

Peripheral Vascular Disease and Outcomes Following Coronary Artery Bypass Graft Surgery

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Hypothesis: There is an increased operative risk in patients with a history of peripheral vascular disease (PVD) who undergo coronary artery bypass grafting (CABG). There are also outcome differences associated with these patients.

Design: A study from a 10-year hospitalization cohort with prospective data collection.

Setting: Multiple hospitals in the Greater Cincinnati area with 1 surgical group of cardiac surgeons.

Participants: Cases were CABG patients with PVD, which was defined as having a history of type 1 neurological injury, prior vascular surgery, or current vascular disease (n=1561). Controls were CABG patients without PVD (n=6328).

Interventions: The study examined 42 potential confounding risk factors and 16 outcome variables.

Results: Twenty-nine potential risk factors were found to be significantly different between CABG patients with and without PVD. Twenty-six confounding risk factors were correlated with 3 factors. Logistic regression analysis showed that even after controlling for sex, significant associative disorders, and other procedures, CABG patients with PVD still experienced more arrhythmias requiring treatment (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.03-1.33; $P=.01$), neurological complications (OR, 1.7; 95% CI, 1.43-2.07; $P<.001$), pulmonary complications (OR, 1.4; 95% CI, 1.23-1.62; $P<.001$), low output (OR, 1.3; 95% CI, 1.09-1.45; $P=.001$), and intraoperative complications (OR, 1.39; 95% CI, 1.06-1.83; $P=.02$).

Conclusions: Patients with a PVD history undergoing CABG had more coexistent risk factors. These patients also exhibited higher rates of cardiac, systemic, renal, neurological, and pulmonary complications.

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IT HAS BEEN WELL DOCUMENTED that a patient with known peripheral vascular disease (PVD) will face substantially increased mortality rates when compared with an individual with nonperipheral vascular disease. To this effect, Criqui et al¹ reported a 3-fold increase in annual mortality rates in patients with the presence of

See Invited Critique at end of article

large-vessel peripheral arterial disease. Because the majority of these documented cases had coronary artery disease and cardiovascular death, many authors have suggested "aggressive" treatment of coronary disease in this patient population, up to and including myocardial revascularization with coronary artery bypass grafting (CABG). Although this suggestion may seem relatively straightforward, there has been little effort to

evaluate the operative risks that present themselves to both these patients and their surgeons. These complications may present both intraoperatively as well as postoperatively when procedures such as CABG are undertaken on a patient with known PVD.

It is crucial to understand the potential short- and long-term complications that may arise in patients with PVD undergoing CABG. Although the association between PVD and increased mortality rates in CABG patients has been generally accepted, there have been no large studies to specifically address this issue. Our study reviewed a cohort of nearly 8000 patients who underwent CABG performed by 1 surgical group.

METHODS

We conducted a cohort study from a 10-year hospitalization cohort (N=11 398) with pro-

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spective data collection. Nurses, physicians, and perfusionists collected data on 225 variables during admission. Data were grouped into sections by demographic, medical history, post-operative, perfusion, and procedure. Using a series of cross-checking questions, 2 individuals audited all data forms for completeness and consistency. To further ensure accuracy and consistency, a physician audited a random 10% of patient forms. Data were then entered into an interactive multi-institutional database (Patient Analysis and Tracking System; Axis Clinical Systems, Portland, Ore).

Included in the study were patients aged 18 years and older undergoing CABG surgery between March 1997 and July 2003 (n=7889). Patients who underwent any surgery other than CABG were excluded. Patients with PVD who underwent CABG had a history of type 1 neurological injury (transient ischemic attack within 3 months or stroke within 3 months), prior vascular surgery, or current vascular disease (n=1561). Peripheral vascular disease classification included patients who had a prior vascular surgery and/or current vascular disease, including carotid, vertebral, innominate, subclavian, thoracic aorta, abdominal aorta, visceral/renal, upper extremity, and lower extremity. There were 6328 CABG patients without PVD.

The study examined 42 potential confounding risk factors and 16 outcome variables. The continuous potential confounding risk factors included age, body surface area, total number of grafts, number of veins, number of left internal mammary artery grafts, number of other arterial grafts, creatinine level, pump time, and cross-clamp time. The dichotomous potential confounding risk factors included the following: sex, race, significant medical disorders, chronic obstructive pulmonary disorder, diabetes, hypertension, history of tobacco use, family history of coronary artery disease, history of neurological disorder, hypercholesteremia, obesity, off-pump CABG, coronary sinus cardioplegia site, surgery for angina or myocardial infarction, surgery for congestive heart failure, surgery for arrhythmia, surgery for coronary anatomy, urgent surgical procedure, hemodynamic status, New York Heart Association functional class, left main greater than 50% cardiac pathologic abnormality, 3-vessel cardiac pathologic abnormality, 2-vessel cardiac pathologic abnormality, 1-vessel cardiac pathologic abnormality, aortic disease, other procedures, left ventricular hypertrophy, left ventricular ejection fraction estimate, ascending aorta proximal site, vein from vein proximal site, internal mammary artery from internal mammary artery proximal site, radial from internal mammary artery proximal site, and coronary quality. **Table 1** lists the definitions for the potential confounding risk factors.

The 16 outcome variables were hours receiving ventilatory support, intensive care unit (ICU) length of stay, total length of hospitalization, arrhythmias requiring treatment, positive cultures, renal complications, sternal wound complications, neurological complications, pulmonary complications, gastrointestinal complications, low output, intra-aortic balloon pump, return to ICU, pulmonary hypertension, intraoperative complications, and mortality. **Table 2** lists the definitions for each of the outcome variables.

To generate the unadjusted risks of each potential confounding risk factor, we performed χ^2 and *t* tests comparing men and women with each of the 42 variables. Correlation coefficients were computed among the significant confounding risk factors. We conducted χ^2 and *t* tests comparing men and women with each of the 16 outcomes. Logistic regression analysis was then used to investigate the adjusted risk between cases and controls with each of the significant outcome variables while controlling for the significant risk factors. We used SPSS statistical software (SPSS Inc, Chicago, Ill) to perform the analyses.

Univariate analysis on potential confounding risk factors revealed 29 significant risk factors (**Table 3**). Patients with PVD who underwent CABG were older ($P<.001$), had a higher creatinine level ($P<.001$) and a lower body surface area ($P<.001$), and required more vein grafts ($P<.001$). Patients with PVD who underwent CABG received fewer left internal mammary grafts ($P<.001$) and fewer other arterial grafts ($P<.001$). There were significantly more women than men undergoing CABG with PVD ($P<.001$). Patients with PVD who underwent CABG had more significant medical disorders ($P<.001$), chronic obstructive pulmonary disorder ($P<.001$), diabetes ($P<.001$), hypertension ($P<.001$), history of tobacco use ($P<.001$), history of neurological disorders ($P=.01$), and obesity ($P=.001$). Patients with PVD who underwent CABG tended to undergo surgery more frequently for congestive heart failure ($P<.001$), coronary anatomy ($P=.03$), left main greater than 50% cardiac pathologic abnormality ($P=.01$), 1-vessel cardiac pathologic abnormality ($P=.02$), aortic disease ($P<.001$), and other procedures ($P<.001$). These patients also were more likely to have abnormal left ventricular hypertrophy ($P<.001$), left ventricular ejection fraction of 39% or less ($P<.001$), and ascending aorta proximal site ($P=.03$). Patients with PVD who underwent CABG had less family history of coronary artery disease ($P<.001$), lower use of retrograde cardioplegia ($P=.05$), and lower New York Heart Association functional class ($P=.01$). They were less likely to have had surgery for angina or myocardial infarction ($P=.001$) and 2-vessel cardiac pathologic abnormality ($P=.005$). Patients with PVD who underwent CABG had fewer urgent surgical procedures ($P<.001$) than CABG patients without PVD. There was no significant difference between CABG patients with and without PVD for the remaining 13 potential confounding risk factors.

Correlation coefficients were calculated for the 29 significant confounding risk factors. Twenty of the risk factors were significantly correlated with sex. These factors include chronic obstructive pulmonary disorder, diabetes, hypertension, history of tobacco use, family history of coronary artery disease, obesity, coronary sinus cardioplegia site, surgery for congestive heart failure, surgery for coronary anatomy, urgent surgical procedure, New York Heart Association functional class, 3-vessel cardiac pathologic abnormality, 1-vessel cardiac pathologic abnormality, aortic disease, left ventricular hypertrophy, left ventricular ejection fraction estimate, number of left internal mammary artery grafts, number of other arterial grafts, age, and body surface area. Five of the remaining 9 factors significantly correlated with significant associative disorders, including history of neurological disorders, surgery for angina or myocardial infarction, left main greater than 50% cardiac pathologic abnormality, number of vein grafts, and creatinine level. Ascending aorta proximal site significantly correlated with other procedures. The correlation resulted in 3 confounding risk factors: sex, significant associative disorders, and other procedures.

There was a significant difference between CABG patients with and without PVD on 13 outcome variables (**Table 4**). Patients with PVD who underwent CABG had

Table 1. Potential Confounding Risk Factors

Variable	Definition
Race	White, other
Sex	Male, female
Significant medical disorder	No, yes (dialysis, gout, long-term steroid use, psychological history, cancer, chronic atrial fibrillation, intermittent atrial fibrillation, ventricular tachycardia/ventricular fibrillation, prior mediastinal radiation)
Chronic obstructive pulmonary disorder	No, yes (mild: no medication; moderate: symptoms on exertion; severe: symptoms at rest)
Diabetes	No, yes
Hypertension	No, yes (diastolic blood pressure >90 mm Hg)
History of tobacco use	No, yes
Family history of coronary artery disease	No, yes
History of neurological disorders	No, yes (seizure, encephalopathy or dementia, neuromuscular symptom, tumor, intracranial hemorrhage, aneurysm, other)
Hypercholesterolemia	No, yes (≥ 200 mg/dL [≥ 5.17 mmol/L], medication)
Obesity	No, yes (>1.5 times ideal weight)
Off-pump CABG surgery	No, yes (off-pump)
Coronary sinus cardioplegia site	No, yes
Surgery	
Angina or myocardial infarction	No, yes (angina or myocardial infarction was reason for surgery)
Congestive heart failure	No, yes (congestive heart failure was reason for surgery)
Arrhythmia	No, yes (arrhythmia was reason for surgery)
Anatomy	No, yes (anatomy was reason for surgery)
Urgency of procedure	Elective, nonelective (urgent, emergent, desperate)
Unstable hemodynamic status	No, yes (stable on IV medications, unstable on IV medications, cardiogenic shock on medications/intra-aortic balloon pump)
NYHA functional class	I, II, III, IV
Cardiac pathologic abnormality	
Left main >50%	No, yes
3 Vessels	No, yes
2 Vessels	No, yes
1 Vessel	No, yes
Aortic disease	No, yes (atherosclerotic, dilated, dissection, calcified, severe, thin, soft, aneurysm, thick wall, old graft, aneurysmal origin of graft)
Other procedures	No, yes (laser, balloon dilation, angioplasty, coronary echo, epicardial color flow, transesophageal color flow, thoracoscopy, aortic echo, carotid endarterectomy, aorto-innominate bypass, lung resection/biopsy, dorsal sympathectomy, thoracotomy incision, abdominal incision, no pump, endoscopic vein harvest)
Abnormal left ventricular hypertrophy	Normal, abnormal (mild, moderate, or severe)
Left ventricular ejection fraction	No, yes (39 or less)
Proximal site	
Ascending aorta	No, yes
Vein from vein	No, yes
Internal mammary artery from vein	No, yes
Radial from internal mammary	No, yes
Coronary quality	Normal, abnormal (thick wall, calcified, diffuse disease distal, clot, endarterectomy required, dissection)
Age	Years
Creatinine level	Milligrams per deciliter (micromoles per liter)
Pump time	Minutes
Cross-clamp time	Minutes
Body surface area	Square meters
Grafts	Total number
Vein graft	Number
Left internal mammary artery graft	Number
Other arterial graft	Number

Abbreviations: CABG, coronary artery bypass grafting; IV, intravenous; NYHA, New York Heart Association.

a longer ICU length of stay ($P=.001$) and a longer total length of hospitalization ($P<.001$). Patients with PVD who underwent CABG experienced more arrhythmias (odds ratio [OR], 1.5; 95% confidence interval [CI], 1.3-1.6; $P<.001$), positive cultures for organisms (OR, 1.7; 95% CI, 1.2-2.6; $P=.005$), renal complications (OR, 2.1; 95% CI, 1.6-2.6; $P<.001$), neurological complications (OR, 2.3; 95% CI, 1.9-2.7; $P<.001$), pulmonary complications (OR, 1.7; 95% CI, 1.5-1.9; $P<.001$), gastrointestinal tract complications (OR, 1.7; 95% CI, 1.1-2.6; $P=.02$), low output (OR,

1.6; 95% CI, 1.4-1.8; $P<.001$), return to ICU (OR, 1.6; 95% CI, 1.1-2.3; $P=.007$), pulmonary hypertension (OR, 1.5; 95% CI, 1.1-2.0; $P<.001$), intraoperative complications (OR, 1.6; 95% CI, 1.3-2.1; $P<.001$), and mortality (OR, 2.1; 95% CI, 1.5-2.8; $P<.001$). There was no significant difference between CABG patients with and without PVD for the remaining 3 outcomes.

Logistic regression analysis showed that even after controlling for sex, significant associative disorders, and other procedures, CABG patients with PVD still experience more

Table 2. Outcome Variables

Hospital Outcome	Definition
Arrhythmias requiring treatment	No, yes (premature ventricular contraction/ventricular tachycardia, atrial fibrillation/atrial flutter, required defibrillation, cardioverted, pacer required/bradycardia, atrial-ventricular disassociation)
Positive cultures for organisms	No, yes (blood, urine, venous lines, arterial)
Renal complications	No, yes (mild: double the preoperative creatinine level; moderate: creatinine level >4.0 mg/dL [353.6 μmol/L]; severe: requiring dialysis)
Sternal wound infections	No, yes (any sternal wound infection, including dehiscence or ones requiring surgery)
Neurological complications	No, yes (any neurological complication, including mental status change, stroke, peripheral nerve, seizure, transient ischemic attack); type 1 stroke: mild hemispheric, severe hemispheric, severe other (brain stem); type 2 stroke: mild mental status, severe mental status, confusion only
Pulmonary complications	No, yes (any pulmonary complication with the exception of mild atelectasis)
Gastrointestinal complications	No, yes (any including severe gastrointestinal bleeding, perforated ulcer, cholecystitis, hepatitis, pancreatitis, bowel obstruction, ileus, ischemic bowel)
Low output	No, yes (mild: dopamine ≤2 μg/kg per minute; moderate: pressures 1 time; severe: pressures ≥2 times; IABP and pressures; IABP and pressures 2 times)
Intra-aortic balloon pump	No, yes (before catheterization, before surgery, at surgery, postoperatively in ICU, attempted/failed)
Return to ICU	No, yes
Pulmonary hypertension	No, yes (pulmonary pressure ≥60 mm Hg)
Intraoperative complications	No, yes (dissection, hemorrhage, prebypass arrhythmia, cardiac laceration, cardiac dilation, air embolism, myocardial infarction, aorta tear, postbypass arrest, valve trauma, postbypass arrhythmia, internal mammary artery/radial/other harvest not satisfactory, redo valve prosthesis, protamine reaction, cut patient CABG, additional incision required)
Mortality	No, yes
Ventilator time in operating room	Hours receiving ventilatory support
Length of stay in ICU	Time in hours of stay
Total hospital length of stay	Duration in days from operation to discharge stay

Abbreviations: CABG, coronary artery bypass grafting; IABP, intra-aortic balloon pump; ICU, intensive care unit; NYHA, New York Heart Association.

negative outcomes. Patients with PVD who underwent CABG had more arrhythmias requiring treatment (OR, 1.7; 95% CI, 1.03-1.33; $P=.01$), neurological complications (OR, 1.7; 95% CI, 1.43-2.07; $P<.001$), and pulmonary complications (OR, 1.4; 95% CI, 1.23-1.62; $P<.001$). They also experienced low output (OR, 1.3; 95% CI, 1.09-1.45; $P=.001$) and more intraoperative complications (OR, 1.39; 95% CI, 1.06-1.83; $P=.02$). There was a significant difference between CABG patients with and without PVD on total hospital stay (OR, 0.96; 95% CI, 0.94-0.97; $P<.001$) and ICU length of stay (OR, 1.002; 95%

Table 3. Univariate Analysis of 29 Significant Confounding Risk Factors

Control	PVD	No PVD	P Value
Female sex, No. (%)	554/1561 (36)	1876/6328 (30)	<.001
Significant associate disorders, No. (%)	448/1560 (29)	1309/6316 (21)	<.001
Chronic obstructive pulmonary disorder, No. (%)	405/1560 (26)	889/6317 (14)	<.001
Diabetes, No. (%)	617/1560 (40)	1930/6318 (31)	<.001
Hypertension, No. (%)	1151/1558 (74)	4110/6318 (65)	<.001
History of tobacco use, No. (%)	988/1385 (71)	3269/5488 (60)	<.001
Family history of coronary artery disease, No. (%)	871/1420 (63)	3857/5759 (67)	<.001
History of neurological disorders, No. (%)	49/1558 (5)	232/6309 (4)	.01
Obesity, No. (%)	263/1551 (17)	1307/6302 (21)	.001
Coronary sinus cardioplegia site, No. (%)	413/1445 (29)	1810/5790 (31)	.05
Surgery, No. (%)			
Angina or myocardial infarction	1368/1511 (91)	5655/6071 (93)	.001
Congestive heart failure	107/1511 (7)	277/6071 (5)	<.001
Anatomy	91/1511 (6)	282/6071 (5)	.03
Urgent surgical procedure, No. (%)	366/1512 (24)	1856/6075 (31)	<.001
Cardiac pathologic abnormality, No. (%)			
Left main >50%	172/1510 (11)	558/6067 (9)	.01
2 Vessels	176/1510 (12)	876/6067 (14)	.005
1 Vessel	55/1510 (4)	309/6067 (5)	.02
Aortic disease, No. (%)	489/1500 (33)	1156/6028 (19)	<.001
Other procedures, No. (%)	319/1506 (21)	990/6057 (16)	<.001
Abnormal left ventricular hypertrophy, No. (%)	877/1491 (59)	3220/6025 (54)	<.001
Left ventricular ejection fraction of ≤39, No. (%)	367/1490 (25)	1185/6000 (20)	<.001
Proximal site ascending aorta, No. (%)	878/1507 (58)	3337/6062 (55)	.03
NYHA functional class, %			
I	13	15	.01
II	26	25	
III	36	79	
IV	18	28	
Age, mean ± SD, y	68.5 ± 9.3	63.7 ± 10.9	<.001
Body surface area, mean ± SD, m ²	1.9 ± 0.2	2.0 ± 0.2	<.001
Creatinine level, mean ± SD, mg/dL	1.4 ± 1.3	1.1 ± 2.5	<.001
Vein graft, mean ± SD, No.	1.9 ± 1.3	1.7 ± 1.3	<.001
Left internal mammary artery graft, mean ± SD, No.	0.9 ± 0.6	1.0 ± 0.6	<.001
Other arterial graft, mean ± SD, No.	0.4 ± 0.8	0.5 ± 0.9	<.001

Abbreviations: ICU, intensive care unit; NYHA, New York Heart Association; PVD, peripheral vascular disease.

SI conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

CI, 1.001-1.003; $P<.001$). After controlling for risk factors, there was no significant difference between CABG patients with and without PVD for mortality, intraoperative complications, pulmonary hypertension, gastrointestinal tract complications, renal complications, positive cultures for organisms, or return to ICU.

Table 4. Univariate Analysis of 13 Significant Hospitalization Outcome Variables

Outcome	PVD	No PVD	P Value
Arrhythmias requiring treatment, No. (%)	736/1559 (47)	2351/6308 (37)	<.001
Positive cultures for organisms, No. (%)	34/1543 (2)	79/6269 (1)	.005
Renal complications, No. (%)	116/1557 (8)	232/6311 (4)	<.001
Neurological complications, No. (%)	276/1560 (18)	536/6312 (9)	<.001
Pulmonary complications, No. (%)	569/1560 (37)	1555/6313 (25)	<.001
Gastrointestinal tract complications, No. (%)	29/1559 (2)	69/6308 (1)	.02
Low output, No. (%)	1082/1555 (70)	3674/6303 (58)	<.001
Return to the ICU, No. (%)	43/1557 (3)	108/6307 (2)	.007
Pulmonary hypertension, No. (%)	70/1499 (5)	182/6029 (3)	.001
Intraoperative complications, No. (%)	89/1509 (6)	216/6068 (4)	<.001
Mortality, No. (%)	61/1559 (4)	120/6327 (2)	<.001
Length of hospitalization, mean \pm SD, d	8.9 \pm 8.7	7.2 \pm 5.2	<.001
Length of stay in ICU, mean \pm SD, h	57.7 \pm 137.8	42.2 \pm 82.6	.001

Abbreviations: ICU, intensive care unit; PVD, peripheral vascular disease.

COMMENT

The presence of PVD plays a significant role in the potential morbidity and mortality of patients undergoing CABG. In this study of nearly 8000 patients who underwent CABG, patients with PVD fared significantly worse on 13 of the 16 outcomes examined. Even after controlling for significant risk factors, CABG patients with a PVD history were more likely to experience complications.

Of note, there are 2 previous studies by Birkmeyer et al^{2,3} that obtained similar findings to our own. The first of these studies found that CABG patients with a PVD history had a nearly 20% five-year mortality while the same risk was roughly 8% for those without known PVD. Even after adjusting for confounding variables such as age and more advanced cardiac disease, it was still noted that patients with a history of PVD had a mortality rate nearly 2 times as high as those without.⁴ These findings hinged on data from an earlier study conducted by several of the same authors, which again found, after adjusting for confounding variables, that CABG patients with PVD showed a 71% increase in in-hospital mortality rate over that of those without. This study was undertaken with a cohort of little more than 3000 patients and found that in-hospital mortality rates with CABG were 2.4-fold higher in those with indicators of PVD vs those without.⁵ It is important to note that this study was composed of data from 5 separate tertiary care centers. Although these studies support our findings, they were each based on a cohort of approximately a quarter the size of our own study population. Potentially, patients with PVD may have an increased morbidity and mortality secondary to noncardiac issues

such as strokes or macrovascular occlusions such as mesenteric ischemia.

There are several potential limitations to this study. One possible limitation is the actual classification of patients into the PVD group, defined as having history of type 1 neurological injury (transient ischemic attack within 3 months or stroke within 3 months), prior vascular surgery, or current vascular disease. Peripheral vascular disease included patients with prior vascular surgery or current vascular disease for carotid, vertebral, innominate, subclavian, thoracic aorta, abdominal aorta, visceral/renal, upper extremity, or lower extremity. Some previous studies have included more than a dozen possible categories for PVD patients while others have included only 3 or 4 clinical or historical factors to describe the PVD category. These variances on what actually categorizes a patient as having a PVD history can serve to either overquantify or underquantify the number of PVD patients incorporated into the respective study. By keeping our requirements for PVD labeling relatively specific and obvious, if anything, we may have underspecified the number of PVD patients in our cohort.

Although a link between PVD and CABG complications had already been established, this study has aided in the further qualification of this association. This information could further prepare those who are trusted with the care of these patients to not only better treat but also better anticipate and possibly even prevent these potential complications.

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