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Risk of venous thromboembolic events following inferior vena cava resection and reconstruction

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Objective: **The perioperative risk of an acute venous thromboembolism (VTE) event after inferior vena cava (IVC) reconstruction is unknown. We sought to describe VTE outcomes of our 15-year IVC reconstruction experience.**
Methods: **We performed a retrospective institutional review of all patients who underwent IVC reconstruction (September 1999-October 2014) and describe perioperative VTE outcomes.**
Results: **Sixty-five patients (mean age 58 ± 2 years) underwent IVC reconstruction (primary repair, 25%; patch, 43%; graft, 32%), most commonly for renal cell carcinoma (51%) and retroperitoneal sarcoma (22%). The overall incidence of perioperative VTE was 22% (n = 14), including isolated deep vein thrombosis (DVT) in 9% (n = 6) and pulmonary embolism in 12% (n = 8; 4 with concomitant DVT). Median time to diagnosis was 6 days (range, 1-37 days). Most VTE patients were symptomatic (57%; 8 of 14), including lower extremity edema in 50%, acute desaturation in 43%, and hemodynamic compromise in 36%. No patient died as a result of his or her VTE. There was a trend for more overall VTE events in patients who underwent graft reconstruction (primary, 13%; patch, 18%; graft, 33%; $P = .06$). VTE was also significantly associated with larger tumor size, renal vein reimplantation, and blood transfusions ($P \leq .05$). Late complications of VTE included lower extremity edema in two patients and graft thrombosis in one patient.**
Conclusions: **IVC reconstruction can be performed safely with low VTE-associated morbidity. Routine anticoagulation might not be warranted in these patients, but early postoperative screening for DVT should be considered, especially in cases with large tumor burden or when graft reconstruction is performed. (J Vasc Surg 2016;63:1004-10.)**

Inferior vena cava (IVC) resection and reconstruction during tumor removal has been previously shown to be safe and effective.[1-14] Retroperitoneal malignancies, most commonly renal cell carcinoma or sarcoma, frequently extend into the IVC in advanced cases, at which point neoadjuvant chemoradiation is minimally effective.[2] In these cases, en bloc resection of the tumor, IVC, and related structures is necessary. Although IVC ligation is an option,[15,16] recent reports advocate for caval repair or reconstruction to allow for the complete resection of the tumor.[2-6] Collateral networks are frequently compromised during the dissection of large retroperitoneal tumors, thereby leading to lower extremity sequestration. IVC reconstruction can mitigate this morbidity by allowing for optimal venous drainage from the lower body.

IVC resection and reconstruction can be completed using a range of surgical techniques, including use of cardiopulmonary or veno-venous bypass in cases of projected hemodynamic instability.[1,8-10,17] In cases in which bypass is not required, proximal and distal venous control is usually obtained via cross-clamp.[7] In all instances, there is a perceived risk of thrombus formation because of venous stasis, which is usually an indication for intraoperative systemic heparinization.[5]

In contrast, the indications for postoperative systemic anticoagulation after IVC resection or reconstruction are less clear; no formal guidelines exist on this topic. Certain centers advocate for routine anticoagulation in patients who undergo IVC resection and reconstruction in an effort to decrease the complications associated with a postoperative venous thromboembolism (VTE) event.[2,3,5,18] However, the perioperative risk of acute VTE after IVC reconstruction has not been well described to our knowledge. The aim of the current study was to describe the risk of perioperative VTE after IVC reconstruction.

METHODS

Patient cohort. We performed a retrospective review of a prospectively maintained database of all patients who underwent IVC repair and/or reconstruction at our institution between September 1999 and October 2014. The

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Johns Hopkins institutional review board approved this study. Informed consent for data collection and follow-up was obtained from all patients.

Patient demographic data, tumor characteristics, intraoperative details, and postoperative outcomes were abstracted from the existing database. Specifically, data regarding postoperative VTE were recorded, including symptoms, time to diagnosis, and perioperative and long-term postoperative complications. All reported postoperative VTE events were new VTE occurrences (ie, patients with known preoperative deep vein thrombosis [DVT] were only diagnosed with postoperative VTE if they developed a DVT or pulmonary embolism [PE] at a site different from that of their original thrombus). All VTE events were diagnosed on the basis of imaging (either duplex ultrasound or computed tomography). At our institution, we do not use a standardized postoperative DVT surveillance algorithm after IVC repair; imaging studies are performed on the basis of patient symptoms, clinical status, and physician preference.

Surgical techniques. The surgical techniques used for IVC resection and reconstruction, including indications for intraoperative bypass support, were determined according to the degree of IVC tumor involvement as previously described.[1] In brief, primary repair was performed when the expected IVC narrowing was <50%, patch repair was used in cases in which expected IVC narrowing was >50%, and IVC graft reconstruction was performed in cases in which complete resection of the IVC wall was necessary. For the sake of brevity, all cases of IVC repair (primary or patch) and graft reconstruction are referred to collectively as "IVC reconstruction" throughout the remainder of this report.

Intraoperative heparinization (100 U/kg) was administered in all cases before vascular cross-clamping, and redosed to maintain an activated clotting time >250 seconds until physiologic flow was restored. All patients received heparin subcutaneously (5000 U) every 8 hours for DVT prophylaxis postoperatively. Use of postoperative acetylsalicylic acid or antiplatelet medications was determined on the basis of pre-existing cardiovascular patient risk factors. Postoperative systemic anticoagulation was reserved for patients who experienced VTE events confirmed with imaging (either computed tomography or duplex ultrasound).

Statistical analysis. All data are presented as mean ± standard error of the mean or count (%) as appropriate. Univariable analyses including *t* tests (continuous variables) and χ^2 or Fisher exact test (categorical variables) were used to compare pre-, peri-, and postoperative variables for patients with VTE after IVC repair vs those without. Survival and graft patency were compared using Kaplan-Meier survival analyses and log-rank tests. Multivariable analysis was not performed because of the overall low number of VTE events (n = 14). All statistical analyses were performed using JMP version 9.0 (SAS Institute, Cary, NC). Statistical significance was defined as $P \leq .05$.

RESULTS

Patient cohort. Overall, 65 patients underwent IVC repair or reconstruction over the 15-year study period (primary repair, 25%; patch, 43%; graft, 32%; Fig 1). Mean age was 57.6 ± 1.9 years, 68% of patients (n = 44) were male, and 86% were white (n = 50). Indication for surgery was most commonly renal cell carcinoma (51%; n = 33) and retroperitoneal sarcoma (22%; n = 14), followed by germ cell tumor (9%; n = 6), paraganglioma (6%; n = 4), adrenal carcinoma (5%; n = 3), and other carcinoma (5%; n = 2). Two patients (3%) required IVC repair for an IVC filter complication. Bypass support was used in 32% of cases (n = 21), including veno-venous bypass in 20% (n = 13) and cardiopulmonary bypass in 12% (n = 8). A complete summary of patient demographic and baseline characteristics is shown in Table I.

VTE events. The overall incidence of perioperative VTE was 22% (n = 14), including isolated DVT in 9% (n = 6) and PE in 12% (n = 8; 4 with concomitant DVT). The median time to diagnosis was 6 days (range, 1-37 days). There was a general upward trend in the number of IVC cases performed each year throughout the course of the study period, with similar upward trends in the number of VTE events and the number of screening duplex ultrasound examinations performed (Fig 2). Overall, there was no significant change over time in the proportion of IVC reconstructions performed compared with the number of VTE events recorded per year ($P = .25$).

More than half of patients with VTE were symptomatic (57%; n = 8 of 14), including lower extremity edema in 50% (n = 7), acute desaturation in 43% (n = 6), and hemodynamic compromise in 36% (n = 5). The remainder of patients (43%; n = 6) were diagnosed with VTE using early postoperative lower extremity DVT screening duplex, which was performed in 65% of cases (n = 42). All patients with postoperative VTE and no contraindications for systemic anticoagulation (79%; n = 11) were treated with warfarin for a mean of 3.6 ± 0.7 months.

Factors associated with VTE. Patients who suffered from VTE were of similar age, sex, and race compared with patients without VTE (all P = not significant [NS]; Table I). Eleven patients (17%) had a history of DVT and/or PE, and 16 patients (25%) had IVC thrombosis preoperatively. Of these, postoperative VTE occurred in 3 patients (27%) and 5 patients (31%), respectively. There were no differences in patient comorbidities, initial presenting symptoms, indication for surgery, preoperative adjuvant therapy use, or preoperative antiplatelet and/or anticoagulation use between groups (all P = NS; Table I).

VTE was significantly associated with larger tumor size ($P = .04$), reimplantation of one or more renal veins ($P = .003$), and more blood product transfusions ($P = .05$; Table II). Intraoperative use of cardiopulmonary or veno-venous bypass, estimated blood loss, level of reconstruction, and conduit size did not significantly affect VTE outcomes (all P = NS; Table II). There was a trend for more overall VTE events in patients who underwent graft reconstruction, but this was also not statistically significant (primary: 13%, n = 2; patch: 18%, n = 5; graft: 33%, n = 7; test for trend $P = .06$).

Outcomes. One patient developed cardiopulmonary failure and required ventilation, but no patient died as a result of his or her VTE. Other perioperative complications