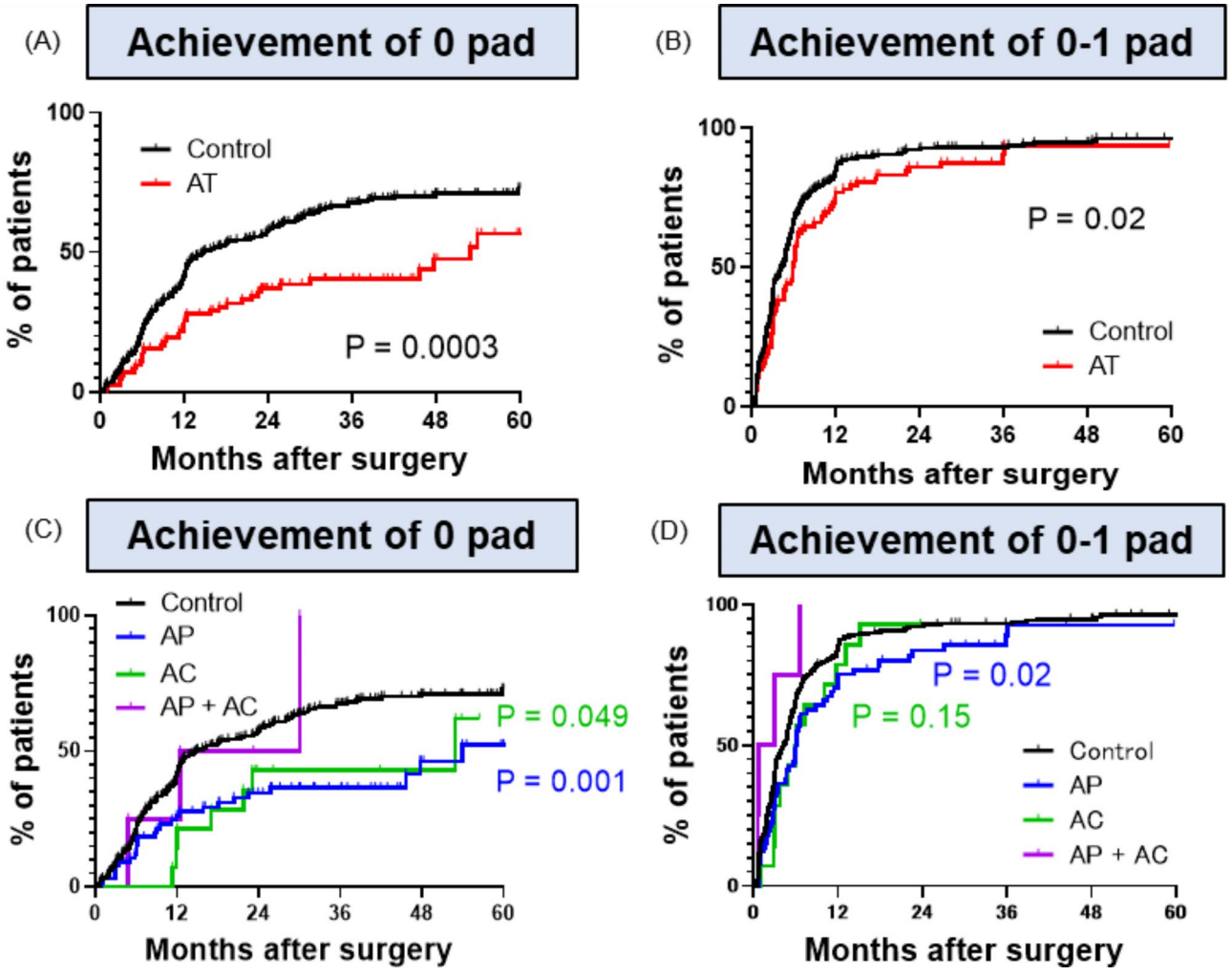

Fig. 2 Comparison of continence recovery after RARP between antithrombotic agent adherents and non-adherents. Continence recovery in relation to the control group in terms of 0 pad use (**A**: compared with the entire AT group; **C**: compared with the AP, AC, and AP + AC groups) and 0–1 pad use for safety (**B**: compared with the entire AT group; D: compared with the individual subgroups (AP, AC, and AP + AC groups)). The black, red, blue, green, and purple lines indicate the control, AT, AP, AC, and AP + AC groups, respectively. AT: antithrombotic; AP: antiplatelet; AC: anticoagulant

adverse effect on wound repair. In fact, AP and AC are the agents with the strongest negative effects on wound healing among various classes of drugs [28]. AC agents are associated with lower implant–engraftment rates in the dental area [29] and lower wound-healing rates for foot gangrene in patients with diabetes [30], which supports this concept. In the present study, patients taking AT agents were more likely to experience anastomotic leakage after RARP compared with the control group, which may be attributed to the poor wound healing observed in such patients. A prolonged inflammatory phase caused by a prolonged wound-healing process, as well as anastomotic leakage itself, may damage the urethral muscle and related tissues that are involved in continence, which may result in poor recovery of urinary continence. Another possibility is that electrocoagulation is over-performed in the AT group, to maintain adequate hemostasis. Coagulation may damage the muscles and nerves located around the urethra and levator ani muscles, which may lead to poor urinary continence recovery. Surgeons may need to consider the balance between hemostasis and tissue damage. The AT cohort had a relatively small number of patients who underwent the nerve-sparing techniques, and since nerve sparing is associated with better urinary continence recovery [20], this may influence continence recovery. Patients with cardiovascular risks are known to have lower sexual function [31], and in this study, nerve-sparing techniques were performed on patients with preserved preoperative sexual function. Therefore, the number of patients in the AT group who underwent nerve-sparing techniques might have been small. However, undergoing nerve-sparing was not associated with urinary continence recovery in the present study (Table 5). This could be explained by

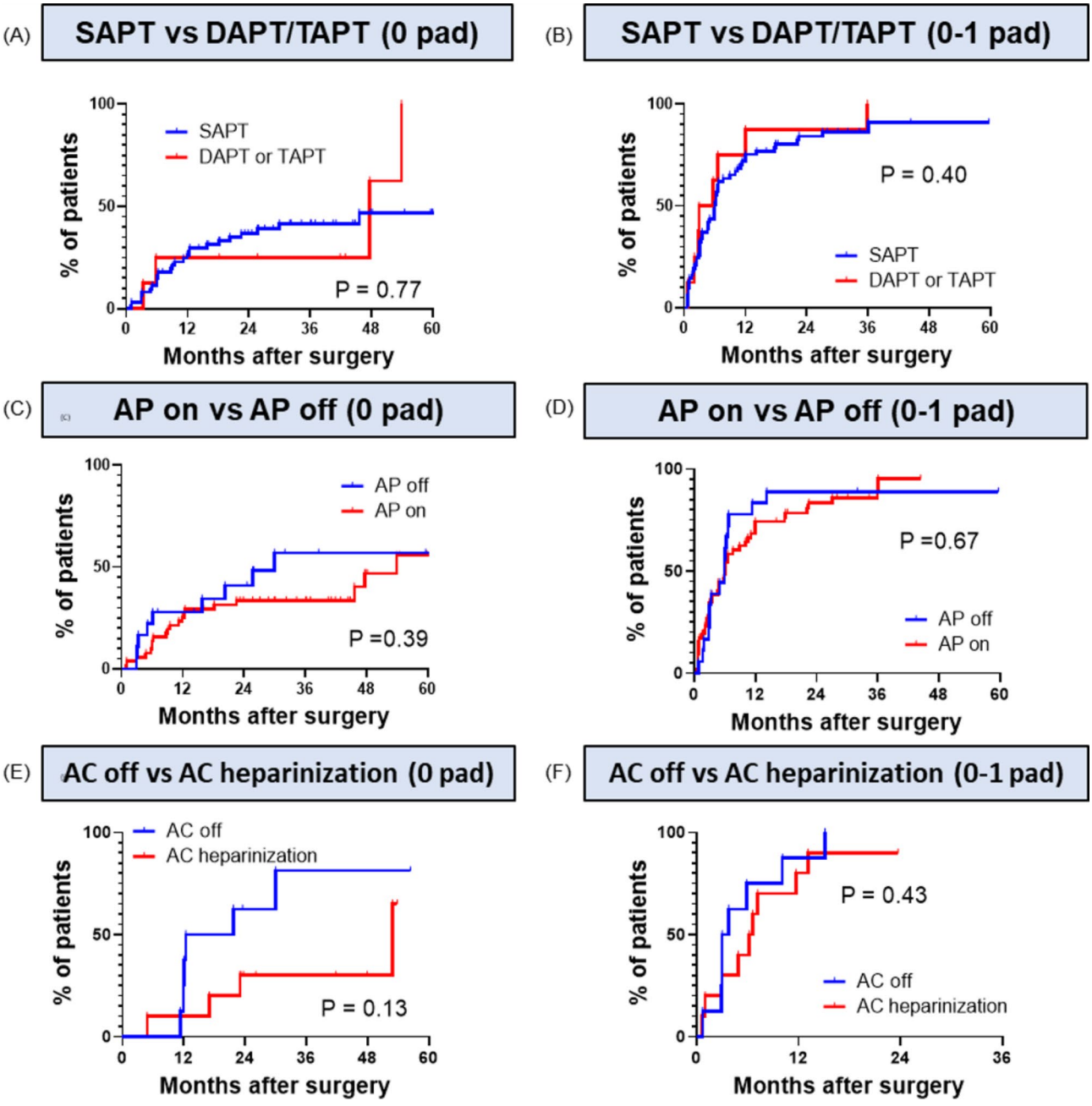

Fig. 3 Comparison of continence recovery based on the number of antithrombotic medications taken and perioperative management. (**A**, **B**) Comparison of continence recovery according to the number of AP agents. (**A**) 0 pad achievement, (**B**) 0–1 pad achievement. The blue and red lines indicate single and multiple medications, respectively. (**C**, **D**) Comparison of continence recovery based on the perioperative management of AP agents. (**C**) 0 pad achievement rate, (**D**) 0–1 pad achievement rate. The blue line indicates patients who discontinued AP agent use during the perioperative period, whereas the red line indicates patients who underwent surgery under continuous medication. (**E**, **F**) Comparison of continence recovery based on the perioperative management of AC agents. (**E**) 0 pad achievement rate, (**F**) 0–1 pad achievement rate. The blue line indicates patients who discontinued AC use during the perioperative period, whereas the red line indicates patients who underwent surgery with heparin replacement of AC

the fact that nine surgeons with varying levels of RARP experience performed this surgery, which may negate the effect of nerve-sparing because multiple factors, including the surgeon's experience, affect continence recovery [32]. Older age and larger prostate volume were reported to be negatively associated with urinary continence recovery [14–16]. Higher age and larger prostate volume in the AT cohort might negatively affect urinary continence recovery. However, these factors were not associated with continence recovery in the present study (Table 5). Additionally, there was a significant difference in preoperative PSA levels between the two

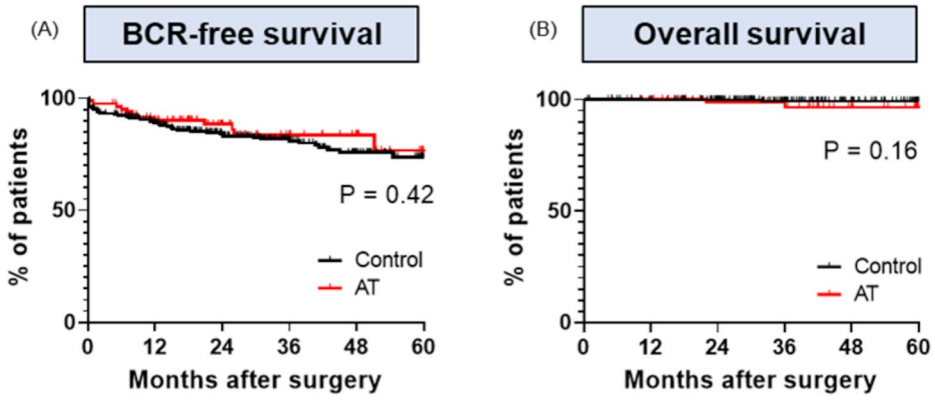

Fig. 4 Comparison of oncological outcomes between antithrombotic agent adherents and non-adherents. BCR-free survival (**A**) and overall survival (**B**) in the control group vs. the AT group. The black and red lines indicate the control group and the AT group, respectively. BCR: biochemical recurrence; AT: antithrombotic

Table 5 Univariate and multivariate analysis of factors contributing to pad-free after RARP

Parameters	Univariate		Multivariate	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (y.o.)	0.99 (0.97–1.01)	0.33		
BMI (kg/m^2)	0.96 (0.92–1.01)	0.13		
Serum PSA (ng/mL)	0.98 (0.97-1.00)	0.048	0.99 (0.97-1.00)	0.17
Nerve sparing (Yes vs. No)	1.15 (0.82–1.57)	0.41		
Lymph node dissection (Yes vs. No)	0.77 (0.45–1.24)	0.32		
Clinical T Stage (≥T3 vs. ≤T2)	0.64 (0.42–0.94)	0.03	0.74 (0.48–1.10)	0.15
NCCN risk (≥ high vs. ≤ intermediate)	0.91 (0.70–1.18)	0.49		
Prostate volume (cm^3)	1.00 (1.00–1.00)	0.10		
Medication for BPH (Yes vs. No)	1.29 (0.93–1.75)	0.11		
Medication for DM (Yes vs. No)	0.92 (0.64–1.30)	0.65		
Taking AT agents (Yes vs. No)	0.53 (0.36–0.74)	0.0004	0.55 (0.38–0.78)	0.001

Cox regression models were used for univariate and multivariate analyses

RARP: robot-assisted radical prostatectomy; HR: hazard ratio; CI: confidence interval; BMI: body mass index; PSA: prostate-specific antigen; NCCN: National Comprehensive Cancer Network; BPH: benign prostate hyperplasia; DM: diabetes mellitus; AT: antithrombotic

groups. Higher PSA levels might lead to more aggressive approaches in the AT group. The PSA level was one of the factors associated with urinary continence recovery in the univariate analysis, but it was not in the multivariate analysis (Table 5).

There are some limitations in this study. First, as this was a retrospective analysis, there was a bias in patient selection. Although comorbidity could affect continence recovery [15], assessment of comorbidity, such as the Charlson Comorbidity Index, was not possible in the present study due to a lack of data. Future clinical studies need to incorporate these factors. Regarding surgical techniques, the operations were performed by nine surgeons with varying levels of RARP experience, which may have affected the results. Further studies with a larger number of cases are needed to strengthen the evidence of this study.

Conclusion

Taking AT agents was associated with poor urinary continence recovery after RARP, which may help the decision-making process regarding the selection of the optimal therapeutic strategy for patients with Pca taking AT agents.

Abbreviations

AP	Antiplatelet
AC	Anticoagulant
AT	Antithrombotic
BCR	Biochemical recurrence
BMI	Body mass index
BPH	Benign prostate hyperplasia

CI	Confidence interval
CT	Computed tomography
DM	Diabetes mellitus
HR	Hazard ratio
MRI	Magnetic resonance imaging
NCCN	National Comprehensive Cancer Network
Pca	Prostate cancer
PLND	Pelvic lymph node dissection
PSA	Prostate specific antigen
PSM	Positive surgical margin
QOL	Quality of life
RARP	Robot-assisted radical prostatectomy
RS-RARP	Retzius-sparing robot-assisted radical prostatectomy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12894-024-01594-6.

Supplementary Material 1

Acknowledgements
We thank Drs. Takanori Hayase, Kosuke Kazashi, and Kohei Mito of Jichi Medical University Saitama Medical Center for helpful discussion.

Author contributions
Data curation was performed by M.O, S.W., K.Y, S.M., Y.N., T.K. and K.S. M.O. analyzed data. M.O. and S.W. designed the study, wrote the main manuscript text, and prepared all figures and tables. T.M. supervised the study. All authors reviewed and approved the manuscript.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

Data availability
The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Preoperative written informed consent was obtained from all participants and this study was approved by the Institutional Review Board and Ethics Committee of Jichi Medical University Saitama Medical Center (RinS20-058).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 29 December 2023 / Accepted: 16 September 2024
Published online: 28 September 2024

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