Symptomatic Venous Thromboembolism is Associated with Inferior Survival among Patients Undergoing Nephrectomy with Inferior Vena Cava Tumor Thrombectomy for Renal Cell Carcinoma

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Abbreviations and Acronyms

DVT = deep venous thrombosis
IVC = inferior vena cava
OS = overall survival
PE = pulmonary embolism
RCC = renal cell carcinoma
TT = tumor thrombectomy
VTE = venous thromboembolism

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Purpose: We investigated the incidence and survival impact of symptomatic venous thromboembolism after nephrectomy with inferior vena cava tumor thrombectomy.

Materials and Methods: We retrospectively reviewed the records of 183 patients who underwent nephrectomy with inferior vena cava tumor thrombectomy (level I-IV) for renal cell carcinoma between 2000 and 2010. Postoperative venous thromboembolism was defined as symptomatic bland thrombus or embolism confirmed on imaging. The cumulative incidence of venous thromboembolism was estimated by the Kaplan-Meier method. Associations of clinicopathological features with time to thromboembolism after surgery and all cause mortality were evaluated on multivariable analysis with Cox models.

Results: Symptomatic venous thromboembolism developed in 55 patients a median of 23 days (IQR 5–142) postoperatively, including pulmonary thrombosis in 24, deep venous thrombosis in 17, bland inferior vena cava thrombosis in 13 and portal vein thrombosis in 1. The cumulative incidence of thromboembolism 30, 90 and 365 days following surgery was 17%, 22% and 27%, respectively. A history of smoking (HR 2.15, 95% CI 1.09–4.24, p = 0.028), ECOG (Eastern Cooperative Oncology Group) performance status 1 or greater (HR 2.15, 95% CI 1.17–3.93, p = 0.013), hypercoagulability disorder (HR 5.12, 95% CI 1.93–13.59, p = 0.001) and bulky lymphadenopathy at surgery (HR 4.84, 95% CI 1.87–12.51, p = 0.001) was significantly associated with an increased risk of venous thromboembolism on multivariable analysis. Postoperative venous thromboembolism was significantly associated with an increased risk of all cause mortality (HR 1.53, 95% CI 1.04–2.23, p = 0.029).

Conclusions: Venous thromboembolism after nephrectomy and tumor thrombectomy is common within 90 days of surgery. Symptomatic venous thromboembolism in this population is independently associated with a greater risk of mortality.

Key Words: kidney; thromboembolism, venous; nephrectomy; carcinoma, renal cell; vena cava, inferior

Despite considerable evolution in the management of RCC with IVC thrombus, this diagnosis continues to carry a morbid overall outlook. Disease progresses within 1 year in 80% of untreated cases and the surgical complication rate exceeds 50% in contemporary series.[1,2]

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Periprocedural VTE is a particularly relevant concern, given the intimate involvement of the central venous system by tumor and often by bland thrombus.[3] Preoperative PE and DVT were reported in 4.4% of patients with IVC involvement, although in the context of early recognition and adequate preoperative anticoagulation such events may not necessarily preclude surgery or portend poor postoperative outcomes.[4] Conversely intraoperative dislodgment of the caval thrombus correlates with surgery related death with a 60% mortality rate in a recent series.[5] These findings underscore the importance of presurgical screening and optimization as well as meticulous surgical technique to minimize the risks of VTE in this patient cohort.

The clinical significance of postoperative VTE after nephrectomy with IVC TT remains under studied. Although groups at many multicenter studies have reported the incidence of postoperative in-hospital and 30-day complications, descriptions of sequelae related to individual events are often omitted from analyses.[6] Considering that postoperative VTE is intimately linked with mortality after several major abdominal and pelvic procedures, including radical cystectomy, the lack of corresponding data on nephrectomy with IVC TT represents a critical void in the literature since it precludes an understanding of potentially modifiable risk factors surrounding thromboembolic events in this population.[7,8]

We investigated the incidence and clinical impact of symptomatic VTE after nephrectomy with IVC TT. We hypothesized that postoperative VTE contributes to mortality risk and to this end we explored clinical and pathological predictors of VTE in an effort to improve patient risk stratification.

METHODS

Following institutional review board approval we queried the nephrectomy registry at our institution to identify patients with RCC and IVC tumor thrombus (level I-IV) who underwent nephrectomy with TT between 2000 and 2010. Immediate preoperative magnetic resonance imaging or computerized tomography was rereviewed by 2 abdominal radiologists to characterize the IVC tumor thrombus, including the presence of bland thrombus. Preoperatively all patients underwent routine computerized tomography of the chest. Patient demographics, surgical features (IVC transection, or placement of a patch graft or tube interposition), and clinical and pathological characteristics of the tumor (size, 2010 primary tumor, regional lymph node and distant metastases classifications, Mayo classification of tumor thrombus level and nodal disease burden) were evaluated. Bulky lymphadenopathy was defined by the presence of retroperitoneal adenopathy with radiographic evidence of compression of the renal vein ostia or IVC causing vessel wall deviation as interpreted by the radiologist.

Data on a VTE or a bleeding event in the postoperative period as well as anticoagulation in the preoperative and postoperative settings were collected retrospectively. A VTE event was defined as the development of a symptomatic bland thrombus or embolism not related to the IVC tumor thrombus, which was confirmed by imaging. A bleeding event was defined as symptomatic bleeding in a critical area or organ.

Outcome measures were survival free of a VTE, survival free of a bleeding event and OS following surgery. Followup of each outcome measure was calculated from the time of surgery.

Clinical and pathological characteristics are summarized with the median and IQR, and the frequency and percent for continuous and categorical variables, respectively. Survival free of and the cumulative incidence of VTE or a bleeding event and OS were estimated by the Kaplan-Meier method. Associations of features studied with time to VTE were evaluated with Cox proportional hazards regression models. A multivariable model of time to VTE was developed using stepwise selection with $p = 0.05$ set for a feature to enter or leave the model. Associations of VTEs and bleeding events which developed during followup with time to death from any cause were also evaluated using Cox models with VTEs and bleeding events analyzed as time dependent covariates. Statistical analyses were performed using SAS®. All tests were 2-sided with $p < 0.05$ considered statistically significant.

RESULTS

A total of 183 patients underwent nephrectomy with IVC TT for RCC with a level I-IV IVC tumor thrombus during the study period. Supplementary tables 1 and 2 (http://jurology.com/) show baseline patient characteristics. Tumor thrombus was defined as level I, II, III and IV in 31%, 38%, 16% and 15% of cases, respectively.[9] A thromboembolic event occurred prior to surgery in 25 patients (14%) with 2 experiencing such an event after the RCC diagnosis. All 25 cases required therapeutic anticoagulation prior to surgery. No intraoperative PEs were identified.

At a median of 23 days postoperatively (IQR 5–142) 55 patients experienced VTE with a cumulative incidence of 17%, 22% and 27% at 30, 90 and 365 days after surgery. Thromboembolic events included PE in 24 cases, DVT in 17, bland IVC thrombosis in 13 and portal vein thrombosis in 1. VTE developed postoperatively in 6 of 32 patients (19%) who received inpatient subcutaneous heparin prophylaxis, 38 of 106 (36%) who did not receive any anticoagulation and 11 of 45 (24%) on therapeutic anticoagulation prior to VTE (supplementary table 3, http://jurology.com/). The VTE-free survival rate 1, 2 and 5 years postoperatively was 73% (95% CI 67–80), 70% (95% CI 63–78) and 60% (95% CI 51–71), respectively (fig. 1).

On multivariable analysis a significantly increased risk of postoperative VTE was observed in individuals