

Perioperative cardiovascular risk stratification of patients with diabetes who undergo elective major vascular surgery

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Background: The importance of diabetes mellitus (DM) as an independent risk factor for perioperative cardiac morbidity after vascular surgery is controversial. This study examined the impact of DM on perioperative outcomes and length of stay in patients who underwent major vascular surgery.

Methods: Patients who underwent elective aortic reconstruction (n = 2792), lower extremity bypass (n = 3838), carotid endarterectomy (n = 5522), and major amputation (n = 3883) from 1997 to 1999 were identified in the National Surgical Quality Improvement Program database of the Department of Veterans Affairs. Outcomes assessed were death, cardiovascular complications (myocardial infarction, stroke, need for cardiopulmonary resuscitation), and length of stay. Multivariable logistic and linear regression models were used to control for patient demographics, procedure type, comorbidities, and diabetic complications.

Results: Before adjustment for potential confounders, patients with diabetes had a higher incidence rate of perioperative death (3.9% versus 2.6%; $P = .001$) and cardiovascular complications (3.3% versus 2.6%; $P = .01$) when compared with patients without diabetes. After controlling for comorbid conditions, procedure type, and diabetic complications, only patients with DM who underwent treatment with insulin were at statistically increased risk for cardiovascular complications (odds ratio [OR], 1.48; 95% CI, 1.15 to 1.91). Neither DM treated with insulin (OR, 1.10; 95% CI, 0.85 to 1.41) nor DM treated with oral medications (OR, 0.96; 95% CI, 0.73-1.28) was an independent risk factor for death. Important independent risk factors for death included several conditions that are commonly associated with diabetes, including proteinuria, elevated creatinine level, history of congestive heart failure, and history of cerebrovascular accident. DM was also found to increase length of stay by as much as 38% even after adjustment for comorbidities.

Conclusion: Patients with diabetes have a higher incidence rate of death and cardiovascular complications. However, after controlling for specific comorbid conditions, the only independent association was between patients with insulin treatment and the risk of cardiovascular complications. DM does not appear to be an independent risk factor for postoperative mortality. All patients with diabetes, regardless of insulin use, have a prolonged length of stay after major vascular surgery. (*J Vasc Surg* 2002;35:894-901.)

Perioperative cardiovascular morbidity and mortality continue to be the leading cause of death and complications after major vascular surgery. Consequently, considerable attention has been paid to the identification of risk factors associated with increased cardiac complications. Patients with diabetes mellitus (DM) have frequently been considered to have an elevated risk of cardiac complications compared with patients without diabetes, which justifies a lower threshold for cardiac stress testing.¹ Diabetes has

been classified by the American College of Cardiology/American Heart Association guidelines as an intermediate risk factor that mandates further evaluation in patients who have decreased functional status or are scheduled for high risk surgery, including aortic and peripheral vascular procedures.²

Previous evaluations of the risk of patients with diabetes who undergo specific vascular surgery have not always supported the finding that patients with diabetes are at increased perioperative risk. After controlling for other identified comorbidities with multivariate analysis, some studies have suggested that patients with diabetes do not appear to be at increased risk of death after carotid endarterectomy^{3,4} or aortic surgery.⁵⁻⁷ However, other studies have suggested that an increased risk of perioperative complications exists among patients with diabetes who undergo aortic surgery.⁶ Most evaluations of this issue have suffered from a small number of adverse outcomes (thus limiting statistical power) and incomplete documentation of important comorbidities. Furthermore, despite evidence that the risk of death after coronary artery bypass grafting may vary among patients with diabetes depending on severity of disease,⁸ the impact of risk stratification by degree of dia-

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betic complications (eg, the need for insulin or presence of nephropathy) has not been investigated in patients who undergo noncardiac vascular surgery.

This investigation examined the independent risk of DM on mortality, cardiovascular morbidity, and length of stay (LOS) in patients who underwent vascular surgery. Analyses controlled for comorbid disease, the severity of DM as determined by the need for oral medications or insulin, and the incidence rate of renal complications of DM. The goal of the investigation was to evaluate the hypothesis that the risk of poor outcome is not uniformly high across all patients with DM, and, in the absence of other identifiable risk factors, invasive testing could be limited to patients with diabetes who are identified before surgery as high risk.

MATERIALS AND METHODS

Data sources. All patients who underwent major vascular surgical procedures from 1997 through 1999 were identified from the Department of Veterans Affairs (VA) Patient Treatment File (PTF) database. Data were abstracted for patients who underwent four types of procedures with International Classification of Diseases, 9th Revision, Clinical Modification codes: abdominal aortic reconstruction (38.44, 39.25), carotid endarterectomy (38.12, 38.32, 38.42), lower extremity bypass (39.29), and lower extremity major amputation (84.10, 84.15, 84.16, 84.17, 84.18). PTF data included demographic information, condition of patient at discharge, and hospital LOS.

Patient records then were linked to the National Surgical Quality Improvement Program (NSQIP) database of surgical procedures performed at VA hospitals. The NSQIP is a prospective, multicenter observational evaluation project to assess risk-adjusted surgical outcomes within the VA as described in detail elsewhere.^{9,10} This clinical database includes patient demographic information, preoperative comorbidities, intraoperative care, and postoperative outcomes collected by trained surgical clinical nurse reviewers at each of 123 surgical centers. All operations performed with general, spinal, and epidural anesthesia are included in the database unless the patient has been entered into the database for another index procedure within the previous 30 days.

Patients also were matched to a diabetes registry collected as part of the national VA Quality Enhancement Research Initiative (QUERI) in diabetes care.¹¹ The QUERI database includes information on hospitalizations, outpatient visits, selected pharmaceuticals, and all laboratory data for selected tests completed on inpatients and outpatients in the VA system. Where available, these data were used to determine patient diabetic medication, preoperative serum creatinine level, hemoglobin A1c, and degree of proteinuria.

Data linkage was accomplished with scrambled patient identifiers, date of admission, and procedure type. Patient confidentiality was ensured with removal of all patient identifiable information, including scrambled identifiers, after linkage. All patient identifiable data were maintained

in secured systems within the VA and were not provided to the study investigators. This project was approved by the Institutional Review Committee of the VA Ann Arbor Health Care System.

Definition of surgical procedures. Patients were classified into one of four mutually exclusive classifications on the basis of procedure type with the following hierarchy: aortic reconstruction, carotid endarterectomy, lower extremity bypass, and amputation. Therefore, if a patient underwent both an aortic repair and a lower extremity bypass, the patient was considered in the aortic repair category. Importantly, patients whose primary procedure was classified as emergent within the NSQIP database were excluded.

Definition of independent variables. Demographic information collected from the PTF file included patient age, race, and sex. Subjects were considered to have DM if they had any of the following conditions: receipt of insulin or oral hypoglycemic medications before admission; outpatient visits, including a diagnosis of DM on two occasions; or a previous inpatient stay with a discharge diagnosis of DM. The DM classification was divided into three categories: insulin-treated DM, oral-treated or diet-treated DM, and no DM. Because the vast majority of patients within the VA have type 2 DM, it should be noted that most of the patients treated with insulin in this study have type 2 diabetes. The databases are unable to identify which patients with insulin treatment have type 1 diabetes, but unpublished audits of the QUERI diabetes registry suggest that less than 3% of VA patients with DM have type 1 DM.

Additional independent variables were defined with NSQIP definitions: history of congestive heart failure within 1 month of surgery; history of chronic obstructive pulmonary disease resulting in 1 or more of conditions of functional disability, chronic bronchodilator therapy, or forced expiratory volume in 1 second of less than 75% of predicted; history of a transient ischemic attack; history of a cerebrovascular accident (embolic, thrombotic, hemorrhage) with residual motor, sensory, or cognitive deficit; ethanol abuse of greater than two drinks per day in the 2 weeks before admission; current smoker; ventilator use before surgery; steroid therapy before surgery; and dialysis before surgery. Further details can be found in previous published reports from the NSQIP project.¹² In addition, because the NSQIP data did not contain a field for hypertension, patients were classified as hypertensive on the basis of identification of a diagnostic code for hypertension in prior inpatient or outpatient evaluations (PTF database).

Preoperative laboratory data were examined for evidence of chronic renal insufficiency, proteinuria, and poorly controlled DM. An elevated creatinine level, identified with the NSQIP set, was considered to be greater than or equal to 2.0. Proteinuria was defined as a value of 2+ or greater on dipstick, greater than 30 mg/24 hours on urine collection, or greater than 100 µg/mL. Patients without preoperative laboratory values were assigned normal values in multivariate analysis. This was on the basis of the finding that most patients have normal values and the assumption

that routine laboratory tests were not obtained in healthier patients, who would be more likely to have normal values. Preoperative urine protein values were available for 47% of patients with diabetes (42% of all patients), and preoperative creatinine values were recorded for 94% of patients with diabetes (94% of patients overall).

Because this investigation was designed to improve preoperative risk stratification on the basis of the severity of diabetes, only variables that would be available to the clinician before surgery were included in the model. Therefore, we did not include intraoperative and postoperative data that had been collected in the NSQIP or diabetes registry in our model. Besides proteinuria and hemoglobin A1c data, no data element was missing for more than 3.6% of the population.

Definition of surgical outcomes. The three primary outcomes assessed in this analysis were defined with NSQIP data. Death was defined with the condition of patient at discharge. Cardiovascular complications were defined as acute myocardial infarction that occurred during surgery or within 30 days of surgery, cardiac arrest necessitating cardiopulmonary resuscitation in the operating room, intensive care unit (ICU), ward, or out-of-hospital within 30 days, or an embolic, thrombotic, or hemorrhagic cardiovascular accident with motor, sensory, or cognitive dysfunction within 30 days.¹² The combined outcome was defined as death or cardiovascular complication or both.

Statistical analysis. Differences in baseline characteristics and clinical outcomes among patients with and without diabetes were evaluated with χ^2 testing for categorical variables and two-tailed Student *t* tests for continuous variables. Subsequently, multivariable logistic regression models were developed for each of the three primary outcomes. The model was developed with sequentially adding progressively more detailed clinical variables. The independent association of insulin-treated or orally treated diabetes with surgical outcomes was determined after sequentially adjusting for (1) procedure type, (2) patient demographics, and (3) general comorbidities. A subsequent model was developed for the subset of patients with diabetes that examined proteinuria and elevated glycosylated hemoglobin to determine their prognostic significance. Finally, the impact of DM on hospital LOS and ICU LOS was determined with linear regression. To account for the significant right skew in LOS and ICU LOS data, the data were transformed with logarithm as the dependant variable.

Model performance was assessed with formal goodness-of-fit (Hosmer-Lemeshow) tests.¹³ The Hosmer-Lemeshow test compares the expected and observed events in 10 equal subgroups defined by the deciles of predicted risk. A statistically nonsignificant goodness of fit statistic is evidence of model discriminant capacity. All models showed evidence of excellent model calibration with both visual and statistical inspection. Appropriate first-degree interaction terms were examined and did not improve model fit as assessed with receiver operating curve values, including interaction terms between procedure type and

Table I. Characteristics of patients undergoing major vascular surgical procedures in VA hospitals from 1997 to 1999

	<i>Patients with DM</i>	<i>Patients without DM</i>	<i>P value</i>
No.	7871	8164	
Age (y)	67.6 ± 9	66.8 ± 9	.001
Male gender	99.0%	98.8%	.257
White race	74.4%	84.0%	.001
Hypertension	87.7%	79.6%	.001
History of stroke with neuro	14.1%	17.4%	.001
History of stroke without neuro	7.6%	6.5%	.019
History of transient ischemia attack	12.6%	17.9%	.001
Congestive heart failure	8.1%	3.2%	.001
Chronic obstructive pulmonary disease	17.8%	22.0%	.001
Creatinine level >2.0	12.5%	4.3%	.001
Dialysis	5.6%	0.8%	.001
Ventilation before surgery	0.4%	0.4%	.910
Smoker	36.3%	54.7%	.001
Active use of ethanol	6.8%	13.6%	.001
Steroid use	2.4%	2.5%	.600
Proteinuria	18.9%	5.9%	.001
DM necessitating insulin	41.5%	N/A	
DM necessitating oral medication	34.7%	N/A	
HbA1c 6.2 - 8.0	15.0%	N/A	
HbA1c 8.0 - 9.5	10.9%	N/A	
HbA1c > 9.5	10.9%	N/A	
HbA1c-missing	52.0%	N/A	

N/A, Not applicable; *neuro*, neurologic deficit; HbA1c, hemoglobin A1c.

diabetes. Data were analyzed with Stata v. 6.0 (Stata Corporation, College Station, Tex).

RESULTS

Records for 17,290 major vascular surgical procedures in the nation's VA hospitals were available for review. After exclusion of patients who underwent emergency operations (*n* = 1250), a total was left of 14,525 unique patients who underwent 16,035 procedures. Patients with DM constituted 49% of these patients, of whom 42% were undergoing treatment with insulin before operation and 35% were undergoing treatment with oral hypoglycemic agents alone.

Patient characteristics differed significantly among patients with and without diabetes (Table I). In particular, patients with diabetes were older, were less likely to be white, and had a significantly higher incidence rate of important comorbid conditions. In addition, patients with diabetes were less likely to smoke, use alcohol, have chronic obstructive pulmonary disease, or have had a stroke.

Before adjustment for patient factors, patients with diabetes who underwent vascular procedures were found to have a higher incidence rate of the combined outcome of death or cardiovascular complications (5.8% versus 4.3%; *P* = .001), death alone (3.9% versus 2.6%; *P* = .001), and cardiovascular complications (3.3% versus 2.6%; *P* = .011; Table II). A higher rate of the combined outcome (death or cardiovascular complications) also was found with individ-

Table II. Death or cardiovascular complications of major vascular procedures performed in VA hospitals from 1997 to 1999

	<i>Patients with DM</i>	<i>Patients without DM</i>	<i>P value</i>
Vascular procedures performed			
Carotid endarterectomy	2210 (40%)	3312 (60%)	
Aortic reconstruction	744 (27%)	2048 (73%)	
Lower extremity bypass	2120 (55%)	1718 (45%)	
Amputation	2797 (72%)	1086 (28%)	
Death or cardiovascular complication			
All procedures	458 (5.8%)	352 (4.3%)	.001
Carotid endarterectomy	78 (3.5%)	83 (2.5%)	.027
Aortic reconstruction	39 (5.2%)	118 (5.8%)	.600
Lower extremity bypass	93 (4.4%)	47 (2.7%)	.007
Amputation	248 (8.9%)	104 (9.6%)	.49
Death			
All procedures	304 (3.9%)	212 (2.6%)	.001
Carotid endarterectomy	19 (0.9%)	18 (0.5%)	.16
Aortic reconstruction	22 (3.0%)	73 (3.6%)	.43
Lower extremity bypass	57 (2.7%)	32 (1.9%)	.09
Amputation	206 (7.4%)	89 (8.2%)	.38
Non-fatal cardiovascular events			
All procedures	260 (3.3%)	214 (2.6%)	.011
Carotid endarterectomy	75 (3.4%)	77 (2.3%)	.017
Aortic reconstruction	25 (3.4%)	76 (3.7%)	.66
Lower extremity bypass	63 (3.0%)	24 (1.4%)	.001
Amputation	97 (3.5%)	37 (3.4%)	.92

ual vascular operations for patients with DM who underwent both carotid endarterectomy (3.5% versus 2.5%; $P = .027$) and lower extremity bypass (4.4% versus 2.7%; $P = .007$).

However, analysis of the combined outcome (death or cardiovascular complications) revealed that only patients with diabetes who needed insulin treatment were at higher risk of death or cardiovascular complications when compared with patients without diabetes (odds ratio [OR], 1.37; $P = .001$) after adjustment for patient demographics (age, sex, and race) and procedure type (Table III). After adjustment for confounding comorbidities, patients with oral hypoglycemic treatment alone did not have a significantly greater risk of death or complications (OR, 1.15; $P = .18$), and patients with diabetes who needed insulin treatment appeared to be at a mildly increased risk of the combined outcome (death or nonfatal cardiovascular complication; OR, 1.22; $P < .06$). Comorbid conditions that predicted a higher odds of postoperative death or cardiovascular complication included increased age, history of stroke with neurologic deficit, chronic obstructive pulmonary disease, steroid use, preoperative ventilation, congestive heart failure, and elevated creatinine level. In this data set, those patients with a clinical diagnosis of hypertension had a lower risk of an adverse outcome (OR, 0.75; $P = .005$).

Similar findings were evident when the association between diabetes and the risk of death was examined separately from nonfatal complications (Table IV). Patients with insulin-treated DM were at increased risk of death after adjustment for demographic factors and procedure type (OR, 1.25; $P = .046$), but no residual effect was seen

after accounting for other comorbidities and renal insufficiency (OR, 1.10; $P = .45$).

Patients with diabetes with insulin treatment also had a significant increase in the odds of development of postoperative nonfatal cardiovascular complications (Table V). After adjustment for demographic factors and procedure type, diabetes treated with insulin had an OR of 1.71 ($P < .001$). Inclusion of other known comorbidities, including renal insufficiency, into the model reduced, but did not eliminate, the independent association between diabetes needing insulin and a greater risk of cardiovascular complications (OR, 1.48; $P = .002$). However, patients with oral hypoglycemic agent treatment alone were not at significantly increased risk (OR, 1.22; $P = .14$) for cardiovascular complications. Comorbid conditions that did predict higher odds of postoperative cardiovascular complications included a history of stroke with neurologic deficit, congestive heart failure, and elevated creatinine level.

In a subset analysis including only patients with diabetes, patients who underwent treatment with insulin had a trend toward higher rates of cardiovascular complications (OR, 1.28; $P = .10$) but not death or the combined outcome (Table VI). This analysis is consistent with the findings of the overall analysis, in that it suggests that insulin-treated diabetes is a minor risk factor for cardiovascular complications but not death and that non-insulin treated DM is not an independent risk factor at all. Also consistent with the overall analysis, other clinical risk factors are more predictive of perioperative morbidity and mortality, including stroke with neurologic deficit, preoperative ventilation, steroid use, and chronic renal failure. Significant proteinuria is a marker of an increased risk of death

Table III. Impact of diabetes on risk of combined outcome (death or cardiovascular complications) after vascular surgical procedures

Risk factor	Combined outcome (OR; 95% CI)		
	Adjusted for procedure type	Additionally adjusted for demographic factors	Additionally adjusted for comorbidities
Insulin-treated DM	1.31 (1.09 - 1.56)*	1.37 (1.13 - 1.64)*	1.22 (0.99 - 1.49)
Oral-treated DM	1.10 (0.89 - 1.35)	1.07 (0.87 - 1.32)	1.15 (0.93 - 1.43)
AAA	0.66 (0.53 - 0.82)*	0.74 (0.59 - 0.92)*	0.97 (0.77 - 1.22)
Carotid	0.32 (0.27 - 0.40)*	0.33 (0.26 - 0.40)*	0.40 (0.32 - 0.51)*
Lower extremity bypass	0.40 (0.32 - 0.49)*	0.43 (0.35 - 0.53)*	0.53 (0.43 - 0.65)*
Age		1.04 (1.03 - 1.05)*	1.04 (1.03 - 1.05)*
Race not white or black			1.32 (1.02 - 1.70)†
Black race			0.83 (0.66 - 1.03)
Ventilation			5.62 (3.12 - 10.1)*
Creatinine level >2.0			2.15 (1.68 - 2.70)*
CHF			1.98 (1.56 - 2.50)*
Steroid therapy			1.56 (1.06 - 2.29)†
Stroke with neuro deficit			1.56 (1.29 - 1.88)*
COPD			1.18 (0.99 - 1.42)
Hypertension			0.75 (0.62 - 0.92)*

C-statistic = 0.72.

Variables not shown ($P > .10$): sex, smoking, alcohol use, prior stroke without neurologic deficit, history of transient ischemic attack. Amputation was used as comparison procedure.

OR = 1.0.

* $P < .01$.

† $P < .05$.

AAA, Abdominal aortic aneurysm; *neuro deficit*, neurologic deficit; *COPD*, chronic obstructive pulmonary disease; *CHF*, congestive heart failure.

Table IV. Impact of diabetes on risk of death after vascular surgical procedures

Risk factor	Death (OR; 95% CI)		
	Adjusted for procedure type	Additionally adjusted for demographic factors	Additionally adjusted for comorbidities
Insulin-treated DM	1.18 (0.95 - 1.47)	1.25 (1.00 - 1.56)†	1.10 (0.85 - 1.41)
Oral-treated DM	0.89 (0.69 - 1.17)	0.99 (0.77 - 1.30)	0.96 (0.73 - 1.28)
AAA	0.45 (0.35 - 0.59)*	0.50 (0.39 - 0.66)*	0.68 (0.51 - 0.91)*
Carotid	0.08 (0.06 - 0.12)*	0.08 (0.06 - 0.12)*	0.12 (0.07 - 0.17)*
Lower extremity bypass	0.29 (0.23 - 0.38)*	0.32 (0.25 - 0.42)*	0.42 (0.32 - 0.54)*
Age		1.05 (1.04 - 1.06)*	1.04 (1.03 - 1.06)*
Ventilation			6.94 (3.82 - 12.6)*
Creatinine level > 2.0			2.51 (1.88 - 3.38)*
CHF			1.96 (1.48 - 2.59)*
Steroid therapy			1.81 (1.16 - 2.81)*
Stroke with neuro deficit			1.59 (1.26 - 2.02)*
COPD			1.34 (1.07 - 1.67)*
Hypertension			0.71 (0.56 - 0.91)*

C-statistic = 0.80.

Variables not shown ($P > .10$): sex, black race, other race, smoking, stroke without neurologic deficit, hemoglobin A1c level, alcohol use; history of transient ischemic attack. Amputation was used as comparison procedure.

OR = 1.0.

* $P < .01$.

† $P < .05$.

AAA, Abdominal aortic aneurysm; *CHF*, congestive heart failure; *neuro deficit*, neurologic deficit; *COPD*, chronic obstructive pulmonary disease.

(OR, 1.44; $P = .02$). We then used this analysis to stratify the diabetic population. We considered patients with diabetes at high risk if they had any of the previous major independent risk factors. With this criterion, the patients with diabetes at high risk represent 44% of the entire

population. Among patients with non-insulin treated diabetes, only 39% of patients had preoperative risk factors for cardiovascular complications.

Finally, we examined the effect of DM on hospital resource use. In bivariate comparisons, patients with DM

Table V. Impact of diabetes on risk of nonfatal cardiovascular complications (stroke, myocardial infarction, need for cardiopulmonary resuscitation) after vascular surgical procedures

Risk factor	Cardiovascular complications (OR; 95% CI)		
	Adjusted for procedure type	Additionally adjusted for demographic factors	Additionally adjusted for comorbidities
Insulin-treated DM	1.65 (1.31 - 2.09)*	1.71 (1.34 - 2.16)*	1.48 (1.48 - 1.91)*
Oral-treated DM	1.24 (0.96 - 1.60)	1.21 (0.93 - 1.56)	1.22 (0.94 - 1.59)
AAA	1.29 (0.96 - 1.61)	1.47 (1.09 - 1.95)*	1.91 (1.41 - 2.58)*
Carotid	0.93 (0.72 - 1.20)	0.96 (0.74 - 1.23)	1.13 (0.85 - 1.52)
Lower extremity bypass	0.70 (0.53 - 0.93)†	0.77 (0.58 - 1.02)	0.92 (0.69 - 1.22)
Age		1.04 (1.03 - 1.05)*	1.04 (1.03 - 1.05)*
Race not white or black		1.56 (1.15 - 2.11)*	1.62 (1.19 - 2.20)*
CHF			2.31 (1.71 - 3.12)*
Creatinine level > 2.0			1.74 (1.26 - 2.39)*
Stroke with neuro deficit			1.63 (1.30 - 2.05)*

C-statistic = 0.68.

Variables not shown ($P > .10$): sex, black race, smoking, chronic obstructive pulmonary disease, without neurologic deficit, ventilation, history of transient ischemic attack, alcohol use, and dialysis. Amputation was used as comparison procedure.

OR = 1.0.

* $P < .01$.

† $P < .05$.

AAA, Abdominal aortic aneurysm; CHF, congestive heart failure; neuro deficit, neurologic deficit.

Table VI. Cardiovascular death and complications in patients with diabetes

Risk factor	Combined outcome	Death	Cardiovascular complications
Insulin-treated DM	1.09 (0.87 - 1.39)	1.16 (0.85 - 1.57)	1.28 (0.95 - 1.70)
AAA	1.10 (0.69 - 1.73)	0.89 (0.49 - 1.62)	1.78 (1.03 - 3.07)†
Carotid	0.61 (0.43 - 0.85)*	0.16 (0.08 - 0.30)*	1.52 (1.03 - 2.24)†
Lower extremity bypass	0.70 (0.53 - 0.92)†	0.53 (0.37 - 0.75)*	1.24 (0.88 - 1.76)
Age	1.04 (1.02 - 1.05)*	1.04 (1.02 - 1.05)*	1.04 (1.02 - 1.05)*
Ventilation	4.84 (2.10 - 11.1)*	6.40 (2.71 - 15.0)*	
Creatinine level > 2.0	2.17 (1.59 - 2.97)*	2.57 (1.77 - 3.74)*	1.95 (1.28 - 2.96)*
CHF	2.13 (1.58 - 2.88)*	2.21 (1.55 - 3.15)*	2.24 (1.51 - 3.23)*
Race not white or black			1.65 (1.09 - 2.50)†
Steroid therapy	1.87 (1.07 - 3.28)†	2.32 (1.22 - 4.41)*	
Stroke with neuro deficit	1.35 (1.04 - 1.77)†	1.38 (1.00 - 1.93)†	
Proteinuria		1.45 (1.06 - 1.97)†	
Hypertension	0.50 (0.38 - 0.68)*	0.45 (0.32 - 0.64)*	0.66 (0.44 - 1.00)*

Data shown as OR (95% CI).

Variables shown include insulin status, procedure adjustments, and all comorbid conditions with $P < .10$. Non-insulin dependent DM and amputation were used as comparison procedure.

OR = 1.0.

* $P < .01$.

† $P < .05$.

AAA, Abdominal aortic aneurysm; CHF, congestive heart failure; neuro deficit, neurologic deficit.

had significantly longer LOS. By procedure, patients with diabetes who underwent abdominal aortic aneurysm repair, carotid endarterectomy, and lower extremity bypass all had significantly longer LOS when compared with patients without diabetes (Table VII). In multivariate analysis controlling for demographic factors, comorbidities, and procedure type, diabetes needing insulin treatment increased LOS by 25% ($P < .001$) and diabetes controlled with oral agents increased LOS by 18% ($P < .001$), compared with patients without DM. In addition, longer ICU stays also

were with associated with diabetes needing insulin (9% increase; $P < .001$) and diabetes controlled with oral hypoglycemic agents (10% increase; $P = .01$; data not shown).

DISCUSSION

Examination of crude mortality rates, even after adjustment for basic demographic factors and procedure specific risks, suggests that patients with diabetes have a significantly higher rate of complication and death after certain

Table VII. Impact of diabetes on hospital LOS after major vascular surgery

	Diabetes	Nondiabetes	P value	Increase in LOS (%)*	
				Diabetes with insulin	Diabetes with Oral medications alone
All procedures	21 (11)	13 (7)	.001	25% ($P < .001$)	18% ($P < .001$)
Carotid endarterectomy	7 (3)	5 (2)	.001	17% ($P = .01$)	14% ($P = .03$)
AAA repair	16 (10)	14 (9)	.031	26% ($P = .01$)	10% ($P = .03$)
Lower extremity bypass	22 (13)	16 (8)	.001	38% ($P < .001$)	32% ($P < .001$)
Amputation	33 (20)	34 (16)	.82	18% ($P < .001$)	6% ($P = .22$)

Data shown are mean (median) expressed as days.

*Controlling for demographic characteristics, cardiovascular comorbidities, and chronic renal insufficiency.

AAA, Abdominal aortic aneurysm.

vascular surgery procedures. However, most of this incremental risk reflects the higher levels of specific comorbidities commonly found in patients with diabetes that can be easily identified before surgery. Patients with diabetes were significantly more likely to have congestive heart failure, renal insufficiency, renal failure needing dialysis, and proteinuria, and each of these were found to be a risk factor for poor surgical outcome. After controlling for these comorbidities, neither insulin-treated nor oral medication-treated DM appeared to increase the risk of postoperative death. Complications of DM, including renal insufficiency and proteinuria, were strong predictors of perioperative death. In contrast, DM did appear to be a moderate independent risk factor for nonfatal cardiovascular complications, but this increased risk was confined to patients with diabetes with insulin treatment. Among patients with diabetes with insulin treatment, the odds of development of a nonfatal cardiovascular complication were almost 50% higher than that of patients without diabetes independent of other risk factors. Of note, both patients with insulin-treated and oral agent-treated diabetes had prolonged LOS when compared with patients without diabetes independent of other risk factors.

The finding that DM is not a significant independent risk factor for perioperative death but is an independent predictor of postoperative complications may, in part, explain previous conflicting reports. Although some investigations of carotid endarterectomy^{3,4} lower extremity bypass,¹⁴ and aortic aneurysm surgery⁷ suggest that diabetes does not convey an increased risk of death, other analyses do show higher levels of postoperative complications.^{1,6} To date, no previous investigation has considered the impact of diabetes severity, and analysis of comorbidities and complications has been limited. The need for insulin in type 2 DM, renal insufficiency, or proteinuria (even in the absence of an elevated creatinine level) conveys significantly elevated risks and could be used to identify patients with diabetes at high risk. Other markers of diabetes severity, including glycosylated hemoglobin level, do not convey increased postoperative risk, even at the highest levels.

Although DM does not appear to independently impact postoperative mortality rates, the significant risk of long-term cardiac morbidity caused by DM could poten-

tially be used to justify a more aggressive preoperative evaluation in this setting. In a previous study, DM was found to significantly increase the odds of death at 4 years (OR, 1.8; $P = .03$).¹⁴ DM also has been found to be one of two preoperative risk factors that strongly correlated with late postoperative cardiac events among patients for vascular surgery followed for 2 years ($P < .001$).¹⁵ Although this analysis suggests the diagnosis of diabetes does not a priori raise the risk of vascular surgery, this finding should not decrease physician vigilance in the medical or surgical management of coronary artery disease and hypertension in these patients.¹⁶

Even with controlling for other cardiovascular risk factors, patients with diabetes appear to have longer LOS for each of the surgical procedures examined. In previous investigations, diabetes increased the LOS among patients who underwent carotid endarterectomy (6.1 versus 4.8 days; $P = .01$).⁴ The increased LOS reported in this study may reflect the increased complexity of caring for patients with diabetes (eg, the higher risk of wound complications, metabolic derangements, and the complexity of medication management). Given that increased LOS is a marker for higher resource use, reimbursement for care of patients with diabetes who undergo vascular procedures should probably reflect the increased costs associated with their care, even in the absence of greater risk of postoperative death.

This investigation is limited by several factors. First, because this analysis used cohort data, it is possible that mainly patients with diabetes at lower risk underwent operations. However, given the high incidence rate of other comorbid diseases found in this population, including end stage renal disease needing dialysis and congestive heart failure, it appears unlikely that surgeons were routinely selecting only healthy patients with diabetes. Second, no electrocardiographic data were available; therefore, it was not possible to adjust the analyses for other recognized risk factors, including symptomatic ventricular arrhythmias, rapid supraventricular arrhythmias, high-grade atrial ventricular venous block, preexisting q waves, or evidence of left ventricular hypertrophy.² However, these factors would most likely bias the results toward the null hypothesis and are unlikely to increase the independent impact of

diabetes on cardiac death. The potential exists that this information could diminish the odds of perioperative cardiovascular complications among patients with DM who undergo insulin treatment. Third, the patients considered in this VA investigation were primarily male, thus limiting the generalization of these findings to female and nonveteran patients.

In summary, although patients with DM do appear to be at increased risk after vascular surgery, this risk is principally a reflection of the higher incidence rate of comorbid disease in patients with diabetes, particularly congestive heart failure and chronic renal insufficiency. Cardiovascular complications are higher in the subgroup of patients with diabetes who are undergoing insulin treatment, have significant proteinuria, or have renal insufficiency. Consideration of special testing to assess perioperative risk should be targeted to these patients with diabetes at high risk, who comprised about 40% of patients with diabetes in this study, rather than applied generally to all patients with DM.

REFERENCES

1. Eagle KA, Coley CM, Newell JB, Brewster DC, Darling RC, Strauss HW, et al. Combining clinical and thallium data optimizes preoperative assessment of cardiac risk before major vascular surgery. *Ann Intern Med* 1989;110:859-66.
2. Eagle KA, Brundage BH, Chaitman BR, Ewy GA, Fleisher LA, Hertzler NR, et al. Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol* 1996;27:910-48.
3. Ballotta E, Da Giau G, Renon L. Is diabetes mellitus a risk factor for carotid endarterectomy? A prospective study. *Surgery* 2001;129:146-52.
4. Akbari CM, LoGerfo FW. Diabetes and peripheral vascular disease. *J Vasc Surg* 1999;30:373-84.
5. Berry AJ, Smith RB III, Weintraub WS, Chaikof EL, Dodson TF, Lumsden AB, et al. Age versus comorbidities as risk factors for complications after elective abdominal aortic reconstructive surgery. *J Vasc Surg* 2001;33:345-52.
6. Treiman GS, Treiman RL, Foran RF, Cossman DV, Cohen JL, Levin PM, et al. The influence of diabetes mellitus on the risk of abdominal aortic surgery. *Am Surg* 1994;60:436-40.
7. Dardik A, Lin JW, Gordon TA, Williams GM, Perler BA. Results of elective abdominal aortic aneurysm repair in the 1990s: a population-based analysis of 2335 cases. *J Vasc Surg* 1999;30:985-95.
8. Brooks MM, Jones RH, Bach RG, Chaitman BR, Kern MJ, Orszulak TA, et al. Predictors of mortality and mortality from cardiac causes in the bypass angioplasty revascularization investigation (BARI) randomized trial and registry. For the BARI Investigators. *Circulation* 2000;101:2682-9.
9. Khuri SF, Daley J, Henderson W, Hur K, Gibbs JO, Barbour G, et al. Risk adjustment of the postoperative mortality rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *J Am Coll Surg* 1997;185:315-27.
10. Daley J, Khuri SF, Henderson W, Hur K, Gibbs JO, Barbour G, et al. Risk adjustment of the postoperative morbidity rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *J Am Coll Surg* 1997;185:328-40.
11. Krein SL, Hayward RA, Pogach L, BootsMiller BJ. Department of Veterans Affairs' Quality Enhancement Research Initiative for Diabetes Mellitus. *Med Care* 2000;38:138-48.
12. Khuri SF, Daley J, Henderson W, Barbour G, Lowry P, Irvin G, et al. The National Veterans Administration Surgical Risk Study: risk adjustment for the comparative assessment of the quality of surgical care. *J Am Coll Surg* 1995;180:519-31.
13. Lemeshow S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression models. *Am J Epidemiol* 1982;115:92-106.
14. L'Italien GJ, Cambria RP, Cutler BS, Leppo JA, Paul SD, Brewster DC, et al. Comparative early and late cardiac morbidity among patients requiring different vascular surgery procedures. *J Vasc Surg* 1995;21:935-44.
15. Krupski WC, Layug EL, Reilly LM, Rapp JH, Mangano DT. Comparison of cardiac morbidity between aortic and infrainguinal operations. Study of Perioperative Ischemia (SPI) Research Group. *J Vasc Surg* 1992;15:354-65.
16. Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. *JAMA* 1996;276:1886-92.

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