Risks and Benefits of Pharmacological Prophylaxis for Venous Thromboembolism Prevention in Patients Undergoing Robotic Partial Nephrectomy

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Abbreviations and Acronyms

AHE = adverse hemorrhagic events
BMI = body mass index
CCI = Charlson comorbidity index
CRA = Caprini risk assessment
DVT = deep venous thrombosis
EBL = estimated blood loss
NPP = no pharmacological prophylaxis
PE = pulmonary embolism
PP = pharmacological prophylaxis
RBC = red blood cells
RPN = robotic partial nephrectomy
VTE = venous thromboembolism
WIT = warm ischemia time

Purpose: We investigate the safety and efficacy of pharmacological venous thromboembolism prophylaxis in patients treated with robotic partial nephrectomy at our center.

Materials and Methods: We retrospectively examined our robotic partial nephrectomy database for cases performed between 2006 and 2014. Clinical venous thromboembolism episodes within 6 months from surgery were documented. Patients were stratified according to the administration of pharmacological venous thromboembolism prophylaxis into pharmacological prophylaxis (222) and no pharmacological prophylaxis (762) groups. The groups were compared in terms of perioperative outcomes, complications and adverse hemorrhagic events defined as the administration of 2 or more units of red blood cells, the need for vascular embolization or any procedures related to blood loss.

Results: There were no differences between the pharmacological prophylaxis and no pharmacological prophylaxis groups regarding mean operation time, median warm ischemia time and estimated blood loss. The rates of venous thromboembolism events were comparable between the groups (pharmacological prophylaxis 1.8% vs no pharmacological prophylaxis 2.1%, p=0.75). Overall 90% of venous thromboembolism events occurred within the first postoperative month. In the multivariable regression analysis encompassing pharmacological prophylaxis, perioperative aspirin intake, body mass index, operation time, Charlson comorbidity index, fellowship training and tumor complexity, operation time (OR 1.06, p=0.009) and Charlson comorbidity index (OR 1.28, p <0.0001) were associated with adverse hemorrhagic events.

Conclusions: The administration of pharmacological prophylaxis did not increase the rate of adverse hemorrhagic events. Isolated inpatient administration of pharmacological prophylaxis after robotic partial nephrectomy does not appear to protect against venous thromboembolism postoperatively in that the

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majority of venous thromboembolism events occurred within the first 30 days after surgery. Longer duration of pharmacological prophylaxis for the prevention of venous thromboembolism after robotic partial nephrectomy should be considered.

Key Words: robotics, nephrectomy, prevention and control, venous thromboembolism, organ sparing treatments

VENOUS thromboembolism is the most frequent nonsurgical complication after major urological surgery,[1] encompassing deep vein thrombosis and pulmonary embolism, resulting in approximately 10% of all hospital deaths.[2] Long-term complications of VTE lead to significant morbidity and financial burden.[3] Before the routine practice of mechanical and pharmacological prophylaxis, the incidence of DVT after major urological operations was 10% to 30% while the incidence of PE was reported as 1% to 10%.[4] Due to early mobilization, improved perioperative care and prophylactic practices, we have witnessed a decrease in the incidence of VTE, yet it is still observed at high rates.[5] Age, obesity, history of previous VTE, trauma, lower extremity fracture, advanced age, immobility, and chronic cardiovascular and respiratory diseases are risk factors for VTE in surgical patients.[6,7] In addition, cancer itself is an important risk factor.[8] However, despite the presence of multiple risk factors for VTE, the routine use of PP after major surgeries might be avoided due to the notion that PP might increase the bleeding risk associated with surgery. In a meta-analysis of data from 69 studies including general, urological and orthopedic surgery, PP was shown to reduce the risk of VTE by 50%, but increased major postoperative bleeding by 50%, supporting this bias.[9]

There is a paucity of data regarding the safety and efficacy of routine PP in patients undergoing robotic partial nephrectomy. Thus, we investigated the efficacy of pharmacological VTE prophylaxis and the safety of this approach in patients treated with RPN at a single, high volume center.

MATERIALS AND METHODS

After institutional review board approval the records of patients who underwent RPN at our institution between 2006 and 2014 were examined. Information on patient characteristics (demographics, ASA® [American Society of Anesthesiologists®] grade, BMI, Charlson comorbidity index), tumor description (size, R.E.N.A.L. score), perioperative details (operation time, warm ischemia time, intraoperative and postoperative complications, transfusion rate, length of hospital stay) and pathological data were obtained. Information on prophylaxis regimen and administration details was extracted from medical charts including the medical administration record, intraoperative anesthesiology report and postoperative progress notes. All of the surgeons performing the procedures were experienced with RPN. However, to capture the element of effect of surgeon on the outcomes, surgeons were divided into fellowship trained and nonfellowship trained groups. All RPNs were performed using our previously described technique.[10]

Complications were graded using the Clavien system.[11] Major complications were defined as greater than grade II complications. Adverse hemorrhagic events were defined as the administration of 2 or more units of RBC, or the need for selective vascular embolization or any secondary procedures related to blood loss. Patients with clinical suspicion of DVT and PE underwent immediate imaging protocol including computerized tomography, ventilation-perfusion scan and duplex ultrasonography. Clinical VTE episodes occurring within 6 months of surgery were documented. The time to VTE episode was categorized into the 3 groups of within first 7 days, 8 to 30 days and 31 days to 6 months after RPN. The perioperative VTE risk factors were graded according to CRA score.[12]

Statistical Analysis

For variables with normal distribution the data were presented as mean $\pm$ SD. For variables with nonnormal distribution the data were presented as median (IQR) and the respective groups were compared using Mann-Whitney U test. Categorical variables were compared using the chi-squared test. Multivariable logistic regression analysis models for the identification of factors associated with intraoperative, major and postoperative complications were constructed. Further multivariable logistic regression analysis models for the identification of factors predicting AHE and VTE were created. Analyses were performed using SPSS® v21 software with significance set at $p < 0.05$.

Study Population

Patients receiving therapeutic intravenous anticoagulation were excluded from the study. Patients were stratified according to administration of pharmacological VTE prophylaxis into pharmacological prophylaxis and no pharmacological prophylaxis groups. The VTE prophylactic groups (PP vs NPP) were compared with regard to perioperative outcomes.

Subgroup analysis stratifying patients according to receipt of perioperative antiplatelet treatment was performed. The antiplatelet group included any patient who did not receive prophylaxis and received antiplatelet therapy (aspirin 81 mg) during the perioperative period. Perioperative outcomes in this group were compared with those of patients in the NPP group who did not receive antiplatelet therapy for at least 1 week before surgery.