Lack of Association of Diabetes With Increased Postoperative Mortality and Cardiac Morbidity

Results of 6565 Major Vascular Operations

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Hypothesis: A number of preoperative factors, including diabetes mellitus (DM), have been cited as increasing risk in patients undergoing major vascular operations. In smaller studies at our institution we have not found this to be apparent. This study reviewed all major vascular operations to confirm our bias that DM is not associated with increased mortality or cardiac morbidity.

Design: Case series retrospectively reviewed from a vascular registry established in 1990.

Setting: Tertiary care center.

Patients: Consecutive sample of 6565 patients who underwent lower extremity revascularization or carotid or aortic procedures, grouped by presence or absence of DM.

Main Outcome Measures: Postoperative mortality, congestive heart failure, or myocardial infarction.

Results: Patients with DM made up 62.3% of the population, and those without diabetes, 37.7%. Average age of the DM group was 67.1 years, with 61.3% male and 38.7% female. Average age of the non-DM group was 70.6 years, with 61.8% male and 38.2% female. The rates of overall postoperative mortality, myocardial infarction, and congestive heart failure were 1.14%, 1.59%, and 1.13%, respectively. Comparing the DM with the non-DM group, these rates were 0.96% vs 1.46%, 1.77% vs 1.30%, and 1.13% vs 1.14%, respectively. Using multivariate analysis, the DM group had an inverse relationship to perioperative death, with an odds ratio of 0.53 (P = .01). The factors that were associated with increased mortality were hemodialysis and history of congestive heart failure. Previous myocardial infarction was the only factor that predicted postoperative myocardial infarction. Kaplan-Meier survival curves showed a significantly decreased survival in the DM group during the next 5 years (P < .001).

Conclusions: Diabetes alone does not confer a higher mortality or cardiac morbidity rate with major vascular procedures. However, long-term survival is significantly worse in this group of patients.

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It is well accepted that patients undergoing major vascular operations are at significant risk for perioperative cardiac morbidity and mortality. In an attempt to stratify and potentially alter this risk, multiple studies have evaluated the role of specific preoperative factors in predicting postoperative outcomes. A number of these reports have identified the presence of diabetes mellitus (DM) as at least a minor predictor of a negative outcome. This finding is important because a significant proportion of patients requiring vascular procedures have DM.

Diabetes mellitus has a large impact on US health care, affecting 16 million people nationally, with 800,000 new cases yearly, and generating health care expenditures of approximately $110 billion annually. Diabetes mellitus has been shown to be a significant contributor to coronary and peripheral arterial disease independent of other atherogenic risk factors. Although primarily known for its association with disease of the infrapopliteal circulation, DM also affects the aortoiliac system approximately 15% of the time. Macrovascular disease accounts for 65% to 75% of deaths in the diabetic population, predominantly due to coronary artery disease. For these reasons, DM is often cited as an independent risk factor for predicting perioperative events, including myocardial infarction (MI), congestive heart failure (CHF), and death.

Our institutional affiliation with the Joslin Diabetes Center, Boston, Mass, has yielded data on more than 4000 patients with DM who have undergone vascular procedures. The purpose of this study is to determine whether DM is an independent predictor of postoperative mortality and cardiac morbidity. We report the
PATIENTS AND METHODS

A computerized vascular registry was established in January 1990. Data from all patients who have undergone vascular procedures at the West Campus of the Beth Israel Deaconess Medical Center (formerly the New England Deaconess Hospital), Boston, Mass, were prospectively entered. For the purpose of this report, we reviewed the data of all consecutive patients who underwent major vascular procedures from January 1, 1990, through May 31, 2000. The procedures included carotid, aortic, and lower extremity (LE) revascularizations. Staff vascular surgeons with vascular fellows or general surgery residents performed the 6565 procedures in 5126 patients during this period. Risk factors and results for each patient were entered separately at the time of each operation, since years might have passed between the procedures. Most patients underwent general anesthesia, but we included patients who had surgery under regional anesthesia. Typically, postoperative patients recovered overnight in the postanesthesia care unit or the vascular intermediate care unit (a specialized vascular ward for stable, untubated patients) and then were transferred to the floor. The vascular intermediate care unit is staffed by vascular surgeons and residents. Those patients requiring intubation or pressor medications were treated in the surgical intensive care unit. We excluded no patient because of need for the surgical intensive care unit. Invasive monitoring, including Swan-Ganz catheterization, was used liberally, although specific percentages were not available from the registry.

We also evaluated patient demographics and preoperative risk factors, including history of hypertension (HTN), CHF, hemodialysis or peritoneal dialysis, previous MI, age, sex, and the presence of DM. Data were obtained by means of registry review. Postoperative MI (PMI) and CHF were identified by means of standard clinical variables and entered into the registry by staff, residents, or fellows. Routine measurement of cardiac isoenzyme levels or electrocardiographic monitoring was not performed without symptoms or other clinical indications.

Dates of death were obtained from the registry or from the online Social Security Death Index Database.14

We performed statistical analysis with the aid of StatView software (Version 5.0; SAS Institute Inc, Cary, NC). Independent predictors of untoward postoperative outcomes were sought using logistic regression. Variables were assumed to be significant if the Wald test P value was <.05 and the 95% confidence interval of the odds ratio (OR) did not contain the integer 1. We obtained further correlation using the logistic likelihood ratio test. Survival analysis was performed using the Kaplan-Meier product-limit method. The resulting survival curves were then compared using the Cox-Mantel log-rank test, with significant differences assumed at P values of <.05.

experience with 6565 major vascular operations over a 10-year period at a single tertiary care center in an effort to further define preoperative risk stratification.

Table 1. Clinical Characteristics of the DM vs Non-DM Groups*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DM Group</th>
<th>Non-DM Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>67.1</td>
<td>70.6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61.3</td>
<td>61.8</td>
</tr>
<tr>
<td>Female</td>
<td>38.7</td>
<td>38.2</td>
</tr>
<tr>
<td>HTN</td>
<td>66.3</td>
<td>63.8</td>
</tr>
<tr>
<td>Previous MI</td>
<td>34.2</td>
<td>27.7</td>
</tr>
<tr>
<td>Previous CHF</td>
<td>22.1</td>
<td>8.3</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, all values are given as percentages. DM indicates diabetes mellitus; HTN, hypertension; MI, myocardial infarction; and CHF, congestive heart failure.

Table 2. Multivariate Analysis of Risk Factors for Perioperative Mortality in 6565 Procedures*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>P Value</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>.01</td>
<td>0.53 (0.33-0.86)</td>
</tr>
<tr>
<td>Previous CHF</td>
<td>.004</td>
<td>2.19 (1.29-3.71)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>.006</td>
<td>3.03 (1.39-6.62)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>.06</td>
<td>1.57 (0.98-2.51)</td>
</tr>
<tr>
<td>HTN</td>
<td>.82</td>
<td>1.06 (0.64-1.74)</td>
</tr>
<tr>
<td>Male sex</td>
<td>.61</td>
<td>0.89 (0.55-1.42)</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>.46</td>
<td>2.14 (0.29-16.41)</td>
</tr>
</tbody>
</table>

*Boldface type indicates statistical significance. CI indicates confidence interval. Other abbreviations are given in the footnote to Table 1.

RESULTS

PATIENTS

Mean age of the patients was 69.3 years (range, 17.6-96.5 years). Other overall characteristics of the patients with regard to preoperative risk factors are listed in the following tabulation:

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>61.4</td>
</tr>
<tr>
<td>Female</td>
<td>38.6</td>
</tr>
<tr>
<td>DM</td>
<td>62.3</td>
</tr>
<tr>
<td>HTN</td>
<td>65.1</td>
</tr>
<tr>
<td>Previous CHF</td>
<td>16.8</td>
</tr>
<tr>
<td>Previous MI</td>
<td>31.2</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>3.7</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>0.6</td>
</tr>
</tbody>
</table>

The population was divided into 2 groups, patients with and without DM. Their characteristics are listed in Table 1.

The overall rates of mortality, MI, and CHF in the 6565 procedures were 1.14%, 1.59%, and 1.13%, respectively. When we compared the DM with the non-DM group, these rates were 0.96% vs 1.46%, 1.77% vs 1.30%, and 1.13% vs 1.14%, respectively. Using logistic regression analysis (Table 2), only 2 factors, hemodialysis and preoperative CHF, predicted perioperative mortality, with ORs of 3.03 (P < .006) and 2.19 (P = .004), respectively. Diabetes mellitus had an inverse effect on the rate of death, with an OR of 0.53 (P = .01). With regard to cardiac morbidity, a history of MI correlated with an increase in PMI (OR, 2.0; P < .001). Preoperative HTN and CHF pre-
COMMENT

Our report finds that patients with DM have a lower rate of perioperative mortality after major vascular procedures than patients without DM (OR, 0.53). Even when stratified by procedure type (carotid, aortic, and LE), no statistically significant differences were found in perioperative mortality between the DM and non-DM groups. Thus, by means of multivariate analysis, DM was not identified as an independent positive predictor of perioperative mortality. This finding was maintained when we corrected for the younger overall age of the DM population by the inclusion of age as an independent variable in the logistic regression analysis.

This finding contradicts previous reports indicating that DM confers a higher risk in patients presenting for vascular surgery. Eagle et al² examined patients undergoing vascular procedures to identify preoperative risk factors and concluded that diabetes was one of 5 independent predictors of postoperative cardiac events and death. That study found that patients with diabetes had a risk of 2.6 times that of nondiabetic patients for adverse outcomes.²

Our data do not support the association of DM with increased perioperative mortality, but similar findings, such as hemodialysis predicting a higher perioperative mortality rate and a history of MI correlating with an increased PMI, were supported by our study.

We report a very low mortality rate in patients undergoing vascular surgery: 0.96% and 1.46% in DM and non-DM groups, respectively. These numbers are lower expected than previously reported and may be due to improvements in patient selection and surgical technique.
than those of several reports, including one from the Cleveland Clinic, Cleveland, Ohio, showing a 4.4% overall mortality in those patients younger than 75 years undergoing vascular procedures. In that same study, however, mortality after LE and carotid surgery were 2.2% and 1.5%, respectively. Since our registry contains a disproportionate number of these potentially lower-risk procedures (>80% were LE or carotid procedures), this could account for the overall very low mortality. In addition, in the presumed higher-risk group (patients undergoing aortic procedures), most of the cases are elective infrarenal repairs. However, the prior presumption that DM confers a higher perioperative risk was studied in patients undergoing these same procedures.

From the available data, it is unclear why patients without DM had a significantly higher perioperative mortality than those with DM. The standard preoperative routine at our institution involves liberal consultation from cardiologists for patients with and without DM, with additional evaluation by the endocrine specialists from the Joslin Diabetes Center for those patients with DM. Intraoperative invasive monitoring with frequent Swan-Ganz catheterization is used. Postoperatively, patients spend 1 to 3 days in a specialized vascular nursing unit. An unintentional but preferential use of invasive monitoring, preoperative cardiac evaluation, or longer length of stay in the vascular unit may occur in patients with DM, possibly accounting for the results. Unfortunately, we do not have any data on differences in complication rates in those patients with and without invasive monitoring. In addition, specifics about the preoperative cardiac work-up, with interpretation of the extent of coronary artery disease, were not included in the registry. It is also unclear whether patients with DM were more likely to receive perioperative β-blockade, which could partly explain the results. The report by Mangano et al showed that in patients with DM, atenolol use was associated with similar survival rates to those of patients without DM, whereas DM patients receiving placebo had a 4-fold increase in mortality.

In regard to perioperative, nonfatal cardiac events, an inherent error may exist in this retrospective single-center report. Our registry only captures events reported by residents, fellows, and staff. Routine postoperative electrocardiographic monitoring and cardiac isoenzyme measurements were not performed. Therefore, it is likely that silent postoperative cardiac events were incompletely captured. Patients with DM are known to have an increased incidence of silent myocardial disease, which could partly account for the lack of increased cardiac morbidity in this study in patients with DM. However, clinically apparent perioperative cardiac morbidity clearly was not increased by DM, which was further emphasized by the low mortality rates.

As already discussed, survival after operation was similar between the DM and non-DM groups, but during the course of the next 5 years, the DM group showed significantly decreased survival. Again, this finding is similar to reports of an average life expectancy of up to 15 years less in patients with DM than in the general population. The reason(s) accounting for the significantly depressed long-term survival in DM is not apparent, because the cause of death was not available for all patients. Some event related to surgery that does not cause immediate mortality might start a sequence of events that eventually leads to their deaths. This possibility is analogous to the finding in the study by Mangano et al, in which those patients not receiving short-term perioperative β-blockade did not have an increased 30-day mortality but had a significantly depressed 2-year survival. Further studies have to be conducted with the aim to find those modifiable factors leading to the dismal long-term survival in patients with DM undergoing vascular surgery.

**CONCLUSIONS**

This single-institution study represents the first time, to our knowledge, that DM has not been found to be a clear predictor of perioperative death and morbidity after vascular surgery. The presence of DM should not preclude a patient from being considered for any vascular surgery procedure.

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**REFERENCES**

James Menzoian, MD, Boston, Mass: This manuscript by Dr. Hamdan and his associates at the Beth Israel Deaconess represents a very informative review of a large number of patients undergoing vascular surgical procedures, including leg bypasses, carotid artery surgery, and aortic procedures. It is especially important because it is well established that vascular patients represent a high risk for perioperative morbidity and mortality due to the fact that the underlying pathophysiologic process is atherosclerosis, and since this is a systemic disease, the incidence of coronary artery disease in our patients is very high. It has been assumed that diabetics have an especially high risk for perioperative morbidity and mortality following vascular surgical procedures. This current study obviously refutes that principal. I have some questions of Dr Hamdan.

One of the obvious problems with your data is your assessment of MI, since you did not perform routine serial EKGs or serial cardiac enzyme assessments. This is especially bothersome, since it is well known that patients with diabetes often do not experience chest pain during an episode of myocardial ischemia.

Secondly, you never addressed the issue of age. Your diabetics were on average 3 years younger than your nondiabetics, and it seems to me that it would be appropriate to do some sort of adjustment, because this could represent a confounding variable.

Third, the very interesting fact that your diabetics had a very low operative mortality but a higher 5-year mortality is rather curious. Can you speculate what is this all about?

And at the risk of offending my dear friend, Dr. Yeston, this Swan-Ganz catheter thing, this sort of damned-if-you-do and damned-if-you-don’t Swan-Ganz catheter—you imply that its placement could somehow be associated with their lower morbidity in your diabetic patients. Maybe you could tell me about any data that you have for this conclusion, because I am also aware of data that Swan-Ganz catheters keep people in ICU longer and make their lungs wetter, but I would be curious to know how you think this may have played a beneficial role.

I do like this paper. Anytime you can do 6000 operations on vascular surgery patients with an operative mortality of less than 1%, you have some very interesting data. Perhaps further dissecting these data can help us better care for the patients with diabetes and peripheral vascular disease.

Jeremy Morton, MD, Portland, Me: I do not want to scoop Robert Clough and the paper that he is going to give tomorrow morning on the Northern New England experience, but we found the incidence of diabetes in that group of a substantial number of patients to be only 30%. It was curious to me that your incidence was 62%. Our results are not really dissimilar to yours in terms of the effect of diabetes on mortality, but one of the things that we have looked at fairly closely—and I wonder if you have looked at the same thing—is the difference levels of diabetes. Did you differentiate between diabetics controlled with oral agents, insulin-dependent diabetes, and diabetics with sequelae to see if that lack of effect on mortality applied to each of those categories?

Dr Hamdan: In regards to Dr Menzoian’s question regarding the low MI rate and the incidence of likely silent MIs in diabetics, it is a very apt comment. In the manuscript, I actually make a point of discussing the fact that all we can say about the MI rate is from a clinical standpoint. Myocardial infarctions that are picked up in this study are still comparative, and there is no significant difference in diabetics and nondiabetics. There is no question that there may be a number of MIs missed that are not reported. It is very possible that missed MIs would be higher in diabetic patients, especially since this is a 10-year longitudinal study and now we have troponin levels, etc.

In regard to age, we did use age in our logistic regression, and based on the findings from that, the 3-year difference in age between the diabetics and nondiabetics did not change the results. The diabetics still had a statistically significant decrease in mortality rate.

As far as the 5-year mortality being so high with the perioperative mortality being low, I agree it is a worrisome finding, and, as far as speculation, the obvious thing would be to just say that even though you are able to get them through the surgery and through the perioperative period, they still have a higher level of underlying disease and more profound disease. Another interesting point that I obviously have no data on, just to quote another paper, Dr. Mangano’s paper, on perioperative β-blockade actually showed no difference in perioperative mortality, but if you followed the patients for 2 years, their mortality at 6 months and 2 years is markedly less if you have just a week of β-blockers. The speculation regarding that was catecholamine surge at the time of surgery may alter coronary plaque and cause plaque rupture. I am not necessarily postulating that is the case here, but there may be something that occurs at the time of surgery with diabetics that we are not picking up that decreases their long-term survival.

As far as Swan-Ganz catheters, I agree it would be nice if we had specific data on it, and I do not have the specific numbers. I hope Dr. Cady does not mind me quoting him as one of my mentors when he would say on rounds, “Would you get that Swan out of my patient? Every time one of my guys has that yellow thing in him, he seems to do worse.” I do not really know what the answer is, other than we definitely do use a lot of Swan-Ganz catheters. The more important thing is that we try to use them; in other words, not just have them in there, try to limit the amount of fluid we use in these patients.

As far as why there are so many diabetics, that is just due to our long-term association with the Joslin Diabetic Clinic, and in fact years ago the number would be closer to 80% or 90%. As far as level of diabetes, I do not have that specific information. We did a limited look at it and it did not seem to make a difference, although your last question about sequelae—certainly patients with hemodialysis did worse in this study and in other studies, and most of our patients on hemodialysis are diabetic.