Impact of Anticoagulant and Antiplatelet Drugs on Perioperative Outcomes of Robotic-assisted Partial Nephrectomy

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OBJECTIVE To evaluate the impact of anticoagulant (AC) or antiplatelet (AP) therapy on the morbidity of robot-assisted partial nephrectomy (RAPN).

MATERIALS AND METHODS From 2011 to 2015, we retrospectively analyzed a prospectively maintained institutional review board–approved database of RAPN from 2 academic departments of urology. We evaluated the occurrence of overall complications and hemorrhagic complications (pseudoaneurysm, arteriovenous fistula, hematoma, transfusion). Patients with therapeutic AC or AP, stopped or not before surgery, were compared with patients without therapeutic AC or AP. A logistic regression model was used to identify predictors of complications.

RESULTS Out of 533 patients who underwent RAPN, 70 had AC or AP (50% aspirin, 25% clopidogrel, 28% AC, 8% direct oral AC). Clopidogrel, AC, and direct oral AC were always stopped preoperatively. Aspirin was continued in 25% of the cases. In univariate analysis, overall complications (39.2% vs 17.4%; $P = .001$) and hemorrhagic complications (32.7% vs 9.6%; $P < .001$) were higher in patients on AC or AP. Hospital stay was longer in the group with therapeutic AC or AP treatment (5.1 vs 3.9 days; $P < .001$). In multivariate analysis, predictors of complications were intake of therapeutic AC (odds ratio [OR] = 4.3, IC95% [1.2-15.9], $P = .03$) and tumor size (OR = 1.8, IC95% [1.3-7.2], $P = .03$). Patients on aspirin tended to have more complications (OR = 2.4; IC95% [0.4-9.3]; $P = .15$).

CONCLUSION AP and therapeutic AC increase the morbidity of RAPN. These treatments should be taken into account in treatment decision-making algorithm of small renal masses. UROLOGY 99: 118–122, 2017. © 2016 Elsevier Inc.

With the aging of the population, many people with cardiovascular conditions are being treated with oral anticoagulants (AC) or antiplatelet (AP) drugs.[1] These medications can be difficult to handle in case of a surgical intervention. They usually have to be stopped before the operation, which can increase the risk of thrombosis or embolism. Furthermore, when resumed in the postoperative period, they can increase the risk of postoperative bleeding.

Hemorrhagic complications (HC) (bleeding, hematoma, arteriovenous fistula, pseudoaneurysm) can occur during or after partial nephrectomy (PN) in up to 5%-10% of the cases.[2-4] When patients are taking AP or therapeutic AC, the risk of hemorrhage is supposedly higher, although data on this topic are very limited.[5] For that reason, the optimal management of therapeutic AC or AP before and after PN remains unknown.

Robot-assisted PN (RAPN) has spread significantly worldwide and is now the most popular mini-invasive technique used to perform PN. It has been reported that RAPN could be associated with a decreased risk of bleeding compared with open PN,[6,7] possibly because of enhanced vision and better quality of renal parenchyma repair.

Our primary objective was to evaluate the impact of therapeutic AC or AP on RAPN perioperative morbidity. We hypothesized that patients with therapeutic AC or AP would have an increased risk of HC. Our secondary objective was to try and discern whether the timing of resumption of therapeutic AC or AP after RAPN had any influence on the occurrence of an HC.

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MATERIALS AND METHODS

Study Population

We made a retrospective analysis of 2 prospectively maintained, institutional review board–approved databases. These databases included all RAPN performed between January 2010 and June 2015 at 2 academic departments of urology. Patients were divided into 2 groups: patients taking therapeutic AC or AP before surgery (group A), and patients without AP or therapeutic AC (group B).

We precisely looked at whether therapeutic AC or AP had been stopped before surgery, and the exact moment when it had been restarted postoperatively.

The following data were collected: surgeon's experience (categorized as <20 procedures, between 20 and 50 procedures, and >50 procedures for each single surgeon), operative time, warm ischemia time, pedicle clamping technique (off-clamp, early unclamping, or standard unclamping[8]), estimated blood loss (EBL), blood transfusion, and length of hospital stay. Estimated glomerular filtration rate was evaluated using the Modification of Diet in Renal Disease.[9] Tumor complexity was assessed using the RENAL nephrometry score.[10] Complications were reported according to the European Association of Urology guidelines[11] and classified using the Clavien-Dindo score.[12] Major complications were defined as a Clavien score ≥3. HC were defined as the occurrence of an arteriovenous fistula, a pseudoaneurysm, or a hematoma requiring transfusion. All postoperative thrombotic or embolism events were recorded, including pulmonary embolism, thrombophlebitis, acute coronary syndrome, and stroke.

Perioperative Management of AC or AP

Perioperative management of AC or AP was not standardized and was left at the anesthesiologist and surgeon's discretion based on estimated cardiovascular risk of the patient. All patients taking therapeutic AC were switched to a low molecular weight heparin (LMWH) before surgery; international normalized ratio was measured on the day of surgery to ensure normalization. In patients taking clopidogrel, the drug was either stopped preoperatively or switched to aspirin (75 mg daily). For patients taking aspirin (75 mg daily), the drug was either stopped or continued perioperatively at the same dosage. Therapeutic AC and AP were resumed postoperatively according to surgeon's decision. All patients who were not under therapeutic anticoagulation underwent prophylaxis of venous thromboembolism using LMWH (enoxaparin 40 mg once per day for 30 days postoperatively) according to the guidelines of the American College of Chest Physicians,[13] even when they were under AP therapy.

Criteria for blood transfusions were a hemoglobin level below 9 g/dL and persistent hypotension.

Statistical Analysis

Means and standard deviations were reported for continuous variables, and proportions were used for nominal variables. Comparisons between groups were performed using χ^2 test and Fisher exact test for discrete variables and Mann-Whitney *U* test for continuous variables. Subgroup analyses were performed to assess the impact of each independent AC or AP on RAPN outcomes. Multiple linear regression analysis was applied to define clinical parameters associated with EBL. A logistic regression model was used to assess predictors of hemorrhagic and overall complications. A sensitivity analysis was performed by matching patients under AC or AP with patients without AC or AP in a 1:1 fashion according to RENAL score, tumor size, and American Society of Anesthesiologists score.

For continuous variables, odds ratios (ORs) were expressed as a range (per change in regressor over entire range). Statistical analyses were performed using JMP v.10.0 software (SAS Institute Inc, Cary, NC). All tests were 2-sided, with a significance level set at $P < .05$.

RESULTS

Patient Demographics

There were 530 patients who underwent RAPN. Among them, 70 (13.2%) were taking therapeutic AC or AP before surgery (group A). Patients' characteristics are summarized in Table 1. Most patients' characteristics were similar on both institutions (Supplementary Table S1). Tumor size and RENAL score were comparable in both groups. Distribution of therapeutic AC and AP treatments in group A was as follows: 50% aspirin, 25% clopidogrel, 28% oral AC (Coumadin or warfarin), and 8% direct oral AC (DOAC) (apixaban, dabigatran, or rivaroxaban). Indications of AC or AP are summarized in Supplementary Table S2.

Table 1. Patients' characteristics

	Patients Under AC or AP N = 70	Patients Without AC or AP N = 463	*P* Value
Mean (SD) age, y	66.6 ± 0.5	59.7 ± 1.4	.001*
Mean (SD) BMI	27.03 ± 1.5	27.07 ± 0.6	.98
Mean (SD) ASA score	2.5 ± 0.5	1.7 ± 0.6	.001*
Number of patients under AC	20 (28%)	—	—
Number of patients under NOAC	6 (8%)	—	—
Number of patients under aspirin	35 (50%)	—	—
Number of patients under clopidogrel	18 (25%)	—	—
Mean (SD) tumor complexity according to RENAL nephrometry score	6.6	7.2	.07
Mean (SD) tumor size, mm	32.1 ± 1.8	32.8 ± 0.7	.70
Pathologic subtype			.96
Renal cell carcinoma	36 (60%)	224 (60.5%)	
Others	24 (40%)	46 (39.5%)	

Patients under anticoagulant (AC), novel oral anticoagulant (NOAC), or antiplatelet (AP) therapy, and patients without AC, NOAC, or AP therapy.

* Statistically significant.