Coronary artery bypass grafting in diabetics: A growing health care cost crisis

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ABSTRACT

Objectives: To determine 4-decade temporal trends in the prevalence of diabetes and cardiovascular risk factors among patients undergoing coronary artery bypass grafting (CABG) and to compare in-hospital outcomes, resource utilization, and long-term survival after CABG in diabetics versus nondiabetics.

Methods: From January 1972 to January 2011, 10,362 pharmacologically treated diabetics and 45,139 nondiabetics underwent first-time CABG. Median follow-up was 12 years. Direct technical cost data were available from 2003 onward ($n = 4679$). Propensity matching by diabetes status was used for outcome comparisons. Endpoints were in-hospital adverse events, resource utilization, and long-term survival.

Results: Diabetics undergoing CABG increased from 7% in the 1970s to 37% in the 2000s. Their outcomes were worse, with more ($P < .05$) in-hospital deaths (2.0% vs 1.3%), deep sternal wound infections (2.3% vs 1.2%), strokes (2.2% vs 1.4%), renal failure (4.0% vs 1.3%), and prolonged postoperative hospital stay (9.6% vs 6.0%); and their hospital costs were 9% greater (95% confidence interval 7%-11%). Survival after CABG among diabetics versus nondiabetics at 1, 5, 10, and 20 years was also worse: 94% versus 94%, 80% versus 84%, 56% versus 66%, and 20% versus 32%, respectively. Propensity-matched patients incurred similar costs, but the prevalence of postoperative deep sternal wound infections and stroke, as well as long-term survival, remained worse in diabetics.

Conclusions: Diabetes is both a marker for high-risk, resource-intensive, and expensive care after CABG and an independent risk factor for reduced long-term survival. These issues, coupled with the increasing proportion of patients needing CABG who have diabetes, are a growing challenge in reining in health care costs. (J Thorac Cardiovasc Surg 2015;150:304-12)

Four-decade trend in prevalence of diabetes among patients undergoing primary isolated coronary artery bypass grafting. Each circle represents a yearly percentage, and the solid line is the locally estimated scatterplot smoother (loess) estimate.

Central Message

Increasingly, patients needing CABG have diabetes, a marker for high-risk, resource-intensive, expensive care after CABG, and an independent risk factor for reduced long-term survival, creating a growing challenge to health care cost reduction.

Perspective

The proportion of patients needing CABG who have diabetes has increased to nearly 40% of all patients undergoing CABG at our institution. The procedure is more resource intensive and expensive for diabetics than for nondiabetics, partly because of postoperative complications. However, when surgeons present the risks and benefits of CABG to diabetic patients, they should explain that CABG offers the best chance for long-term survival.

See Editorial Commentary page 313.

See Editorial page 284.

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Diabetes is an emerging worldwide epidemic that affects 382 million people,¹ including 25.8 million in the United States alone.² In 2013, global health expenditures resulting from diabetes were estimated at \$548 billion and are expected to exceed \$627 billion by 2035.¹ In the United States, the total economic burden of diabetes was \$245 billion in 2012.³ Because coronary artery disease is

Abbreviation and Acronym

CABG = coronary artery bypass grafting

common in diabetics,⁴ it is an important driver of diabetes-related health care cost.³

As the prevalence of diabetes has risen, cardiovascular disease associated with it has increased as well.⁵ Today, diabetics represent an important subset of patients undergoing coronary artery bypass grafting (CABG), an expensive procedure. Therefore, we sought to determine 4-decade temporal trends in the prevalence of diabetes and cardiovascular risk factors for patients undergoing CABG, compare overall in-hospital adverse outcomes, hospital resource utilization and costs, and long-term survival after CABG in diabetics versus nondiabetics, then compare these same factors in diabetics versus nondiabetics who have similar high-risk profiles using propensity matching.

METHODS

Patients

From January 1, 1972, to January 1, 2011, 57,278 patients underwent first-time isolated CABG at Cleveland Clinic. Data on the presence or absence of pharmacologically treated diabetes mellitus (insulin or oral hypoglycemic agent) were available for 55,501 (97%) of these patients: 45,139 nondiabetics and 10,362 diabetics.

Patients were identified, and preoperative, operative, and postoperative variables (Appendix E1) were retrieved from the prospective Cleveland Clinic Cardiovascular Information Registry. This database is populated concurrently with patient care and has been approved for use in research by the institutional review board, with the requirement for patient consent waived.

Variables and Definitions

A coronary artery system was considered meaningfully stenotic if it contained a $\geq 50\%$ -diameter obstruction. Incomplete revascularization was defined as failure to graft any coronary system containing $\geq 50\%$ stenosis, or both left anterior descending and circumflex coronary systems for $\geq 50\%$ left main trunk stenosis. Left ventricular function was echocardiographically graded as normal (ejection fraction $\geq 60\%$), mild dysfunction (ejection fraction 40%-59%), moderate dysfunction (ejection fraction 25%-39%), or severe dysfunction (ejection fraction $< 25\%$).

Endpoints

Endpoints were: (1) in-hospital adverse outcomes defined as in the Society of Thoracic Surgeons national database (www.ctsnet.org/file/rptDataSpecifications252_1_ForVendorsPGS.pdf); (2) in-hospital direct technical costs (the sum of direct preoperative, operative, and postoperative costs), both total and broken down according to resource utilization areas; and (3) time-related mortality. Actual direct technical cost data (not charge data), exclusive of physician professional salaries, were obtained from Decision Support Services of Cleveland Clinic. Data were available for patients from only 2003 onward ($n = 4679$: 1776 diabetics and 2903 nondiabetics). Costs were corrected to constant 2011 dollars.⁶ Indirect costs, including institutional costs and capital equipment costs used for all operations, could not be estimated on a per patient basis and are not included, but they were assumed to be distributed uniformly across groups.

Vital status after hospital discharge was obtained by routine anniversary follow-up questionnaires supplemented with data from the Social Security Death Master File,⁷ accessed on October 27, 2011, with a closing date of

April 27, 2011. A total of 714,709 patient-years of follow-up data were available for analyses. Median follow-up was 11.8 years, with 25% of survivors followed for > 21 years, and 10% for > 30 years.

For diabetic patients, 86,153 patient-years of follow-up data were available for analyses, with a median follow-up period of 7.5 years; 25% of survivors were followed for > 12 years, and 10% for > 18 years. For nondiabetic patients, 628,556 patient-years of follow-up data were available for analyses, with a median follow-up period of 13 years; 25% of survivors were followed for > 24 years, and 10% for > 31 years.

Statistical Analysis

Temporal trends. Four-decade temporal trends in the prevalence of diabetes and cardiovascular risk factors among patients undergoing CABG were assessed using plots of yearly percentages or averages over time. A nonparametric locally estimated scatterplot smoother, PROC LOESS (SAS Institute, Cary, NC), was used to smooth these temporal trends.

In-hospital adverse outcomes. Comparisons of outcomes after CABG between diabetics and nondiabetics, unmatched and propensity matched, were made using the χ^2 test for categorical endpoints.

Resource utilization and total direct technical cost. Hours in the intensive care unit and postoperative and total hospital lengths of stay had right-skewed distributions, so the Wilcoxon rank-sum test, and the median score test for continuous endpoints, were used for comparisons between diabetics and nondiabetics. To identify the relative difference in direct technical costs, we estimated the ratio of the median cost between the 2 groups. The percentile bootstrap confidence method⁸ was used to estimate 95% confidence intervals. This procedure was applied to the overall and matched cohorts.

Long-term survival. Survival was assessed nonparametrically, using the Kaplan-Meier method, and parametrically, using a multiphase hazard model.⁹ The latter involved resolving the number of hazard phases for instantaneous risk of death (hazard function), and estimating shaping parameters. (For details, see www.lerner.ccf.org/qhs/software/hazard.) Because the shape of time-varying risk of death may differ for diabetics versus nondiabetics, we constructed separate hazard models for each group.

Propensity-score matching. Although overall assessment of outcomes in diabetics compared with nondiabetics represents the realities of the real world, diabetics as a group present with a higher-than-average risk profile. We therefore treated diabetes as a “natural experiment,”¹⁰ comparing outcomes of propensity-matched diabetics and nondiabetics.¹¹⁻¹³ This comparison was accomplished in 2 steps. First, a parsimonious multivariable logistic regression was used to identify differences in preoperative characteristics of diabetic versus nondiabetic patients, to obtain insight into these differences (see Appendix E1 for a list of variables analyzed). Bootstrap bagging for variable selection with automated analysis of 500 resampled datasets was used to accomplish this, followed by tabulation of the frequency of both single factors and closely related clusters of factors.¹⁴ We retained factors that occurred in $\geq 50\%$ of the bootstrap models (Table E1). The C-statistic for this parsimonious model was .83.

Second, the parsimonious model was augmented into a saturated propensity model by including patient characteristics that were not statistically significantly different between groups. These characteristics were demographic, cardiac, and noncardiac comorbidities not represented (see Appendix E1). The C-statistic for this model was .84.

A propensity score representing the probability of diabetes—group membership given the variables included in the propensity model, regardless of whether the patient had diabetes—was then calculated for each patient. A greedy matching strategy based on the propensity scores alone was used to match diabetic with nondiabetic patients, yielding 8926 well-matched pairs (86% of possible matches; Figure E1). Diabetes

cases with propensity scores that deviated >0.10 from those of nondiabetes cases were considered unmatched. Standardized differences demonstrated that covariable balance was achieved across nearly all variables (Figure E2).

Using a similar approach, separate propensity matching was done between the subset of diabetics and nondiabetics undergoing an operation in the period from 2003 to 2011, during which cost data were available. This yielded 1368 well-matched pairs (77% of possible matches).

Missing values. Several variables examined in multivariable analyses had missing values. We used fivefold multiple imputation¹⁵ with a Markov chain Monte Carlo technique to impute missing values (SAS PROC MI; SAS Institute, Cary, NC). In multivariable modeling, for each imputed complete dataset, we estimated regression coefficients and their variance-covariance matrix. After this step, following Rubin,¹⁵ we combined estimates from the 5 models (SAS PROC MIANALYZE; SAS Institute, Cary, NC) to yield final regression coefficient estimates, the variance-covariance matrix, and *P* values.

Presentation. Continuous variables are summarized by mean $\pm$ SD, or equivalent 15th, 50th (median), and 85th percentiles when the distribution of values is skewed. Analyses were performed using SAS statistical software, version 9.1 (SAS Institute, Cary, NC) and R (version 3.0.2). Uncertainty is expressed by confidence limits (CLs) equivalent to ± 1 SE (68%).

RESULTS

Compared with nondiabetics, diabetic patients undergoing CABG were older and more likely to be overweight, and more likely to be women. In addition, they were more likely to have a history of heart failure, peripheral arterial disease, carotid disease, hypertension, renal failure, stroke, and advanced coronary artery disease (Table 1).

Temporal Trends

The proportion of patients presenting for CABG who have diabetes increased from 7% per year in the 1970s to 37% in the 2000s (Central Image). The cardiovascular risk factor profile also changed during this time, more so for diabetics than nondiabetics. Today, patients are likely to be older (Figure 1, A) and obese (Figure 1, B); to have had a stroke (Figure 1, C); and to have hypertension (Figure 1, D), peripheral arterial disease (Figure 1, E), lower total cholesterol (Figure 1, F), higher high-density lipoprotein cholesterol (Figure 1, G), lower triglycerides (Figure 1, H), and more-advanced coronary artery disease (Figure 1, I) (see Table E1).

Overall Outcomes

In-hospital adverse outcomes, and resource utilization and direct technical costs. Diabetics had higher in-hospital mortality and greater occurrence of deep sternal wound infection, stroke, atrial fibrillation, renal failure, and respiratory failure (Table 2). Hours spent in the intensive care unit and of length of stay >14 days were higher in diabetics than nondiabetics (Table 2). As a result, the total cost of CABG was 9% greater (95% CI, 7%-11%) in diabetics. Most of this difference was due to higher costs of

clinical and laboratory testing, diagnostic imaging, pharmacy services, and nursing care (Figure 2).

Long-term survival. The instantaneous risk of death was high immediately after CABG, decreased over the ensuing 6 months, and then gradually increased for both diabetics and nondiabetics (Figure 3, A), resulting in early divergence of their survival curves (Figure 3, B). In addition, late hazard was elevated in diabetics; thus, ever-increasing divergence of survival was observed out to at least 20 years. Among diabetics, overall survival at 6 months, 1, 5, 10, 15, and 20 years after CABG was 95%, 94%, 80%, 54%, 31%, and 18%, respectively. In contrast, for nondiabetics, it was 97%, 97%, 90%, 76%, 59%, and 42%, respectively ($P < .0001$).

Comparison of Diabetics with Similar High-Risk Nondiabetics

In-hospital adverse outcomes, and resource utilization and direct technical costs. After matching, the incidence of deep sternal wound infection and stroke remained significantly higher among diabetics (Table 2). After propensity matching, no significant difference remained in total cost of CABG between diabetics and nondiabetics (Figure 2). Hours spent in the intensive care unit were similar, but length of stay >14 days remained higher for diabetics (Table 2).

Long-term survival. Among propensity-matched patients, instantaneous risk of death (hazard function) was similar for both diabetics and nondiabetics until 1 year after surgery, after which risk of death was greater for diabetics (Figure 3, C). Early survival was similar between the 2 groups, but late survival was worse for diabetics (Figure 3, D). Late survival continued to diverge as long as patients were followed, because of the substantial difference in late hazard for at least 20 years after CABG. Survival of diabetics at 6 months, 1, 5, 10, 15, and 20 years after operation was 96%, 94%, 80%, 56%, 35%, and 20%, respectively, versus 96%, 94%, 84%, 66%, 47%, and 32% for nondiabetics.

DISCUSSION

Principal Findings

This study shows that the proportion of patients presenting for CABG who have diabetes increased each year during the past 4 decades, as did the proportion with cardiovascular risk factors. Thus, compared with diabetics undergoing operation in the 1970s, 1980s, and 1990s, those operated on more recently were more likely to be obese and have more comorbidities and advanced coronary artery disease. For diabetics, CABG was more resource intensive and expensive, and in-hospital adverse events and long-term survival were worse. However, the increase in in-hospital resource utilization was not specific to diabetics, but rather commensurate with that of patients coming to surgery with

TABLE 1. Patient characteristics and revascularization details of nondiabetics and diabetics undergoing coronary artery bypass grafting

Characteristic	Nondiabetics (n = 45,139)		Diabetics (n = 10,362)		P value
	n	No. (%) or mean $\pm$ SD	n	No. (%) or mean $\pm$ SD	
Demographics					
Age (y)	45,139	60 $\pm$ 10	10,362	63 $\pm$ 9.7	<.001
Male	45,139	37,626 (83)	10,362	7249 (70)	<.001
Body mass index (kg/m ²)	27,739	28 $\pm$ 4.7	8883	30 $\pm$ 5.8	<.001
Symptoms and surgical priorities					
NYHA functional class	44,775		10,317		<.001
I		7645 (17)		1800 (17)	
II		16,533 (37)		3982 (39)	
III		4702 (11)		1468 (14)	
IV		15,895 (35)		3067 (30)	
Emergency operation	45,137	1242 (2.8)	10,362	248 (2.4)	.04
Cardiac comorbidity					
Myocardial infarction	45,139	22,916 (51)	10,362	5932 (57)	<.001
Left ventricular dysfunction	42,404		8996		<.001
None		37,013 (87)		6300 (70)	
Mild		2492 (5.9)		948 (11)	
Mild to moderate		514 (1.2)		238 (2.6)	
Moderate		1315 (3.1)		688 (7.6)	
Moderate to severe		492 (1.2)		384 (4.3)	
Severe		578 (1.4)		438 (4.9)	
Preoperative AF or flutter	36,357	411 (1.1)	8967	163 (1.8)	<.001
Heart failure	45,139	2219 (4.9)	10,362	1750 (17)	<.001
Coronary artery disease	35,015	20,687 (59)	7042	3446 (49)	<.001
No. of coronary systems diseased (stenosis $\geq$ 50%)	43,113		9908		<.001
0		366 (0.85)		69 (0.70)	
1		5310 (12)		615 (6.2)	
2		13,807 (32)		2332 (24)	
3		23,630 (55)		6892 (70)	
Left main disease (stenosis $\geq$ 50%)	41,909	6704 (16)	9277	1749 (19)	<.001
Noncardiac comorbidity					
Peripheral arterial disease	45,139	4551 (10)	10,362	1840 (18)	<.001
Carotid disease	45,139	3434 (7.6)	10,362	2278 (22)	<.001
Stroke	45,139	1515 (3.4)	10,362	880 (8.5)	<.001
Hypertension	29,346	17,615 (60)	9077	6966 (77)	<.001
COPD	14,360	1079 (7.5)	6639	584 (8.8)	<.001
Smoking	44,244	24,133 (55)	10,208	5319 (52)	<.001
Creatinine (mg/dL)	13,969	1.2 $\pm$ 0.83	6464	1.3 $\pm$ 1.2	.07
Blood urea nitrogen (mg/dL)	13,954	18 $\pm$ 9.0	6460	22 $\pm$ 12	<.001
Renal dialysis	7375	59 (0.80)	4060	98 (2.4)	<.001
Total cholesterol (mg/dL)	35,236	235 $\pm$ 56	7422	208 $\pm$ 60	<.001
HDL cholesterol (mg/dL)	14,734	40 $\pm$ 12	5283	39 $\pm$ 13	<.001
LDL cholesterol (mg/dL)	9616	128 $\pm$ 46	4309	113 $\pm$ 45	<.001
Triglycerides (mg/dL)	29,248	185 $\pm$ 116	6672	203 $\pm$ 173	.002
Bilirubin (mg/dL)	12,683	0.65 $\pm$ 0.50	5803	0.59 $\pm$ 0.51	<.001
Hematocrit (%)	13,037	40 $\pm$ 5.1	5993	38 $\pm$ 5.5	<.001
Experience					
January 1, 1972 to index operation	45,139	14 $\pm$ 9.5	10,362	21 $\pm$ 9.6	<.001
Revascularization details					
ITA grafts at index operation	45,139		10,362		<.001
None		14,888 (33)		2018 (19)	
Single		25,160 (56)		7570 (73)	
Bilateral		5091 (11)		774 (7.5)	
Complete revascularization*	45,139	40,405 (90)	10,362	9432 (91)	<.001
Cardiopulmonary bypass	45,139	43,761 (97)	10,362	9817 (95)	<.001

Values in "n" columns are numbers of patients with data available. SD, Standard deviation; NYHA, New York Heart Association; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ITA, internal thoracic artery. *Incomplete revascularization was defined as failure to graft any system containing 50% stenosis or both the left anterior descending and circumflex coronary artery systems for 50% left main trunk stenosis.

FIGURE 1. Four-decade trends in prevalence of diabetes and cardiovascular risk factors among patients undergoing primary isolated coronary artery bypass grafting. Each *circle* is a yearly percentage or mean value, and *solid lines* are loess estimates. The factors shown are: (A) age; (B) body mass index; (C) stroke; (D) hypertension; (E) PAD; (F) total cholesterol; (G) HDL cholesterol; (H) triglycerides; and (I) percentage with 3-system disease. PAD, Peripheral arterial disease; HDL, high-density lipoprotein.

a similar extent of comorbidities, but without diabetes. Unadjusted in-hospital and early mortality (1-year) were higher in diabetics than in nondiabetics, but similar for propensity-matched patients with a similar comorbidity profile. Long-term survival was worse in diabetics than in either nondiabetic patients or matched, nondiabetic, high-risk patients. Thus, diabetes is both a marker for high-risk, resource-intensive, and expensive care after CABG, and an independent risk factor for reduced long-term survival.

Trends

In 2010, nearly 40% of those undergoing CABG at our institution were diabetic, paralleling the rising prevalence of diabetes in the general population. However, the increasing use of percutaneous coronary intervention for revascularization, and the choice of CABG as the preferred revascularization strategy for diabetics, could also have been contributing factors.¹⁶ Although cardiovascular

disease-related morbidity and mortality has clearly been reduced in the United States over the past 50 years, the cardiovascular disease burden attributable to diabetes has increased.⁵ Current estimates are that 18.8 million people in the United States have been diagnosed with diabetes, and 7 million remain undiagnosed.² In addition, nearly 79 million people aged ≥ 20 years have prediabetes,² a condition that places them at increased risk of developing diabetes and cardiovascular disease.¹⁷

We also observed a change in the cardiovascular risk-factor profile over time. Diabetics undergoing CABG in recent years are more likely to be obese and to have more-advanced coronary artery disease than those operated on in the 1970s, 1980s, and 1990s. In addition, they are more likely to have hypertension, one component of metabolic syndrome, together with diabetes, hyperlipidemia, and obesity—all risk factors for coronary artery disease.¹⁸ Obesity is now considered a national epidemic and is of particular importance as a well-recognized contributor to

TABLE 2. In-hospital outcomes after coronary artery bypass grafting: overall and propensity matched

Outcome	Overall					Propensity matched				
	Nondiabetic (total n = 45,139)		Diabetic (total n = 10,362)		P value	Nondiabetic (total n = 8926)		Diabetic (total n = 8926)		P value
	n	No. (%)	n	No. (%)		n	No. (%)	n	No. (%)	
Hospital death	45,139	566 (1.3)	10,362	211 (2.0)	<.001	8926	152 (1.7)	8926	174 (1.9)	.2
Deep sternal wound infection	45,139	526 (1.2)	10,362	239 (2.3)	<.001	8926	116 (1.3)	8926	197 (2.2)	<.001
Septicemia	14,298	226 (1.6)	6633	151 (2.3)	.004	6393	139 (2.2)	5352	113 (2.1)	.8
Stroke	45,139	640 (1.4)	10,362	233 (2.2)	<.001	8926	134 (1.5)	8926	200 (2.2)	<.001
Perioperative MI	45,139	1023 (2.3)	10,362	135 (1.3)	<.001	8926	118 (1.3)	8926	123 (1.4)	.8
Bleeding or tamponade	45,139	1791 (4.0)	10,362	348 (3.4)	.004	8926	271 (3.0)	8926	314 (3.5)	.07
Atrial fibrillation	45,139	5148 (12)	10,362	1979 (19)	<.001	8926	1914 (21)	8926	1672 (19)	<.001
Renal failure	45,139	569 (1.3)	10,362	418 (4.0)	<.001	8926	258 (2.9)	8926	285 (3.2)	.2
Renal failure requiring dialysis	14,298	104 (0.73)	6633	86 (1.3)	<.001	6393	79 (1.2)	5352	60 (1.1)	.6
Prolonged ventilation (>24 h)	3492	320 (9.2)	2100	249 (12)	.001	1838	212 (12)	1563	160 (10)	.2
Length of stay*										
ICU (h)	14,296	24/24/72	631	24/26/95	<.001	6391	24/24/75	5351	24/24/76	<.001
Postoperative (d)	44,014	6.1/8.0/11	10,263	5.9/7.9/12	<.001	8864	5.2/7.0/11	8829	5.9/7.9/11	<.001
Hospital (d)	44,014	7/11/17	10,263	6.3/10/18	<.001	8864	6.3/9.3/16	8829	6.3/10/17	<.001
Prolonged (>14 d)	45,139	2688 (6.0)	10,362	995 (9.6)	<.001	8926	679 (7.6)	8926	785 (8.8)	.004

Values in “n” columns are numbers of patients with data available. P values are given for the median score test. MI, Myocardial infarction; ICU, intensive care unit. *15th/50th/85th percentiles. Median score test was used to compare medians and Wilcoxon rank-sum test to compare tails of distributions.

diabetes. More than one third of US adults are obese,¹⁹ and in the next 20 years, obesity may play a contributing role in an estimated 6 million cases of diabetes.²⁰ On the other hand, diabetics undergoing CABG in recent years had lower total cholesterol, higher high-density lipoprotein cholesterol, and lower triglycerides than did patients operated on in earlier years; this difference may be attributable to better control of lipids in the statin era.

In-Hospital Adverse Outcomes

In-hospital adverse outcomes after CABG were more common in diabetics than nondiabetics. In part, this difference is attributable to diabetic patients being sicker and

having more comorbidities than nondiabetics, because some of the differences, including hospital death, septicemia, renal failure, and respiratory failure, became statistically insignificant after comparison with similar high-risk nondiabetic patients through propensity matching. However, occurrence of deep sternal wound infection and stroke remained significantly higher in diabetics even after matching. Deep sternal wound infection results in prolonged postoperative length of stay and thus increases hospital resource utilization. Strokes may cause permanent disability, resulting in unemployment and thus increasing the indirect cost of diabetes through loss of productivity.

FIGURE 2. Median (triangles) ratio of total direct technical costs (overall and propensity matched) in diabetics versus nondiabetics. Error bars are 95% confidence intervals.

FIGURE 3. Time-related death after primary isolated coronary artery bypass grafting in diabetics and nondiabetics. *Solid lines* are parametric estimates enclosed within dashed 68% confidence bands equivalent to ± 1 SE. The panels show: (A) instantaneous risk of death (overall); (B) survival (overall); (C) instantaneous risk of death (propensity-matched cohort); and (D) survival (propensity-matched cohort). Each *symbol* represents a death; *vertical bars* are confidence limits equivalent to ± 1 SE; and values in parentheses are numbers of patients remaining at risk.

Other studies have also revealed worse hospital and long-term outcomes of CABG in diabetics.^{21,22} The SYNTAX trial showed that at 3 years, diabetes had little effect on outcomes of CABG, and diabetes control (as indicated by baseline hemoglobin A1c levels) was not predictive of major adverse cardiac and cerebrovascular events. In our study, overall postoperative prevalence of stroke and in-hospital death was higher in diabetics, and occurrence of myocardial infarction was higher in nondiabetics. However, after comparison with similar, high-risk, nondiabetic patients, occurrence of death and myocardial infarction was similar in the 2 groups, as was true in the SYNTAX trial, but stroke remained higher in diabetics.²³

Health Care Costs

Our study additionally shows that resource utilization and the actual direct technical cost of CABG were greater in diabetics, mainly because of longer intensive care unit and postoperative stays, and higher costs of clinical and laboratory testing, diagnostic imaging, pharmacy services, and nursing care. Greater severity of disease among diabetics necessitates preoperative admission and more-extensive laboratory and diagnostic workup. Furthermore, managing postoperative adverse events and the resulting increase in postoperative length of stay both lead to higher in-hospital costs.

After using propensity matching to compare similar high-risk, nondiabetic patients, no significant difference between the total cost of CABG in diabetics versus

nondiabetics with a similar high-risk profile was observed, demonstrating that most of the increased cost was due to diabetics being sicker and having more comorbidities. In 2012, \$176 billion was spent on direct health care for diabetics in the United States, with in-hospital care representing 43% of that amount.³ Because heart disease is one of the leading causes of hospitalization in diabetics, a large share of in-hospital costs can be attributed to CABG and its postoperative complications.

Others have also demonstrated the association of diabetes with increased cost of CABG.^{24,25} A study of 114 diabetics and 198 nondiabetics showed that insulin-treated diabetics have longer hospital stays and higher hospital charges than non-insulin-treated diabetics and nondiabetics.²⁴ A recently published study from China also showed that CABG was more costly, with worse long-term results, in diabetics than in nondiabetics.²⁶

Survival

Diabetic patients as a group had a higher early (1-year) risk of death after CABG than nondiabetics, as has been documented by others.²¹ However, an interesting finding of our study is that among propensity-matched patients, early risk was similar to that of nondiabetic high-risk patients with a similar comorbidity profile. Long-term survival, however, was worse in diabetics than in both nondiabetic patients and nondiabetic high-risk patients. Other studies have also demonstrated diabetes to be an independent risk factor for reduced long-term survival after

CABG.^{21,26} Although long-term survival after CABG is worse in diabetics and high-risk nondiabetics, in general, high-risk patients reap the greatest survival benefit from CABG.²⁷ Moreover, using surgical techniques that are associated with better long-term survival after CABG in diabetics could further enhance this survival benefit.²⁸

Diabetes: An Avoidable Economic Burden

Diabetes is a growing threat to the US economy. Diabetic patients' medical expenses are nearly 2.3 times higher than those of nondiabetics,³ and this economic burden is expected to increase as the number of diabetes cases rises. Fortunately, however, this situation is largely preventable. In people with prediabetes, cost-effective lifestyle interventions have been shown to have a positive effect on preventing development of the disease.²⁹⁻³¹ In people with diagnosed diabetes, controlling blood sugar and cardiovascular disease risk factors, such as hypertension and hypercholesterolemia, has been shown to help reduce cardiovascular events.^{32,33} With appropriate use of these approaches, we can help prevent development of diabetes and its complications, reducing the diabetes-related economic burden.

Strengths and Limitations

This study includes 4 decades of patients who underwent CABG at a single, high-volume academic medical center. An advantage of a long observation period is having a long follow-up period, but generalizing these late results to a contemporary patient population may not accurately reflect the changing patient case mix and advances in managing these patients over time. For adjusted comparison of outcomes, propensity-score matching was performed. Although the patient pairs were well matched, any patient factors that significantly affect outcomes after CABG but were not included in the propensity analysis might bias our adjusted results. In addition, circumstances of each death, which may differ among diabetic and nondiabetic patients, were not reliably captured during follow-up inquiries.

CONCLUSIONS

Diabetes is both a marker for high-risk, resource-intensive, and expensive care after CABG and an independent risk factor for reduced long-term survival. These issues, coupled with the annually increasing number of patients needing CABG who are diabetic, present a growing challenge to reining in health care costs, both in the United States and internationally. Diabetic patients, and those with a similar high-risk profile, set to undergo CABG should be made aware that their risks of postoperative complications are higher than average, and measures should be taken to reduce their postoperative complications. Moreover, trying to reverse the diabetes epidemic is important; if left

uncontrolled, it will increase the prevalence of cardiovascular disease and add to the ever-increasing economic health care burden. Research and policies focused on reducing diabetes, and programs that raise awareness about preventive strategies, should be developed and implemented to check rising health care costs.

Conflict of Interest Statement

Dr Sabik is the North American principal investigator for the Abbott Laboratories-sponsored left main coronary disease randomized trial (EXCEL), is on the Society of Thoracic Surgeons Board of Directors, and is on the scientific advisory board of Medtronic. All other authors have nothing to disclose with regard to commercial support.

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Key Words: Coronary artery bypass grafting, diabetes, health care costs

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APPENDIX E1. VARIABLES CONSIDERED IN ANALYSES

Demographics

Age (y)*, sex*, race*, weight (kg), height (cm), weight/height ratio, body surface area (m²), body mass index (kg·m⁻²)*

Symptoms and Surgical Priorities

New York Heart Association functional class (I-IV)*, emergency surgery

Cardiac Comorbidity

Prior myocardial infarction*, atrial fibrillation or flutter*, complete heart block or pacer*, heart failure*, ventricular arrhythmia, left ventricular dysfunction (none, mild, mild to moderate, moderate, moderate to severe, severe)*

Noncardiac Comorbidity

Peripheral arterial disease*, carotid disease*, hypertension*, chronic obstructive pulmonary disease*, history of smoking*, prior stroke*, bilirubin (mg·dL⁻¹)*, total

cholesterol (mg·dL⁻¹)*, high-density lipoprotein (mg·dL⁻¹)*, low-density lipoprotein (mg·dL⁻¹), triglycerides (mg·dL⁻¹)*, creatinine (mg·dL⁻¹)*, blood urea nitrogen (mg·dL⁻¹)*, hematocrit (%)*

Coronary Anatomy

Number of systems diseased (≥50% stenosis)*, left main trunk (LMT) disease, any LMT disease, LMT disease (≥70% stenosis)*, LMT disease (≥50% stenosis)*, left anterior descending coronary artery (LAD) system disease, any LAD system disease, LAD system disease (≥70% stenosis)*, LAD system disease (≥50% stenosis)*, left circumflex (LCx) coronary artery system disease, any LCx system disease, LCx system disease (≥70% stenosis)*, LCx system disease (≥50% stenosis)*, right coronary artery (RCA) system disease, any RCA system disease, RCA system disease (≥70% stenosis)*, RCA system disease (≥50% stenosis)*

Experience

Date of operation (years since January 1, 1972)*

* Variables used in the saturated model to calculate propensity scores.

FIGURE E1. Mirrored histogram of distribution of propensity scores for diabetes and no diabetes (*shaded area* represents matched patient cohorts).

TABLE E1. Factors associated with diabetes among patients undergoing coronary artery bypass grafting (parsimonious model)

Factor	Estimate $\pm$ SE	P value	Reliability (%)
More common in diabetics			
Higher body mass index*	2.09 $\pm$ 0.13	<.0001	100
NYHA functional class IV	0.063 $\pm$ 0.029	.03	67
Cardiac comorbidities			
Heart failure	0.37 $\pm$ 0.045	<.0001	99
More systems diseased†	0.30 $\pm$ 0.027	<.0001	100
LCx system disease‡	0.20 $\pm$ 0.038	<.0001	100
Worse left ventricular function	0.15 $\pm$ 0.011	<.0001	96
Noncardiac comorbidities			
Peripheral arterial disease	0.40 $\pm$ 0.039	<.0001	100
Carotid disease	0.16 $\pm$ 0.040	<.0001	68
Hypertension	0.30 $\pm$ 0.036	<.0001	90
Stroke	0.25 $\pm$ 0.054	<.0001	88
Higher triglycerides§	0.10 $\pm$ 0.0036	<.0001	97
Lower bilirubin	0.49 $\pm$ 0.014	<.0001	75
More common in nondiabetics			
Black or other race¶	0.50 $\pm$ 0.041	<.0001	97
LMT system disease‡	-0.20 $\pm$ 0.055	.0009	100
Smoking	-0.37 $\pm$ 0.026	<.0001	96
Lower cholesterol#	-1.20 $\pm$ 0.07	<.0001	97
Lower hematocrit**	-1.29 $\pm$ 0.057	<.0001	87
Intercept	-2.28 $\pm$ 0.56	.001	

C-statistic = .83. The reliability indicates percentage of times the factor appeared in 500 bootstrap models. *SE*, Standard error; *NYHA*, New York Heart Association; *LCx*, left circumflex coronary artery; *LMT*, left main trunk. *Log(body mass index), logarithmic transformation. † $\geq 50\%$ stenosis. ‡ $\geq 70\%$ stenosis. §(Triglycerides/180)², squared transformation. ||(1/bilirubin), inverse transformation. ¶Black or other race compared with white race. #Log(cholesterol), logarithmic transformation. ** (Hematocrit/40)², squared transformation.

FIGURE E2. Covariable balance plot before and after propensity-score matching on selected covariables (Austin PC, Mamdani MM. A comparison of propensity score methods: a case study estimating the effectiveness of post-AMI statin use. *Stat Med*. 2006;25:2084-106.) Diabetes-like characteristics are on the right; non-diabetes-like characteristics are on the left. *BMI*, Body mass index; *LV*, left ventricular; *PAD*, peripheral arterial disease; *MI*, myocardial infarction; *NYHA*, New York Heart Association; *STD*, standardized.