Prevalence and Risks of Undiagnosed Diabetes Mellitus in Patients Undergoing Coronary Artery Bypass Grafting

Achim H. Lauruschkat, MD; Bert Arnrich, MS; Alexander A. Albert, MD; Jörg A. Walter, PhD; Berthold Amann, MD; Ulrich P. Rosendahl, MD; Tejas Alexander, MD; Jürgen Ennker, MD

Background—Numerous studies have shown that diabetes mellitus (DM) is not identified and, consequently, inadequately treated in a substantial proportion of the patients in the general population. We know very little about the extent and the consequences of undiagnosed diabetes in the risk group of patients with coronary heart diseases. The objective of this study was therefore to determine the prevalence and the risks of undiagnosed DM among patients with coronary artery bypass.

Methods and Results—The data of 7310 patients who have undergone coronary bypass operations between 1996 and 2003 were analyzed. Depending on their diagnosis on admission and their fasting plasma glucose (FPG) level, these patients were classified as known diabetics, undiagnosed diabetics (FPG ≥126 mg/dL), or as nondiabetics (FPG <126 mg/dL) and were compared in terms of their preoperative, intraoperative, and postoperative characteristics. Among the patients with coronary bypass that we examined, we found a prevalence of diagnosed diabetics of 29.6%. The prevalence of patients with undiagnosed DM (FPG ≥126 mg/dL) was 5.2%. In comparison with the other groups (non-DM versus undiagnosed DM versus known DM), the undiagnosed diabetics more frequently required resuscitation (1.7% versus 4.2% versus 1.5%; P < 0.01) and reintubation (2.1% versus 5.0% versus 3.5%; P < 0.01) and often showed a longer period of ventilation >1 day (5.6% versus 10.5% versus 7.4%; P < 0.01). Perioperative mortality rate was highest in this group (0.9% versus 2.4% versus 1.4%; P < 0.01).

Conclusions—This study is the first to publish the prevalence of undiagnosed diabetes mellitus in cardiac surgery. During the perioperative and postoperative courses, these patients displayed a substantially higher morbidity and mortality rate.

(Circulation. 2005;112:2397-2402.)

Key Words: coronary disease ■ diabetes mellitus ■ diagnosis ■ mortality ■ risk factors

As early as 1974, the epidemiological data of the Framingham study have shown that diabetes mellitus—even after accounting for concomitant factors such as age, gender, body mass index (BMI), hypercholesterolemia, nicotine abuse, and arterial hypertension—is one important independent risk factor for the genesis of cardiovascular diseases. Compared with the standard population, diabetics have as much as a 2 to 3 times greater frequency of disorders of the cardiovascular system. Cardiovascular mortality rate among diabetics is 3 times higher than in the standard population. Even in cases of disturbances of the glucose tolerance without clinical diabetes mellitus, coronary insufficiency has been shown to have a higher incidence, and asymptomatic hyperglycemia has been shown to entail a substantially higher risk of cardiovascular death. In the perioperative and postoperative courses of coronary bypass operations, diabetic patients are often at a disadvantage compared with nondiabetic patients. Hospital mortality among diabetics is significantly increased; patients with diabetes mellitus had postoperative strokes more often and spent, on average, more days in hospital. The data of the Second National Health and Nutrition Examination Survey demonstrate a prevalence of diabetes mellitus in the population of the United States of 2% in the group 20 to 34 years of age, with an increase of almost 20% among the patients between 65 and 74 years of age. Among approximately 50% of the diabetics in all age groups, the disease had not been previously diagnosed at the time the study was conducted. Since that time, numerous studies on the prevalence of undiagnosed diabetes mellitus have been published. Current data from Germany show a prevalence of diabetes mellitus of 16.6% among the age group 55 to 74 years, again with the disease having gone unnoticed in half the cases. However, we know very little about the extent and the consequences of undiagnosed diabetes mellitus in high-risk groups such as patients with coronary heart diseases.
studies have to date been published on the prevalence of undiagnosed diabetes mellitus in coronary bypass patients and its impact on the perioperative and postoperative results.

Methods
The study included 7310 patients who had undergone coronary bypass operations at the Heart Institute Lahr/Baden in the period between January 1996 and June 2003. Emergency interventions, combined procedures and "re-do" operations were excluded from the study. Patient care, both at the operative and the postoperative stages, followed the standardized guidelines of our hospital. For each patient included in the present study, 32 preoperative characteristics and 8 postoperative progress values were used from the consolidated database of our Data Mart system. The data were based on the anesthesiological and cardiosurgical quality assurance and the laboratory data of the clinical chemistry.

Definitions
The following definitions, essentially applied in analogy with the EuroSCORE, were used for the risk factors investigated: peripheral vascular disease: claudication, previous or planned intervention involving the arteries of the limbs; carotid disease: carotid occlusion or >50% stenosis, previous or planned intervention on the carotids; neurological dysfunction: severely affecting ambulation or day-to-day functioning; chronic obstructive pulmonary disease (COPD): long-term use of bronchodilators or steroids for lung disease; pulmonary hypertension: systolic pulmonary artery pressure >60 mm Hg; recent myocardial infarction: myocardial infarction occurring within 90 days; unstable angina: rest angina requiring intravenous nitrates until arrival in the anesthetic room (patients who were not fully without symptoms under intravenous nitrate medication were declared as "emergency cases" and excluded from the study); stroke: a new focal neurological deficit or coma lasting more than 24 hours, associated with computed tomographic demonstration or recent ischemic cerebral lesion; and cerebral dysfunction: in comparison with the preoperative status, abnormality in behavior and temporal and spatial disorientation that are also clinically conspicuous without specific psychiatric examinations. Diabetes was diagnosed by using the current recommendations by the American Diabetes Association: The determination of the diabetes status in epidemiological studies is based on the measurement of the fasting plasma glucose level (FPG ≥126 mg/dL (7.0 mmol/L)). Patients admitted and diagnosed with diabetes mellitus or treated with oral antidiabetic agents or with insulin before their admission were assessed as having known diabetes. Depending on their FPG level, the remaining patients were classified either as having undiagnosed diabetes (FPG ≥126 mg/dL) or as having no diabetes (FPG <126 mg/dL). These groups of patients were compared in terms of their preoperative characteristics and risk factors and the data of their postoperative progress.

Statistical Analysis
Univariate comparisons between the 3 patient groups investigated (known diabetics, undiagnosed diabetics, and nondiabetics) were performed by using the χ² test for categorical variables and the Mann-Whitney test for continuous variables (SPSS, 12.0). Stepwise logistic regression was used to determine the predictors of the hospital outcomes of interest by minimizing the so-called Akaike Information Criterion. All baseline attributes and 2 additional dichotomous indicator variables encoding the diabetes status were initially used in the regression tasks. To obtain a nondiabetic reference group, the 2 indicator variables were defined as follows: known diabetes mellitus=1 for diagnosed diabetes, 0 otherwise, and undiagnosed diabetes mellitus=1 for undiagnosed diabetes, 0 otherwise. In cases where only 1 indicator variable remained significant in the final model, the counterpart was forced into the model respectively. Model discrimination was evaluated by the area under the receiver operating characteristic curve.

Results
Table 1 shows the distribution of the patients we investigated according to the diagnostic criteria applied. The demographic and clinical characteristics of the nondiabetic coronary patients versus the undiagnosed diabetics and the known diabetics are shown in Table 2.

Baseline Characteristics
On average, diabetic coronary patients in cardiac surgery were significantly older than nondiabetic patients. Women, patients with a higher BMI, and patients with arterial hypertension were significantly overrepresented among the diabetic patients. In this respect, the undiagnosed diabetics did not differ significantly in all aspects from nondiabetic patients, but their data tended to lie between the nondiabetic patients and diagnosed diabetics. Known and undiagnosed diabetics had a significantly higher prevalence of peripheral vascular disease than did nondiabetics. A history of strokes was most frequently found among the group with known diabetes. These patients also had COPD significantly more often than did patients with undiagnosed diabetes and nondiabetic patients with coronary disease.

Clinical Cardiac Parameters and Angiographic Findings
Diabetic patients were more frequently admitted to cardiac surgery with New York Heart Association functional class IV symptoms than were nondiabetic patients, but the highest proportion of patients in NYHA functional class IV was found among the undiagnosed diabetics (8.4% undiagnosed diabetes mellitus versus 6.0% no diabetes mellitus; P=0.06). Patients with restricted left ventricular ejection fraction were found significantly more often among the known diabetics, whereas the known diabetics and the undiagnosed diabetics showed a significantly higher prevalence of coronary 3-vessel diseases than did nondiabetic patients with coronary disease. The frequency of main stem stenoses showed a declining, downward tendency from nondiabetics to undiagnosed diabetics and known diabetics.

Laboratory Parameters
On average, the diabetic group of patients showed higher leukocyte values than those of the nondiabetic patients. Also, we found the highest total cholesterol values among the group of undiagnosed diabetics. The renal function tests (creatinine, urea) showed a rising tendency from nondiabetics over undiagnosed diabetics to known diabetics.

Medication
The medication history also showed a certain heterogeneity. Known diabetics have been treated before surgery more often

### Table 1. Patient Distribution

<table>
<thead>
<tr>
<th>FPG</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;126 mg/dL</td>
<td>4.769 (65.2)</td>
</tr>
<tr>
<td>≥126 mg/dL</td>
<td>380 (5.2)</td>
</tr>
<tr>
<td>Known diabetes</td>
<td>2.161 (29.6)</td>
</tr>
<tr>
<td>Total</td>
<td>7.310 (100)</td>
</tr>
</tbody>
</table>

FPG indicates fasting plasma glucose.

FPG indicates fasting plasma glucose.
TABLE 2. Baseline Characteristics for the 3 Patient Groups in Percent or as Group Average (With Units)

<table>
<thead>
<tr>
<th>Demographic profile</th>
<th>No Diabetes (n=4769)</th>
<th>Undiagnosed Diabetes (n=380)</th>
<th>Known Diabetes (n=2161)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.09</td>
<td>66.34*</td>
<td>66.58†</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>81.2</td>
<td>128.6†</td>
<td>14.4†</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.46</td>
<td>27.92†</td>
<td>28.61†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical history</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, %</td>
<td>73.4</td>
<td>75.0</td>
<td>83.61§</td>
</tr>
<tr>
<td>Carotid disease, %</td>
<td>9.1</td>
<td>11.1†</td>
<td>12.7†</td>
</tr>
<tr>
<td>Past stroke, %</td>
<td>6.2</td>
<td>5.3</td>
<td>9.1†‡</td>
</tr>
<tr>
<td>Neurological dysfunction, %</td>
<td>6.2</td>
<td>6.1</td>
<td>10.2‡</td>
</tr>
<tr>
<td>COPD, %</td>
<td>19.4</td>
<td>19.5</td>
<td>26.01§</td>
</tr>
<tr>
<td>Pulmonary hypertension, %</td>
<td>2.6</td>
<td>2.1</td>
<td>3.4</td>
</tr>
<tr>
<td>Recent myocardial infarction, %</td>
<td>23.7</td>
<td>28.9*</td>
<td>26.9†</td>
</tr>
<tr>
<td>Unstable angina, %</td>
<td>10.4</td>
<td>14.5*</td>
<td>9.8§</td>
</tr>
<tr>
<td>NYHA class 4, %</td>
<td>6.0</td>
<td>8.4</td>
<td>7.7†</td>
</tr>
<tr>
<td>Ejection fraction, 30%–50%, %</td>
<td>28.0</td>
<td>30.8</td>
<td>36.9†‡</td>
</tr>
<tr>
<td>Ejection fraction &lt;30%, %</td>
<td>3.6</td>
<td>2.4</td>
<td>5.8†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Angiographic characteristics</th>
<th>No Diabetes (n=4769)</th>
<th>Undiagnosed Diabetes (n=380)</th>
<th>Known Diabetes (n=2161)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Vessel disease, %</td>
<td>10.5</td>
<td>6.1†</td>
<td>6.8†</td>
</tr>
<tr>
<td>2-Vessel disease, %</td>
<td>32.7</td>
<td>29.5</td>
<td>28.9†</td>
</tr>
<tr>
<td>3-Vessel disease, %</td>
<td>49.0</td>
<td>59.5‡</td>
<td>57.3†</td>
</tr>
<tr>
<td>Main stem disease, %</td>
<td>19.5</td>
<td>17.9</td>
<td>16.5†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dL</td>
<td>13.95</td>
<td>13.94</td>
<td>13.59§</td>
</tr>
<tr>
<td>Erythrocytes, 10¹²/μL</td>
<td>4.53</td>
<td>4.54</td>
<td>4.46§</td>
</tr>
<tr>
<td>Thrombocytes, 10³/μL</td>
<td>234.5</td>
<td>234.4</td>
<td>234.6</td>
</tr>
<tr>
<td>Leukocytes, 10³/μL</td>
<td>7.61</td>
<td>8.03†</td>
<td>7.90†</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>203.7</td>
<td>212.0†</td>
<td>197.5§</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.13</td>
<td>1.19†</td>
<td>1.21†</td>
</tr>
<tr>
<td>Urea, mg/dL</td>
<td>38.77</td>
<td>43.41†</td>
<td>45.49§</td>
</tr>
<tr>
<td>Creatine kinase, U/L</td>
<td>44.14</td>
<td>43.85</td>
<td>44.35†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors, %</td>
<td>47.0</td>
<td>43.9</td>
<td>59.9§</td>
</tr>
<tr>
<td>Aspirin, %</td>
<td>25.6</td>
<td>25.0</td>
<td>24.1</td>
</tr>
<tr>
<td>β-Blockers, %</td>
<td>69.1</td>
<td>63.4*</td>
<td>64.5†</td>
</tr>
<tr>
<td>Diuretics, %</td>
<td>17.6</td>
<td>21.6</td>
<td>31.9§</td>
</tr>
<tr>
<td>Nitrates, %</td>
<td>62.0</td>
<td>62.1</td>
<td>61.5</td>
</tr>
</tbody>
</table>

Tests on group equivalence are performed by using the χ² test (for categorical data) and Mann-Whitney test (for continuous variables). Significant difference of undiagnosed or known diabetes to no-diabetes group: *P<0.05, †P<0.01.

Significant difference of known diabetes to undiagnosed diabetes group: ‡P<0.05, §P<0.01.

n indicates No. of cases remaining after listwise deletion of cases with any missing values (initial frequencies: age, 0.1%; body mass index, 0.2%; carotid disease, 3.4%; past stroke, 4.8%; chronic obstructive pulmonary disease, 3.4%; pulmonary hypertension, 1.8%; recent myocardial infarction, 3.1%; New York Heart Association class IV, 1.8%; hemoglobin, 2.2%; erythrocytes, 2.5%; thrombocytes, 2.4%; leukocytes, 2.7%; total cholesterol, 3.8%; creatinine, 2.2%; urea, 2.7%; creatine kinase, 2.2%; ACE inhibitors, 2.6%; aspirin, 2.6%; β-blockers, 2.6%; diuretics, 2.6%; nitrates, 2.6%; others, 0%).

TABLE 3. Hospital Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No Diabetes</th>
<th>Undiagnosed Diabetes</th>
<th>Known Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary resuscitation, %</td>
<td>1.7</td>
<td>4.2†</td>
<td>1.5§</td>
</tr>
<tr>
<td>Renal failure-dialysis, %</td>
<td>1.7</td>
<td>2.9</td>
<td>4.8↑</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>1.4</td>
<td>2.1</td>
<td>2.3↑</td>
</tr>
<tr>
<td>Cerebral dysfunction, %</td>
<td>4.7</td>
<td>6.3</td>
<td>8.2↑</td>
</tr>
<tr>
<td>Reintubation, %</td>
<td>2.1</td>
<td>5.0†</td>
<td>3.5↑</td>
</tr>
<tr>
<td>Ventilation time &gt;1 day, %</td>
<td>5.6</td>
<td>10.5†</td>
<td>7.4↑</td>
</tr>
<tr>
<td>Intensive care unit stay &gt;3 days, %</td>
<td>27.0</td>
<td>28.7</td>
<td>35.1↑</td>
</tr>
<tr>
<td>30-Day mortality rate, %</td>
<td>0.9</td>
<td>2.4†</td>
<td>1.4*</td>
</tr>
</tbody>
</table>

With ACE inhibitors and diuretics, whereas the non-diabetic patients with coronary disease had been given β-blockers more often than the diabetic patient groups.

Hospital Outcome

At the postoperative stage, undiagnosed diabetics needed resuscitation significantly more often than the other patient groups examined (no diabetes mellitus, 1.7% versus undiagnosed diabetes mellitus, 4.2% versus known diabetes mellitus, 1.5%), see Table 3. Among the known diabetic patients with coronary disease, postoperative renal failure requiring dialysis occurred significantly more often (4.8%) than in nondiabetics (1.7%) or the undiagnosed diabetics (2.9%). Perioperative strokes occurred more often among diabetic patients with coronary disease (2.3%) than among nondiabetics (1.4%). Also, cerebral dysfunction occurred significantly more often among these patients (8.2%) than in non-diabetic patients with coronary disease (4.7%).

Diabetics required postoperative reintubation more often (3.5%) than nondiabetics (2.1%), with the rate of reintubation being highest among the undiagnosed diabetics (5.0%). The number of patients requiring respiration for periods longer than 1 day was also highest among these patients (no diabetes mellitus, 5.6%, versus undiagnosed diabetes mellitus, 10.5%, versus known diabetes mellitus, 7.4%). The number of patients staying in the intensive care unit for postoperative periods longer than 1 day was also highest among these patients (no diabetes mellitus, 27.0%, versus undiagnosed diabetes mellitus, 28.7%, versus known diabetes mellitus, 35.1%). Known and undiagnosed diabetics showed a significantly higher 30-day mortality rate, with the highest mortality rate found in the group of undiagnosed diabetics (no diabetes mellitus, 0.9%, versus undiagnosed diabetes mellitus, 2.4%, versus known diabetes mellitus, 1.4%).

Table 4 shows the 4 resulting stepwise logistic regression models for hospital outcomes in which undiagnosed diabetes remained significant in the final model. The results show that undiagnosed diabetes mellitus can be considered as an independent risk factor for (1) longer respiration times, (2) more frequent reintubations, (3) resuscitation at the postoperative stage, and (4) an increased 30-day mortality rate.
Ventilation time
Reintubation†
diagnoses in younger years.
ities but may also suggest more comprehensive preoperative
demographic changes and changes in the assignment modal-
26.7% (1998). The reasons for this phenomenon are found in
with coronary bypass in recent years from 18.6% (1990) to
consistent rise in the prevalence of diabetes among patients
LVEF (COPD), leucocytes, creatine kinase, urea, unstable angina, LVEF 30% to 50%, LVEF
levels, and unstable angina, recent myocardial infarc-
tion, total cholesterol, 2-vessel disease, LVEF 30% to 50%, LVEF <30%, β-blockers; area under ROC, 0.69.
Further covariates (full model): Age, COPD, neurological dysfunction, leucocytes, creatine kinase, urea, unstable angina, recent myocardial infarction, total cholesterol, 2-vessel disease, LVEF 30% to 50%, LVEF <30%, β-blockers; area under ROC, 0.70.
Further covariates (full model): Age, past stroke, COPD, leucocytes, urea, main stem disease, LVEF 30% to 50%, LVEF <30%; area under ROC, 0.77.

Discussion
The prevalence of diagnosed diabetes mellitus in the patient
population investigated by us was 29.6%. The prevalence of
undiagnosed diabetes was 5.2%. Taking these patients into
consideration, the total share of diabetic patients with coro-
nary disease rose to 34.8%. Abramov et al14 reported a
consistent rise in the prevalence of diabetes among patients
with coronary bypass in recent years from 18.6% (1990) to
26.7% (1998). The reasons for this phenomenon are found in
demographic changes and changes in the assignment modal-
ities but may also suggest more comprehensive preoperative
diagnoses in younger years.

Baseline Characteristics
Diabetic patients showed a significantly higher prevalence of
the known cardiovascular risk factors such as raised BMI, age, and arterial hypertension. The results obtained by Taub-
ert et al15 show a progression of cardiovascular risk factors
over the various categories ranging from “nondiabetics” over
“undiagnosed diabetics” through to “known diabetics.” The
data from other authors showed a higher prevalence of
overweight and other cardiovascular risk factors, mainly in
the group of undiagnosed diabetics.8,9,16 The observation that
diabetic patients with coronary disease have peripheral vas-
cular disease significantly more often is also described by
other authors.17,18 Stroke in the patient history was found
significantly more often among the group of known diabetics.
The more advanced age of diabetic patients must be taken
into account in this context, considering that it is accompa-
nied by advancing atherosclerosis, the higher risk of embolic
events, and by changes in the cerebral vessels and in the
blood flow autoregulation.19

Clinical Cardiac Parameters and
Angiographic Findings
The data obtained in the present study demonstrated that
diabetics are more frequently admitted with NYHA func-
tional class IV symptoms and often have a lower ejection
fraction than nondiabetic patients with coronary disease.
These results are consistent with the observations made by
many other authors.1,5,17,20 Patients with a longer duration of
the diabetic disorder more often showed signs of diabetic
neuropathy, which, in turn, may result in myocardial infarc-
tions progressing painlessly or atypically or manifest them-
theselves as cardiac insufficiency, cardiac shock, or arrhyth-
ia.21 This means that the diagnosis is more difficult and that
the adequate therapy is often initiated with a delay. Zarich et
al22 reported that more than 90% of the ischemic episodes
progressed asymptomatically among the diabetic patients
they observed. This high number of asymptomatic ischemic
episodes could result in these patients later being diagnosed
as nondiabetic and consequently admitted to cardiac surgery
at an advanced stage of coronary heart disease. Consequently,
we found a significantly higher number of patients with
冠状动脉3- vessel disease among the diabetic coronary pa-
tients (see Table 2).

Laboratory Parameters and Medication
The highest mean total cholesterol values (see Table 2) were
found among the group of undiagnosed diabetics, a result that
is also reported by other authors9,16 and could suggest that
these patients have hitherto not been treated commensurately
with their risk profile. ACE inhibitors and diuretic medication
is found significantly more often among the known diabetic
patients with coronary disease (unfortunately, proper data on
statin medication were not available).

The progressive abnormalities in renal function tests as
seen in diabetics compared with undiagnosed diabetics is not
surprising, as a higher incidence of diabetic nephropathy
would be expected among those having diabetes for a longer
time.

Hospital Outcome
The results of the present study showed that neurological
damage and states of disorientation in the postoperative
course of coronary bypass operations occurred significantly
more often among known diabetics. Studies have demon-
strated that diabetics show subclinical but objectively mea-
surable impairments of the cognitive cerebral functions23 that
correlate directly with the duration of the disorder.24 These
patients are particularly at risk during cardiac surgery inter-

<table>
<thead>
<tr>
<th>Diabetes Status</th>
<th>No. of Events</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary resuscitation†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed DM</td>
<td>16</td>
<td>2.51</td>
<td>2.38</td>
<td>1.37–4.15</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Known DM</td>
<td>33</td>
<td>0.89</td>
<td>0.78</td>
<td>0.52–1.19</td>
<td>0.25</td>
</tr>
<tr>
<td>Reintubation†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed DM</td>
<td>19</td>
<td>2.41</td>
<td>1.89</td>
<td>1.12–3.19</td>
<td>0.02</td>
</tr>
<tr>
<td>Known DM</td>
<td>76</td>
<td>1.67</td>
<td>1.25</td>
<td>0.92–1.72</td>
<td>0.16</td>
</tr>
<tr>
<td>Ventilation time &gt;1 day‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed DM</td>
<td>40</td>
<td>1.98</td>
<td>1.75</td>
<td>1.21–2.53</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Known DM</td>
<td>159</td>
<td>1.33</td>
<td>1.01</td>
<td>0.82–1.26</td>
<td>0.90</td>
</tr>
<tr>
<td>Mortality§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed DM</td>
<td>9</td>
<td>2.80</td>
<td>2.23</td>
<td>1.04–4.79</td>
<td>0.04</td>
</tr>
<tr>
<td>Known DM</td>
<td>31</td>
<td>1.68</td>
<td>1.17</td>
<td>0.72–1.91</td>
<td>0.54</td>
</tr>
</tbody>
</table>

For each outcome, the crude OR (resulting from simple logistic models where only the 2 indicator variables undiagnosed diabetes mellitus [DM] and Known DM were included) and the adjusted OR with additional covariates and the area under the receiver operating curve (ROC) given in the footnote are presented. Confidence intervals and P values correspond to the adjusted models, respectively.

*Further covariates (full model): Age, carotid disease, leucocytes, creatine kinase, unstable angina, main stem disease, left ventricular ejection fraction (LVEF) <30%; area under ROC, 0.68.
†Further covariates (full model): Age, chronic obstructive pulmonary disease (COPD), leucocytes, creatine kinase, urea, unstable angina, LVEF 30% to 50%, LVEF <30%; β-blockers; area under ROC, 0.69.
‡Further covariates (full model): Age, COPD, neurological dysfunction, leucocytes, creatine kinase, urea, unstable angina, recent myocardial infarction, total cholesterol, 2-vessel disease, LVEF 30% to 50%, LVEF <30%, β-blockers; area under ROC, 0.70.
§Further covariates (full model): Age, past stroke, COPD, leucocytes, urea, main stem disease, LVEF 30% to 50%, LVEF <30%; area under ROC, 0.77.
ventations. Other authors report that diabetics, in the perioperative course of a bypass operation, are significantly more at risk of having strokes and transient ischemic attacks to fall into permanent coma or to die from stroke or hypoxic encephalopathy. Potential causes include cerebrovascular autoregulation impaired in diabetics under the extracorporeal circulation and a generalized atherosclerosis affecting the aorta, the carotids, and the cerebral arteries. The significantly longer average ventilation time and the high number of reintubations of diabetic patients at the postoperative stage, even after accounting for risk factors such as age, BMI, preexisting COPD, and so forth, was also remarkable. These results are explicable if the lung as a target organ of diabetic microangiopathy is also taken into account.27 Pathological studies involving diabetics found basal lamina thickening both of the alveolar epithelium and of the capillary endothelium.28 Pulmonary dysfunctions—clinically inconspicuous under normal conditions—could, as it were, be “unmasked” by the “capillary leak” and other pathophysiologic conditions developing after the use of extracorporeal circulation.

The rise in hospital mortality rates of diabetic patients that we observed is also reported by other authors.5 Remarkably, the highest mortality rate was found among the group of undiagnosed diabetics. It should be noted, however, that these patients—as shown in Table 2—have a characteristic risk profile without, however, having been appropriately treated as known diabetics. With regard to their vascular status (peripheral vascular disease, carotid disease, past stroke), undiagnosed diabetics appear to be less predisposed than diagnosed diabetics. With regard to the cardiovascular risk factors (age, BMI, arterial hypertension, and so forth) these patients stand between the known diabetics and the nondiabetics. These findings suggest a briefer duration of the disease, which may also explain the omitted diagnosis, particularly because type 2 diabetes is, on average, often diagnosed with a delay of as much as 7 years after the actual onset of the disease.29 The results of the present study show, however, that these patients are exposed to a particularly high risk in the perioperative and postoperative course of coronary bypass operations. It should be noted that the patients we examined do not constitute just any random sample from the total population but, by virtue of their coronary heart disease, have passed through a selection process that also involved extensive preoperative diagnostics before their admission to cardiac surgery. The fact that the proportion of undiagnosed diabetics was so large among these patients may be surprising but is explicable: Levetan et al examined 1034 internistic and surgical hospitalized patients in an inner-city tertiary-care teaching hospital in Washington, DC, and found a rate of 33% of diabetics undiagnosed at the time of admission among the hyperglycemic patients. What surprised the investigators, however, was the discovery that only 7.3% of the previously undiagnosed diabetics were actually diagnosed in the continued course of their hospital stay. The treating physicians presumably believed the cause of the increased blood sugar values to be more a “stress hyperglycemia” as an expression of the acute disease rather than considering the diagnosis of a previously undetected diabetes mellitus. The problem may have been that there are as yet no uniform diagnostic criteria or recommendations for a definite diabetes diagnosis in situations of clinical stress. Husband et al examined patients admitted with suspected acute myocardial infarction and showing increased level of plasma glucose. Among these patients, whose glucose values would certainly have been interpreted often as “stress hyperglycemia” on inpatient admission, a normal glucose tolerance was found in one third of the patients during the follow-up check 1 month later. The study by Norhammar et al22 in the year 2002 confirmed these findings.

In view of the high risk that this disease entails, especially for patients with coronary disease, clinicians are urgently advised to rate hyperglycemia as diabetes mellitus until proof to the contrary is shown.

Because the patient population is not very different from other national heart institutes, the hypothesis arises that our finding can be generalized to a wider field of patients with cardiac disease in the Western industrialized world.

The high proportion of undiagnosed diabetics among patients with coronary disease that we observed could also have some relevance in the analysis of earlier studies. In the past, numerous major studies have tried to establish which revascularization method—bypass surgery or the methods of interventional cardiology (PTCA/stenting)—delivers better results. The investigators of the Bypass Angioplasty Revascularization Investigation (BARI) reported that in the 5-year survival, there were no significant differences between these therapy strategies.35 However, the infarction mortality rate in the subgroup of patients with diabetes mellitus assigned to the coronary surgery group was significantly lower than that in the PTCA group.34 The results of the Northern New England Cardiovascular Disease Study Group,35 published later, and of the Arterial Revascularization Therapy Study (ARTS)36,37 confirmed that coronary surgery leads to significantly better results in diabetic patients. The issue common to all these studies is that the “diabetes mellitus” status was acquired only under categorical terms. The decisive factor in the assignment to this group was the diagnosis made by the admitters, the information given by the patient during anamnesis, and the documented therapy using oral antidiabetic agents or insulin therapy. No objective data such as the FPG values were obtained. The possibility that there might be a relevant group of undiagnosed diabetics was obviously ignored in these studies. One may therefore assume that the unidentified diabetics in the group of the “nondiabetics” will show a pronounced drop in the observable differences between diabetic and nondiabetic patients with coronary disease. Considering the observed high prevalence of undiagnosed diabetics among patients with coronary disease, the conclusion seems evident that diabetics could benefit to a greater extent than previously assumed from bypass operations versus the measures of interventional cardiology.

Furthermore, it is highly recommended that clinical practice and future studies focus on the possibly concealed factor of diabetes mellitus, which can be easily detected by measuring the FPG concentration. Our study emphasizes the importance of this general advice of the American Diabetes Association for the field of coronary surgery.
Acknowledgment

The authors thank Sarah Garner, Renate Böhmer, Peter Mühlecker, and Ulrike Ritzauf (Heart Institute Lahr/Baden) for expert help with data collection.

References


Prevalence and Risks of Undiagnosed Diabetes Mellitus in Patients Undergoing Coronary Artery Bypass Grafting

Achim H. Lauruschkat, Bert Arnrich, Alexander A. Albert, Jörg A. Walter, Berthold Amann, Ulrich P. Rosendahl, Tejas Alexander and Jürgen Ennker

_Circulation_. 2005;112:2397-2402
doi: 10.1161/CIRCULATIONAHA.105.534545

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/112/16/2397

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/