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# Venous thrombosis following pancreaticoduodenectomy with venous resection



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#### ABSTRACT

Background: Addition of en bloc segmental venous reconstruction (VR) to pancreaticoduodenectomy (PD) for venous involvement of pancreatic tumors increases the complexity of the operation and may increase complications. The long-term mesenteric venous patency rate and oncologic outcome has not been well defined.

Methods: Our prospective database was reviewed to assess 90-day postoperative outcomes for patients who underwent PD or PD + VR (September 2004-June 2016). Two independent observers reviewed CT scans to determine long-term vein patiency. In patients with pancreatic ductal adenocarcinoma, the impact of VR on 5-year overall survival was assessed using multivariate Cox proportional hazards regression. Student's t-test was used to evaluate continuous variables and the chi-square test for categorical variables.

Results: Three hundred ninety-three patients underwent PD (51 PD + VR). Patients undergoing PD + VR had longer operations (561  $\pm$  119 versus 433  $\pm$  89 min, P < 0.00001) and greater blood loss (768  $\pm$  812 versus 327  $\pm$  423 cc, P < 0.00001). There was no difference in 90-day mortality, overall postoperative complication rates, complication severity grades, reoperation, readmission, or length of stay. 26.7% experienced venous thrombosis. Most thromboses occurred in the first year after surgery, but we also observed late thrombosis in 1 patient after 89-month follow-up. Among 135 patients with pancreatic ductal adenocarcinoma, survival was significantly longer in the PD-alone group (31.3 months [95% confidence interval: 22.9-40.0] versus 17.0 [95% confidence interval: 13.0-19.1],  $p_{\log - {\rm rank}} = 0.013$ ).

Conclusions: PD + VR does not increase short-term morbidity, but venous thrombosis is frequent and can occur long after surgery. Survival is inferior when VR is required especially in the absence of neoadjuvant chemotherapy.

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## Introduction

Although the morbidity and mortality associated with pancreaticoduodenectomy (PD) has declined since the first report of this procedure in 1935, it remains a challenging operation. The proximity of the pancreas to major vessels often leads to their involvement with tumors of the pancreas. In these cases, experienced pancreatic surgeons have advocated PD with *en bloc* resection of the portal and/or superior mesenteric vein (SMV). Several centers have reported feasibility and safety of combining PD with venous reconstruction (VR). <sup>1-3</sup> However, other larger series, including a recently published cohort analysis of the National Surgical Quality Improvement Program database, have demonstrated increased postoperative morbidity and mortality with the inclusion of VR. <sup>4</sup>

The aims of the present study were to (1) determine perioperative morbidity and mortality rates for patients undergoing PD with or without VR at our institution, (2) determine long-term vein patency rates by examining postoperative imaging of patients who underwent PD + VR, and (3) evaluate oncologic outcomes following PD with or without VR among patients with pancreatic ductal adenocarcinoma (PDAC).

### **Methods**

All patients who underwent PD at our institution from September 2004 through June 2016 were identified and retrospectively reviewed from our prospectively maintained database. Baseline demographics, clinical characteristics, and outcome data were obtained. Specific demographic data included age at the time of diagnosis, gender, and race/ ethnicity. The presence of comorbid conditions, such as hypertension, diabetes mellitus, renal insufficiency, chronic pancreatitis, coronary artery disease, chronic obstructive pulmonary disease, and obesity were recorded, as were clinical characteristics such as presenting symptoms and specific laboratory values. The American Society of Anesthesiologists classification score, operative time, estimated intraoperative blood loss, and intraoperative transfusion data were recorded. Details of the procedure and intraoperative characteristics of the pancreas, such as texture and pancreatic duct size, were also reviewed. Pathologic details including the pathologic diagnosis, lymph nodes positive, and the status of the resection margin were recorded.

Patients were all operated on in a largely uniform manner with VRs and reconstructions performed with the assistance of a vascular surgeon in order to minimize clamp time. We prefer resection of the vein, and only one vein patch was performed over the period. For short-segment resections, an end-to-end anastomosis was performed, and for resections spanning greater than 2 cm in length, an interposition graft using the internal jugular vein was employed. Systemic heparin (5000 U) was given before clamping the vein. The mesenteric artery was not clamped. No venous bypasses were performed. Our institutional anticoagulation strategy includes the previously mentioned intraoperative administration of heparin, which is not reversed at the end of the case, followed by daily aspirin (enteric-coated acetylsalicylic acid

325 mg) started immediately after surgery and continued indefinitely. Prophylactic enoxaparin (40 mg subcutaneously, daily) is initiated on postoperative day 1 and continued for 30 days postoperatively. Aspirin is recommended to be continued indefinitely because we believe there may be a risk of late vein thrombosis, but no data were collected to confirm compliance with this regimen.

The primary outcome of interest included rates of serious (>grade 2) 90-day complications to assess perioperative morbidity and mortality. Operative mortality was defined as any death within 90 days of surgery. All complications were recorded using specific and standardized definitions. Complications were graded in severity using the Common Terminology Criteria for Adverse Events v4.0 (grade 1-5) unless otherwise specified.<sup>5</sup> Pancreatic fistula was graded using the International Study Group of Pancreatic Fistula definition and delayed gastric emptying was defined and graded using the International Study Group of Pancreatic Surgery criteria.<sup>6,7</sup> A descriptive analysis of our entire study population was performed. Univariate comparisons between patients who underwent PD + VR and those who underwent PD alone were then performed for demographic, clinical, operative, and pathologic features. Student's t-test was used to evaluate continuous variables and the chi-square test for categorical variables. A multivariate Cox proportional hazards regression was used using 5-year overall survival to generate 95% confidence interval (CI) and P values. A Kaplan-Meier curve was created, median overall survival for patients with and without VR was calculated, and the p log-rank test was completed. All results were reported with the appropriate summary statistic, measure of dispersion/variance, and measure of statistical significance. P values of <0.05 were considered statistically significant. All statistical analyses were performed using SPSS v24 (IBM Corp, Armonk, NY) or Stata v15 (StataCorp, College Station, TX).

Secondary outcomes included vein patency rates among PD + VR patients. All available computed tomography (CT) scans were obtained for these patients and reviewed by two independent observers. These CT scans were performed for cancer surveillance purposes in almost all cases; of the 45 PD + VR patients who were not lost to follow-up, only two patients' CT scans were performed for abdominal pain or other symptoms. The VR was thereby assessed for patency on each scan to determine patency rates over time. A subset analysis was also performed on patients with PDAC to assess survival among those who underwent PD + VR versus PD alone. Survival was calculated from the date of cancer diagnosis until death or date of last contact, resulting in a median follow-up length that is approximately the same as median overall survival.

#### **Results**

Three hundred ninety-three patients underwent PD with or without VR. Of these, 51 patients (13.0%) underwent PD + VR (Fig. 1). Table 1 displays characteristics of the study population and a comparison of the study groups. There was no statistically significant difference in the age, gender, race, or

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