Concomitant Vascular Reconstruction During Pancreatectomy for Malignant Disease

A Propensity Score–Adjusted, Population-Based Trend Analysis Involving 10 206 Patients

Mathias Worni, MD; Anthony W. Castleberry, MD; Bryan M. Clary, MD; Beat Gloor, MD; Elias Carvalho, MSc; Danny O. Jacobs, MD, MPH; Ricardo Pietrobon, MD, PhD; John E. Scarborough, MD; Rebekah R. White, MD

Objective: To assess trends in the frequency of concomitant vascular reconstructions (VRs) from 2000 through 2009 among patients who underwent pancreatectomy, as well as to compare the short-term outcomes between patients who underwent pancreatic resection with and without VR.

Design: Single-center series have been conducted to evaluate the short-term and long-term outcomes of VR during pancreatic resection. However, its effectiveness from a population-based perspective is still unknown. Unadjusted, multivariable, and propensity score–adjusted generalized linear models were performed.

Setting: Nationwide Inpatient Sample from 2000 through 2009.

Patients: A total of 10 206 patients were involved.

Main Outcome Measures: Incidence of VR during pancreatic resection, perioperative in-hospital complications, and length of hospital stay.

Results: Overall, 10 206 patients were included in this analysis. Of these, 412 patients (4.0%) underwent VR, with the rate increasing from 0.7% in 2000 to 6.0% in 2009 ($P < .001$). Patients who underwent pancreatic resection with VR were at a higher risk for intraoperative (propensity score–adjusted odds ratio, 1.94; $P = .001$) and postoperative (propensity score–adjusted odds ratio, 1.36; $P = .008$) complications, while the mortality and median length of hospital stay were similar to those of patients without VR. Among the 25% of hospitals with the highest surgical volume, patients who underwent pancreatic surgery with VR had significantly higher rates of postoperative complications and mortality than patients without VR.

Conclusions: The frequency of VR during pancreatic surgery is increasing in the United States. In contrast with most single-center analyses, this population-based study demonstrated that patients who underwent VR during pancreatic surgery had higher rates of adverse postoperative outcomes than their counterparts who underwent pancreatic resection only. Prospective studies incorporating long-term outcomes are warranted to further define which patients benefit from VR.

JAMA Surg. 2013;148(4):331-338. Published online December 17, 2012. doi:10.1001/jamasurg.2013.1058

Author Affiliations: Department of Surgery, Duke University Medical Center, Durham, North Carolina (Drs Worni, Castleberry, Clary, Carvalho, Jacobs, Pietrobon, Scarborough, and White) and Department of Visceral Surgery and Medicine, University of Bern, Inselspital, Bern, Switzerland (Drs Worni and Gloor).

PANCREATIC ADENOCARCINOMA is known as one of the most aggressive neoplasms in the gastrointestinal tract, which in 2012 alone will account for an expected 37 390 deaths in the United States.[1] Although nonoperative therapy can marginally prolong survival, surgical resection of the tumor remains the only potentially curative treatment strategy, with reported overall 5-year survival rates of between 14% and 23%.[2-9] The current National Comprehensive Cancer Network guidelines[10] describe tumors as borderline resectable if they meet any of the following criteria: (1) involvement of the superior mesenteric vein and/or portal vein but with "suitable vessel proximal and distal to the area of vessel involvement, allowing for safe resection and reconstruction," (2) no more than short-segment encasement of the hepatic artery, or (3) no greater than 180° involvement of the superior mesenteric artery. For these patients, neoadjuvant therapy is recommended—based on nonuniform National Comprehensive Cancer Network consensus—followed by surgical resection if there is no distant progression and no great likelihood of a positive margin.

See Invited Critique at end of article

Since the first description in 1951 of a reconstruction of the superior mesenteric vein during a pancreatic resection,[11] this method has been increasing in popu-

larity. Owing to substantial improvements in surgical techniques and perioperative management, a number of single-center studies have demonstrated that vascular reconstruction (VR) during pancreatectomy can be safely performed, with short-term outcomes comparable with those of pancreatectomy without VR.[12-17] Most of these studies were performed in highly specialized centers, and it remains unknown whether short-term outcomes for patients undergoing pancreatectomy with and without concomitant VR are also comparable when evaluated in a population-based setting.

Therefore, the aims of this study were to (1) assess trends in the frequency of concomitant VR in patients with pancreatic cancer who underwent pancreatic resections from 2000 through 2009 and (2) compare the short-term adverse outcomes among patients with and without concomitant VR overall and in the subgroup of high-volume centers. We hypothesized that outcomes with and without concomitant VR would be superior in high-volume centers.

METHODS

The Duke University institutional review board approved the study protocol. We conducted a secondary analysis of data from 2000 through 2009 from a national administrative database, the Nationwide Inpatient Sample (NIS), which is part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality.[18] In the United States, the NIS is the largest all-payer inpatient database; 5 million to 8 million patients are included annually. Data from the NIS are based on both clinical discharge diagnoses and resource use for about 20% of all patient discharges per year from nonfederal, short-term, general, and specialty hospitals in the United States. The data set is stratified by various hospital characteristics such as hospital region, urban/rural locations, teaching status, number of beds, and ownership. All hospital discharges are included in this publicly available, accredited database. No personal identifiers are contained in the NIS.

Patients aged 18 years and older with malignant pancreatic neoplasms who underwent pancreatic resection were included in this analysis. First, patients with pancreatic cancer were identified through the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes: 157.0 (malignant neoplasm of the head of the pancreas), 157.1 (body), 157.2 (tail), 157.3 (pancreatic duct), 157.8 (other specified sites of pancreas), and 157.9 (pancreas, part unspecified). Patients who underwent a pancreatic resection were identified using the following *ICD-9* procedure codes: 52.7 (pancreaticoduodenectomy); 52.53 and 52.6 (subtotal and total pancreatectomy, respectively); and 52.51, 52.52, and 52.59 (proximal, distal, and other partial pancreatectomy, respectively). Vascular reconstructions were identified using the following *ICD-9* procedure codes: vascular resection with anastomosis (38.36 [abdominal arteries] and 38.37 [abdominal veins]), vascular resection with replacement (38.46 [abdominal arteries] and 38.47 [abdominal veins]), and other excision of vessel (38.66 [abdominal arteries] and 38.67 [abdominal veins]). Patients were then divided into 2 treatment groups: (1) patients who underwent pancreatectomy without VR or (2) patients who underwent pancreatectomy concomitant with VR. Patients admitted through the emergency department were excluded from the analyses to assure a homogenous sample of patients undergoing elective pancreatic resection for malignant neoplasm of the pancreas including both adenocarcinomas and malignant neuroendocrine tumors.

To account for case-mix differences, patient characteristics were extracted from the data set including age, sex, race/ethnicity (white, African American, Hispanic, and other), ZIP code–related household income ($1-$34 999, $35 000-$44 999, and ≥$45 000), and primary insurance (Medicare, Medicaid, private [health maintenance organization], and other). A comorbidity score was assigned to every patient using the Deyo categorization,[19] a modified comorbidity index adapted from the Charlson Comorbidity Index.[20] The Deyo score was especially developed for administrative data where its accuracy has been validated.[21] We grouped patients by 3 Deyo score categories (2-3, 4-8, or >8). Increasing values of the Deyo score represent patients with quantitatively increasingly severe comorbidities. We also extracted information about hospital region (Northeast, West, Midwest, or South), hospital location and teaching status (urban teaching, urban nonteaching, or rural), and hospital operation volume (in quartiles).

The short-term outcomes available in the NIS that were considered included in-hospital mortality, discharge status (nonroutine vs routine), and length of hospital stay in days. We also assessed intraoperative and postoperative complications, as well as reinterventions defined by *ICD-9* diagnosis and procedure codes as previously described by others (eTable, http://www.jamasurg.com).[22,23]

Differences in characteristics between patients who underwent pancreatectomy with and without VR were assessed using the t test for continuous data and χ^2 test for count data. The unadjusted comparison of postoperative adverse outcomes between the 2 treatment groups was performed using logistic regression analyses, with the adverse outcome of interest as outcome variable and treatment group as predictor. To assess differences among the sum of postoperative complications, we applied negative binomial regression. The predicted length of hospital stay was estimated using linear regression models after converting the values to their natural logarithm. This conversion was necessary because length of hospital stay was highly right skewed. The predicted values were then retransformed and are provided as medians and 95% confidence intervals.[24] The time trend from 2000 through 2009 of concomitant VR was estimated using logistic regression with year of operation (continuous) as predictor and treatment group as outcome.

All unadjusted analyses were repeated 2-fold through (1) multivariable risk adjustment and (2) propensity score (PS) adjustment. For risk adjustment, the potential confounders included were age, sex, race/ethnicity, ZIP code–related income, insurance status, Deyo category, hospital location/teaching status, hospital region, hospital volume, type of pancreatic resection, and year of operation. Propensity score–adjusted analyses were performed to improve information about causal inference between treatment group and outcomes of interest, mimicking a randomized controlled trial. The PS for each subject represents the conditional probability of undergoing vascular resection during pancreatic surgery based on all measured covariates.[25] We included all potential confounders used in the multivariable risk-adjusted analyses to calculate the PS owing to their potential association with the outcome and treatment selection.[26]

To assess short-term outcome differences between patients undergoing pancreatectomy with vs without VR in high-volume hospitals, we performed subgroup analyses restricted to the highest hospital volume quartile using the same statistical methods as just described. We also conducted subgroup analyses among the patients who underwent pancreaticoduodenectomy, the patients most likely to undergo VR during pancreatic surgery.

A significance level (alpha) of 0.05 was used for all analyses; *P* values for all tests were 2-sided. All statistical calculations were performed using Stata/SE version 11.2 (Stata Corp).

RESULTS

Overall, 10 206 patients who underwent pancreatic resection owing to malignant pancreatic neoplasm were included in this analysis. A total of 5069 patients (49.7%) were female and 6198 (60.7%) were white (**Table 1**). Most patients underwent a pancreaticoduodenectomy (n=7283; 71.4%) for pancreatic head tumors (n=6156; 60.3%). In total, 412 patients (4.0%) underwent VR, while the rate among the hospital volume quartiles increased from 1.2% for the lowest quartile to 6.5% for the highest quartile ($P<.001$ for trend). The rate of VR among patients who underwent pancreatic resection for malignant pancreatic disease increased from 0.7% in 2000 to 6.0% in 2009 (PS-adjusted odds ratio [OR] per year, 1.11; 95% CI, 1.06-1.16; $P<.001$) (**Figure**).

In unadjusted analyses, the overall rate of intraoperative complications was higher in patients who underwent pancreatectomy with VR (8.7%) than in patients without VR (5.8%), resulting in an OR of 1.56 (95% CI, 1.10-2.22; *P* = .01) (**Table 2**). The rate of any postoperative complication was higher in the group with VR (49.0%) than in the group without VR (43.4%) (OR, 1.26; 95% CI, 1.03-1.53; *P* = .02). Using negative binomial regression, the predicted number of complications was greater among patients who underwent pancreatectomy with VR than among those who underwent pancreatectomy only (*P* = .008) (**Table 3**). However, no differences in in-hospital mortality (4.6% with VR and 5.1% without VR; *P* = .64) or the reintervention rate (7.8% with VR and 6.1% without VR; *P* = .18) were found (Table 2). The use of blood transfusions did not differ between the 2 groups, although patients with VR received more transfusions of platelets and coagulation factors (OR, 2.88; 95% CI, 1.57-5.28; *P* = .001, and OR, 1.81; 95% CI, 1.27-2.59; *P* = .001, respectively). No difference was detected between pancreatectomies with VR and without VR for median length of hospital stay (11.9 days; 95% CI, 11.2-12.6, and 12.2 days; 95% CI, 12.1-12.4, respectively; *P* = .34).

Given the unadjusted results, we performed multivariable and PS-adjusted analyses (Table 2). Overall, the estimates from multivariable and PS-adjusted analyses were very similar. The rate of intraoperative complications was higher in patients with VR than patients without VR (PS-adjusted OR [PSOR], 1.94; 95% CI, 1.31-2.86; *P* = .001), mainly because of the higher rate of intraoperative hemorrhages (PSOR, 2.67; 95% CI, 1.70-4.20; $P<.001$). Postoperative complications were more frequent in patients with VR than without VR (PSOR, 1.36; 95% CI, 1.09-1.72; *P* = .008). Higher rates of postoperative urinary/renal, pulmonary, and gastrointestinal complications were found in patients with VR compared with patients without VR. The predicted number of complications was also lower in the group without VR (*P* = .002) (Table 3). No differences were found between the 2 groups with respect to mortality and reintervention rate, although the use of blood products was higher in patients with VR than patients without VR. The median length of hospital stay was similar, even after PS adjustment (12.3 days; 95% CI, 11.5-13.2, and 12.3 days; 95% CI, 12.1-12.4, respectively; *P* = .87).

We then performed subgroup analyses on the highest hospital volume quartile; in total, 166 of those patients (6.5%) underwent VR and 2377 (93.5%) underwent pancreatectomy only (**Table 4**). Among VR patients, 48% (n = 79) were coded as having undergone vascular resection alone, 20% (n = 34) vascular anastomosis, and 32% (n = 53) vascular replacement. While there was a trend toward more complex vascular surgery in the highest quartile, the overall distribution of the 3 VR subgroups was not significantly different compared with the lower 3 quartiles (*P* = .11). The rate of intraoperative hemorrhage was again greater in patients with VR than patients without VR (PSOR, 2.74; 95% CI, 1.33-5.61; *P* = .006), although the overall intraoperative complication rates were similar (Table 4). Postoperative complications were more frequent in patients with VR than patients without VR (PSOR, 1.43; 95% CI, 1.00-2.04; *P* = .05), mainly because of a higher rate of urinary/renal (PSOR, 3.33; 95% CI, 1.85-6.01; $P<.001$) and gastrointestinal (PSOR, 1.84; 95% CI, 1.15-2.96; *P* = .01) complications in the group with VR. Finally, in the highest volume quartile, the mortality rate was greater in the group with VR compared with the group without VR (PSOR, 4.32; 95% CI, 2.04-9.18; $P<.001$). While the mortality rate of patients with VR of the highest quartile was similar to those without VR in the other 3 quartiles (adjusted OR, 1.61; 95% CI, 0.56-4.65; *P* = .38), the mortality rate was significantly lower for patients without VR in the highest quartile compared with the others (adjusted OR, 0.36; 95% CI, 0.25-0.52; $P<.001$).

Among patients who underwent pancreaticoduodenectomies (n = 7283), 4.5% (n = 330) underwent VR. Our analysis of in-hospital adverse outcomes conducted through PS adjustment in the context of sensitivity analyses demonstrated similar results for the whole cohort in regard to both OR estimates and *P* values. The only exception was the necessity for blood transfusions (OR, 1.30; 95% CI, 0.99-1.73; *P* = .06), which was no longer significant in this subgroup.

COMMENT

To our knowledge, there have been no published population-based analyses to date investigating short-term outcomes among patients with pancreatic cancer who underwent pancreatic resection with vs without VR in the United States. We found that the annual rate of concomitant VR during pancreatic surgery has increased during the last decade and that these more extensive operations were associated with higher rates of intraoperative and postoperative complications, increased need for blood products, but overall comparable short-term mortality and hospital stay.

The results from the NIS data for both intraoperative and postoperative complications support the claim that these events are more frequent in patients who undergo

Table 1. Patient and Hospital Characteristics for Patients Who Underwent Pancreatic Resection With or Without VR

	No. (%)		
	With VR (n = 412)	Without VR (n = 9794)	*P* Value
Female	207 (50.2)	4862 (49.6)	.86
Age, mean (SD), y	63.9 (10.8)	64.9 (11.8)	.10
Race/ethnicity			
White	280 (68.0)	5918 (60.4)	.004
African American	15 (3.6)	660 (6.7)	
Other	31 (7.5)	1047 (10.7)	
Unknown	86 (20.9)	2169 (22.2)	
Zip code–related income, $			
1-34 999	72 (17.5)	2056 (21.0)	.15
35 000-44 999	91 (22.1)	2340 (23.9)	
≥45 000	240 (58.3)	5160 (52.7)	
Unknown	NS[a]	238 (2.4)	
Insurance status			
Medicare	187 (45.4)	4976 (50.8)	.01
Medicaid	13 (3.2)	487 (5.0)	
Private/HMO	194 (47.1)	3878 (39.6)	
Other/unknown	18 (4.4)	453 (4.6)	
Deyo category			
2-3	122 (29.6)	4276 (43.7)	<.001
4-8	102 (24.8)	2771 (28.3)	
>8	188 (45.6)	2747 (28.1)	
Unknown	0	0	
Hospital location/teaching status			
Rural	3 (0.7)	284 (2.9)	<.001
Urban, nonteaching	40 (9.7)	2007 (20.5)	
Urban, teaching	369 (89.6)	7474 (76.3)	
Unknown	0	29 (0.3)	
Hospital region			
Northeast	71 (17.2)	1973 (20.1)	.02
Midwest	111 (26.9)	2027 (20.7)	
South	134 (32.5)	3400 (34.7)	
West	96 (23.3)	2394 (24.4)	
Unknown	0	0	
Hospital volume quartile			
1	32 (1.2)	2728 (98.8)	<.001
2	79 (3.3)	2301 (96.7)	
3	135 (5.4)	2388 (94.6)	
4	166 (6.5)	2377 (93.5)	
Unknown	0	0	
Tumor location			
Head	299 (72.6)	5857 (59.8)	<.001
Body	32 (7.8)	629 (6.4)	
Tail	9 (2.2)	1270 (13.0)	
Duct/unknown	72 (17.5)	2038 (20.8)	
Pancreatic resection			
Pancreaticoduodenectomy	330 (80.1)	6953 (71.0)	<.001
Total pancreatectomy	40 (9.7)	488 (5.0)	
Other partial resection	42 (10.2)	2353 (24.0)	
Unknown	0	0	
Type of vascular surgery			
Resection	207 (50.2)		
Anastomosis	95 (23.1)		
Replacement	110 (26.7)		
Vascular resection			
Arterial	40 (9.7)		
Venous	372 (90.3)		

Abbreviations: HMO, health maintenance organization; NS, not shown; VR, vascular reconstruction.
[a]The number of patients is not shown as it is below that cited in the Privacy Protection Rule (<10).

VR than those who undergo pancreatectomy only. In contrast, most single-center experiences in the literature report that VR during pancreatectomy does not increase postoperative complication rates.[12-15,17,27-30] This higher rate of postoperative complications did not translate into an increased length of hospital stay; overall, we found no significant difference in mortality between patients with and without VR, which is in agreement with most

of the previous literature.[12,14,15,17,28-31] Only 1 previous study, in which no difference in overall in-hospital mortality was found, reported higher 30-day mortality among patients who underwent concomitant VR.[27] A recent systematic review and meta-analysis, focused only on arterial resections, also found increased mortality rates among patients who underwent VR compared with pancreatectomy alone.[32]

Acknowledging that case-mix differences between these studies and ours may exist, our study is substantially larger than any previous report in the literature. For example, to our knowledge, the largest single-center report was provided by Yekebas and colleagues[12] and evaluated 136 patients with VR compared with 412 patients with VR in our study. This increased statistical power to detect outcome differences might partly explain the divergent results of our current study. One might also speculate that, while the NIS database includes all patients independent of their outcome, single-center experiences are more commonly reported if they have outcomes that are similar between patients with and without VR, a phenomenon well known as reporting bias. A recently presented investigation based on the American College of Surgeons National Surgical Quality Improvement Program also suggested higher morbidity in patients with VR vs patients without VR; additionally, higher overall mortality rates were found in that study.[33] While the National Surgical Quality Improvement Program is based on voluntary participation, the NIS sampling design was specifically aimed at representing the US population. Therefore, trends identified in the NIS can be considered to have a greater degree of external validity, allowing for the evaluation of surgical trends as well as inference in relation to their association with hospital volume, location, and teaching status.

We anticipated that this difference in outcomes would be less apparent among patients who underwent surgical procedures at hospitals within the highest volume quartile. However, not only did the difference in postoperative complications persist, but also mortality risk was significantly increased for patients with VR (6%) compared with patients without VR (<2%) in this subgroup. Therefore, this difference was attributable primarily to decreased mortality in the highest volume quartile of the pancreatectomy-only subgroup relative to lower volume quartiles. Why there was no parallel decrease in mortality in the subgroup of patients with VR cannot be conclusively assessed. More specific information on tumor stage and cause of death is not available from the NIS data set, but the fact that slightly more complex VR cases were performed in the highest quartile might contribute to the relatively higher mortality for patients with VR in this subgroup.

Although there is much controversy regarding the roles of neoadjuvant and adjuvant therapy in localized pancreatic cancer, there is general agreement that complete (R0) resection is necessary for long-term survival. The current National Comprehensive Cancer Network consensus guidelines advocate vascular resection and/or reconstruction when necessary to achieve a R0 resection.[10] Although there is not universal acceptance of this practice, these more liberal recommendations represent a paradigm shift away from vascular involvement being a contraindication to resection. This

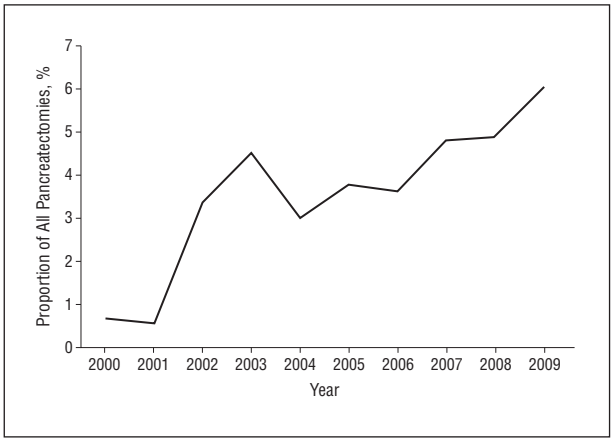

Figure. Trend of the rate of vascular reconstruction among patients who underwent pancreatic resections from 2000 through 2009 in the Nationwide Inpatient Sample database.

shift is reflected in the finding that the use of concomitant VR during pancreatectomy significantly increased from 2000 through 2009. National database studies have revealed that only about 30% of patients with locoregional disease undergo tumor resection.[34,35] The more liberal application of VR might help increase the proportion of patients who are able to undergo complete resection, thus have the potential for long-term survival. Several recent series have demonstrated that long-term survival does not differ when VRs are performed in addition to pancreatectomy.[12,14-17,27,28,31] A recent systematic review and meta-analysis involving patients who underwent arterial resection concomitant with pancreatectomy showed that 1-year and 3-year survival rates were lower than for patients who underwent pancreatectomy only.[32] In response to these findings, we would argue that the best comparison group for long-term survival studies is not patients undergoing resection without VR but rather patients with locally advanced disease undergoing palliative chemotherapy and/or chemoradiation therapy without resection. Even in modern prospective trials of nonsurgical therapy, median survival in locally advanced patients does not exceed 1 year.[36,37] The most compelling way to prove that VR has longer-term benefits would be through a randomized controlled trial comparing surgery vs nonsurgical therapy in patients with vascular involvement. However, it is unlikely that such a trial could be conducted owing to the lack of equipoise on this topic perceived by most clinicians.

Despite the strong external validity of our results, the analysis of administrative data is associated with some inherent limitations. First, we were limited to covariates available within the data set. To mitigate this limitation, we used propensity-scoring techniques, creating a quasirandomized experiment. However, information on variables such as tumor stage, neoadjuvant therapy, and body mass index were not available, and other confounding factors may have been present. For example, it is not possible to ascertain retrospectively whether VR was intended or the result of an intraoperative injury. This uncertainty may have contributed to the increased rates of intraoperative hemorrhage and complications in the VR group. Second, the de-identified nature of the data does not allow confirmation of the type of VR performed. The

Table 2. Short-term Outcomes After Pancreatectomy With VR and Without VR[a]

	No. (%)		Unadjusted Analysis, OR (95% CI)	*P* Value	Multivariable-Adjusted Analysis, OR (95% CI)[b]	*P* Value	Propensity Score–Adjusted Analysis, OR (95% CI)[c]	*P* Value
	With VR	Without VR						
Intraoperative injury	17 (4.1)	263 (2.7)	1.56 (0.94-2.57)	.08	1.78 (1.02-3.09)	.04	1.83 (1.05-3.18)	.03
Intraoperative retained foreign body[d]	0	6 (0.1)	NA	.62	NA	NA	NA	NA
Intraoperative hemorrhage	28 (6.8)	329 (3.4)	2.10 (1.41-3.13)	<.001	2.55 (1.63-4.00)	<.001	2.67 (1.70-4.20)	<.001
Intraoperative complication	36 (8.7)	567 (5.8)	1.56 (1.10-2.22)	.01	1.87 (1.23-2.75)	.002	1.94 (1.31-2.86)	.001
Wound complication	21 (5.1)	348 (3.6)	1.46 (0.93-2.29)	.10	1.03 (0.57-1.88)	.91	1.07 (0.59-1.96)	.82
Infection	64 (15.5)	1593 (16.3)	0.95 (0.72-1.24)	.69	1.00 (0.73-1.38)	.97	1.01 (0.74-1.38)	.97
Urinary/renal complication	39 (9.5)	574 (5.9)	1.68 (1.19-2.36)	.003	2.07 (1.41-3.05)	<.001	2.03 (1.39-2.97)	<.001
Pulmonary complication	74 (18.0)	1328 (13.6)	1.40 (1.08-1.81)	.01	1.65 (1.23-2.22)	.001	1.60 (1.20-2.15)	.002
Gastrointestinal complication	81 (19.7)	1612 (16.5)	1.24 (0.97-1.59)	.09	1.51 (1.14-2.01)	.004	1.54 (1.16-2.03)	.002
Acute pancreatitis	12 (2.9)	395 (4.0)	0.71 (0.40-1.28)	.26	0.73 (0.37-1.45)	.37	0.74 (0.37-1.46)	.38
Cardiovascular complication	41 (10.0)	725 (7.4)	1.38 (0.99-1.93)	.06	1.00 (0.66-1.54)	.99	0.96 (0.63-1.47)	.86
Systemic complication	9 (2.2)	200 (2.0)	1.07 (0.55-2.10)	.84	1.65 (0.82-3.30)	.16	1.59 (0.79-3.19)	.19
Any postoperative complication	202 (49.0)	4246 (43.4)	1.26 (1.03-1.53)	.02	1.38 (1.09-1.74)	.006	1.36 (1.09-1.72)	.008
Mortality	19 (4.6)	502 (5.1)	0.89 (0.56-1.43)	.64	1.62 (0.96-2.71)	.07	1.58 (0.94-2.63)	.08
Blood transfusion	106 (25.7)	2274 (23.2)	1.15 (0.91-1.44)	.24	1.37 (1.05-1.77)	.02	1.36 (1.06-1.75)	.02
Platelet transfusion	12 (2.9)	101 (1.0)	2.88 (1.57-5.28)	.001	3.39 (1.74-6.61)	<.001	3.21 (1.65-6.25)	.001
Transfusion of coagulation factors/serum	35 (8.5)	477 (4.9)	1.81 (1.27-2.59)	.001	1.83 (1.23-2.73)	.003	1.84 (1.24-2.73)	.002
Reintervention rate	32 (7.8)	600 (6.1)	1.29 (0.89-1.87)	.18	1.20 (0.77-1.87)	.42	1.24 (0.80-1.94)	.33

Abbreviations: NA, not applicable; OR, odds ratio; VR, vascular reconstruction.
[a] Unadjusted, multivariable, and propensity score–adjusted analyses were performed (pancreatectomy only: reference group).
[b] Adjustment for year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, region, and volume; and type of pancreatic resection.
[c] Propensity score calculation based on the prediction of having pancreatectomy with VR including year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, region, and volume; and type of pancreatic resection.
[d] Owing to the small number of events for retained foreign body, no adjusted analyses were performed.

Table 3. Predicted Complications After Pancreatectomy With and Without VR

Postoperative Complications, No.	Unadjusted Analysis, No. (%)[a]			%					
				Multivariable-Adjusted Analysis[a,b]			Propensity Score–Adjusted Analysis[a,c]		
	VR	Pancreatectomy Only	*P* Value	VR	Pancreatectomy Only	*P* Value	VR	Pancreatectomy Only	*P* Value
0	210 (51.0)	5548 (56.7)	.008	50.1	56.0	.001	50.8	56.2	.002
1	116 (28.2)	2559 (26.1)		28.6	27.5		28.0	27.1	
2	47 (11.4)	1051 (10.7)		12.7	10.6		12.6	10.7	
3	27 (6.6)	465 (4.8)		5.2	3.8		5.2	3.9	
4	10 (2.4)	144 (1.5)		2.1	1.3		2.1	1.4	
5	2 (0.5)	20 (0.2)		0.8	0.5		0.8	0.5	
6	0	6 (0.1)		0.3	0.02		0.3	0.2	
7	0	1 (0.01)		0.1	0		0.1	0	

Abbreviation: VR, vascular reconstruction.
[a] Based on negative binomial regression.
[b] Adjustment for year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, region, and volume; and type of pancreatic resection.
[c] Propensity score calculation based on the prediction of having pancreatectomy with VR including year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, region, and volume; and type of pancreatic resection.

Table 4. Adverse Postoperative Outcomes for Subgroup of Patients Operated on in the Highest Hospital Volume Quartile

	No. (%)							
	VR (n = 166)	Pancreatectomy Only (n = 2377)	Unadjusted Analysis, OR (95% CI)	*P* Value	Multivariable-Adjusted Analysis, OR (95% CI)[a]	*P* Value	Propensity Score–Adjusted Analysis, OR (95% CI)[b]	*P* Value
Intraoperative injury	5 (3.0)	56 (2.4)	1.29 (0.51-3.26)	.59	2.36 (0.87-6.43)	.09	2.47 (0.93-6.59)	.07
Intraoperative retained foreign body[c]	0	0	NA	NA	NA	NA	NA	NA
Intraoperative hemorrhage	10 (6.0)	66 (2.8)	2.24 (1.13-4.45)	.02	2.80 (1.35-5.80)	.006	2.74 (1.33-5.61)	.006
Intraoperative complication	10 (6.0)	119 (5.0)	1.22 (0.63-2.37)	.56	1.68 (0.83-3.39)	.15	1.70 (0.85-3.40)	.13
Wound complication	9 (5.4)	77 (3.2)	1.71 (0.84-3.48)	.14	0.92 (0.32-2.63)	.87	0.96 (0.34-2.73)	.94
Infection	30 (18.1)	335 (14.1)	1.34 (0.89-2.03)	.16	1.20 (0.74-1.95)	.45	1.17 (0.73-1.89)	.51
Urinary/renal complication	19 (11.5)	99 (4.2)	2.97 (1.77-5.00)	<.001	3.79 (2.06-7.00)	<.001	3.33 (1.85-6.01)	<.001
Pulmonary complication	24 (14.5)	229 (9.6)	1.59 (1.01-2.50)	.05	1.26 (0.73-2.17)	.41	1.24 (0.72-2.13)	.44
Gastrointestinal complication	30 (18.1)	256 (10.8)	1.83 (1.21-2.77)	.005	1.83 (1.13-2.95)	.01	1.84 (1.15-2.96)	.01
Acute pancreatitis	6 (3.6)	85 (3.6)	1.01 (0.44-2.35)	.98	0.89 (0.32-2.54)	.83	0.89 (0.31-2.51)	.82
Cardiovascular complication	22 (13.3)	192 (8.1)	1.74 (1.08-2.79)	.02	1.26 (0.71-2.24)	.43	1.24 (0.70-2.19)	.47
Systemic complication	2 (1.2)	33 (1.4)	0.87 (0.21-3.64)	.85	0.95 (0.22-4.15)	.94	0.94 (0.21-4.12)	.93
Any postoperative complication	82 (49.4)	868 (36.5)	1.70 (1.24-2.33)	.001	1.46 (1.02-2.09)	.04	1.43 (1.00-2.04)	.05
Mortality	10 (6.0)	46 (1.9)	3.25 (1.61-6.56)	.001	4.94 (2.27-10.74)	<.001	4.32 (2.04-9.18)	<.001
Blood transfusion	28 (16.9)	440 (18.5)	0.89 (0.59-1.36)	.60	1.17 (0.74-1.87)	.50	1.15 (0.74-1.79)	.54
Platelet transfusion	3 (1.8)	22 (0.9)	1.97 (0.58-6.65)	.28	2.51 (0.69-9.14)	.16	2.24 (0.63-7.95)	.21
Transfusion of coagulation factors/serum	12 (7.2)	114 (4.8)	1.55 (0.83-2.87)	.17	1.52 (0.77-2.96)	.23	1.57 (0.81-3.05)	.18
Reintervention rate	15 (9.0)	123 (5.2)	1.82 (1.04-3.19)	.04	1.40 (0.70-2.80)	.34	1.39 (0.70-2.77)	.35

Abbreviations: NA, not applicable; OR, odds ratio; VR, vascular reconstruction.

[a] Adjustment for year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, and region; and type of pancreatic resection.

[b] Propensity score calculation based on the prediction of having pancreatectomy with VR including year of operation; age; sex; race/ethnicity; ZIP code–related income; primary insurance; Deyo score; hospital location, teaching status, and region; and type of pancreatic resection.

[c] Owing to the small number of events for retained foreign body, no adjusted analyses were performed.

NIS database relies exclusively on *ICD-9* procedure codes assigned by administrative coders. A broad range of techniques are used for VR, from simple venorrhaphy to often complex interposition vein grafting. Given the inconsistencies in how these techniques are used and described by surgeons in their operative reports, coding inaccuracies certainly exist and limit our ability to analyze the type of reconstruction as a factor. Third, the small number of arterial resections (n = 40) precluded specific subgroup analysis. Because there are technical and oncologic issues that differ between venous and arterial reconstructions, this important topic requires further investigation. Finally, our analyses are limited to in-hospital complications, as our data set does not allow assessment of 30-day or 90-day morbidity. However, we believe that our claims about short-term outcomes are still highly relevant.

In conclusion, in contrast to most single-center analyses, postoperative adverse outcomes following VR were more frequent than following pancreatectomy only in this population-based analysis. This finding persisted in a subgroup analysis focusing on the highest quartile of hospital volume. However, if complete (R0) resection can be achieved through vascular resection, a reasonable increase in perioperative adverse outcomes can be tolerated because this is the only treatment that offers any chance of a cure. Future studies investigating shared decision-making between patients and physicians should be conducted given the trade-offs imposed by the immediate risk for mortality and the potential benefit of long-term survival. Additional population-based investigations including information on long-term survival are also warranted to better understand in which settings vascular resections should be recommended to patients with pancreatic cancer.

Accepted for Publication: September 25, 2012.
Published Online: December 17, 2012. doi:10.1001/jamasurg.2013.1058
Correspondence: Rebekah R. White, MD, Division of Surgical Oncology, Department of Surgery, Duke University Medical Center, PO Box 3247, 489 Seeley G. Mudd

Bldg, Searl Center, Durham, NC 27710 (rebekah.white@duke.edu).

Author Contributions: *Study concept and design:* Worni, Castleberry, Gloor, Pietrobon, and Scarborough. *Acquisition of data:* Worni. *Analysis and interpretation of data:* Worni, Castleberry, Clary, Gloor, Carvalho, Jacobs, Scarborough, and White. *Drafting of the manuscript:* Worni and Scarborough. *Critical revision of the manuscript for important intellectual content:* Castleberry, Clary, Gloor, Carvalho, Jacobs, Pietrobon, Scarborough, and White. *Statistical analysis:* Worni, Castleberry, Carvalho, and Pietrobon. *Administrative, technical, and material support:* Clary, Jacobs, and Scarborough. *Study supervision:* Clary, Gloor, Jacobs, and White.

Conflict of Interest Disclosures: None reported.

Online-Only Material: The eTable is available at http://www.jamasurg.com.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin*. 2012; 62(1):10-29.
2. Oettle H, Post S, Neuhaus P, et al. Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. *JAMA*. 2007;297(3):267-277.
3. Neoptolemos JP, Stocken DD, Bassi C, et al; European Study Group for Pancreatic Cancer. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. *JAMA*. 2010;304(10):1073-1081.
4. Wagner M, Redaelli C, Lietz M, Seiler CA, Friess H, Büchler MW. Curative resection is the single most important factor determining outcome in patients with pancreatic adenocarcinoma. *Br J Surg*. 2004;91(5):586-594.
5. Herman JM, Swartz MJ, Hsu CC, et al. Analysis of fluorouracil-based adjuvant chemotherapy and radiation after pancreaticoduodenectomy for ductal adenocarcinoma of the pancreas: results of a large, prospectively collected database at the Johns Hopkins Hospital. *J Clin Oncol*. 2008;26(21):3503-3510.
6. You DD, Lee HG, Heo JS, Choi SH, Choi DW. Prognostic factors and adjuvant chemoradiation therapy after pancreaticoduodenectomy for pancreatic adenocarcinoma. *J Gastrointest Surg*. 2009;13(9):1699-1706.
7. Lim JE, Chien MW, Earle CC. Prognostic factors following curative resection for pancreatic adenocarcinoma: a population-based, linked database analysis of 396 patients. *Ann Surg*. 2003;237(1):74-85.
8. Corsini MM, Miller RC, Haddock MG, et al. Adjuvant radiotherapy and chemotherapy for pancreatic carcinoma: the Mayo Clinic experience (1975-2005). *J Clin Oncol*. 2008;26(21):3511-3516.
9. Riediger H, Keck T, Wellner U, et al. The lymph node ratio is the strongest prognostic factor after resection of pancreatic cancer. *J Gastrointest Surg*. 2009; 13(7):1337-1344.
10. National Comprehensive Cancer Network. National Comprehensive Cancer Network website. http://www.nccn.org/index.asp. Accessed August 12, 2012.
11. Moore GE, Sako Y, Thomas LB. Radical pancreatoduodenectomy with resection and reanastomosis of the superior mesenteric vein. *Surgery*. 1951;30(3):550-553.
12. Yekebas EF, Bogoevski D, Cataldegirmen G, et al. En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels: perioperative outcome and long-term survival in 136 patients. *Ann Surg*. 2008; 247(2):300-309.
13. Bachellier P, Rosso E, Lucescu I, et al. Is the need for an arterial resection a contraindication to pancreatic resection for locally advanced pancreatic adenocarcinoma? a case-matched controlled study. *J Surg Oncol*. 2011;103(1):75-84.
14. Fukuda S, Oussoultzoglou E, Bachellier P, et al. Significance of the depth of portal vein wall invasion after curative resection for pancreatic adenocarcinoma. *Arch Surg*. 2007;142(2):172-179, discussion 180.
15. Martin RC II, Scoggins CR, Egnatashvili V, Staley CA, McMasters KM, Kooby DA. Arterial and venous resection for pancreatic adenocarcinoma: operative and long-term outcomes. *Arch Surg*. 2009;144(2):154-159.
16. Tseng JF, Raut CP, Lee JE, et al. Pancreaticoduodenectomy with vascular resection: margin status and survival duration. *J Gastrointest Surg*. 2004;8(8): 935-949; discussion 949-950.
17. Turley RS, Peterson K, Barbas AS, et al. Vascular surgery collaboration during pancreaticoduodenectomy with vascular reconstruction. *Ann Vasc Surg*. 2012; 26(5):685-692.
18. Healthcare Cost and Utilization Project. Overview of the Nationwide Inpatient Sample (NIS). http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed August 12, 2012.
19. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
21. Cleves MA, Sanchez N, Draheim M. Evaluation of two competing methods for calculating Charlson's Comorbidity Index when analyzing short-term mortality using administrative data. *J Clin Epidemiol*. 1997;50(8):903-908.
22. Guller U, Hervey S, Purves H, et al. Laparoscopic versus open appendectomy: outcomes comparison based on a large administrative database. *Ann Surg*. 2004; 239(1):43-52.
23. Hu JC, Gu X, Lipsitz SR, et al. Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA*. 2009;302(14):1557-1564.
24. Rutten-van Mölken MP, van Doorslaer EK, van Vliet RC. Statistical analysis of cost outcomes in a randomized controlled clinical trial. *Health Econ*. 1994; 3(5):333-345.
25. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55. doi:10.2307/2335942.
26. Brookhart MA, Schneeweiss S, Rothman KJ, Glynn RJ, Avorn J, Stürmer T. Variable selection for propensity score models. *Am J Epidemiol*. 2006;163 (12):1149-1156.
27. Banz VM, Croagh D, Coldham C, et al. Factors influencing outcome in patients undergoing portal vein resection for adenocarcinoma of the pancreas. *Eur J Surg Oncol*. 2012;38(1):72-79.
28. Riediger H, Makowiec F, Fischer E, Adam U, Hopt UT. Postoperative morbidity and long-term survival after pancreaticoduodenectomy with superior mesentericoportal vein resection. *J Gastrointest Surg*. 2006;10(8):1106-1115.
29. Hartel M, Niedergethmann M, Farag-Soliman M, et al. Benefit of venous resection for ductal adenocarcinoma of the pancreatic head. *Eur J Surg*. 2002;168 (12):707-712.
30. Capussotti L, Massucco P, Ribero D, Viganò L, Muratore A, Calgaro M. Extended lymphadenectomy and vein resection for pancreatic head cancer: outcomes and implications for therapy. *Arch Surg*. 2003;138(12):1316-1322.
31. Harrison LE, Klimstra DS, Brennan MF. Isolated portal vein involvement in pancreatic adenocarcinoma: a contraindication for resection? *Ann Surg*. 1996; 224(3):342-347, discussion 347-349.
32. Mollberg N, Rahbari NN, Koch M, et al. Arterial resection during pancreatectomy for pancreatic cancer: a systematic review and meta-analysis. *Ann Surg*. 2011;254(6):882-893.
33. Castleberry AW, White RR, De La Fuente SG, et al. The impact of vascular resection on early postoperative outcomes after pancreaticoduodenectomy: an analysis of the American College of Surgeons National Surgical Quality Improvement Program database [published online August 30, 2012]. *Ann Surg Oncol*. doi:10.1245/s10434-012-2585-y.
34. Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS. National failure to operate on early stage pancreatic cancer. *Ann Surg*. 2007; 246(2):173-180.
35. Riall TS, Nealon WH, Goodwin JS, et al. Pancreatic cancer in the general population: improvements in survival over the last decade. *J Gastrointest Surg*. 2006; 10(9):1212-1223; discussion 1223-1214.
36. Crane CH, Winter K, Regine WF, et al. Phase II study of bevacizumab with concurrent capecitabine and radiation followed by maintenance gemcitabine and bevacizumab for locally advanced pancreatic cancer: Radiation Therapy Oncology Group RTOG 0411. *J Clin Oncol*. 2009;27(25):4096-4102.
37. Loehrer PJ Sr, Feng Y, Cardenes H, et al. Gemcitabine alone versus gemcitabine plus radiotherapy in patients with locally advanced pancreatic cancer: an Eastern Cooperative Oncology Group trial. *J Clin Oncol*. 2011;29(31):4105-4112.