Trends in Lipid Management Among Patients With Coronary Artery Disease

Has diabetes received the attention it deserves?

OBJECTIVE — To examine lipid management trends for coronary artery disease (CAD) patients with and without diabetes in order to determine whether those with diabetes are beginning to receive aggressive lipid management consistent with their elevated risk.

RESEARCH DESIGN AND METHODS — We used outpatient medical record data from 47,813 CAD patients seen at 295 medical practices participating in the Quality Assurance Program II between 1996 and 1998. Lipid testing rates, lipid treatment rates, and serum lipid concentrations are described for CAD patients with and without diabetes within strata of office visit date.

RESULTS — Lipid testing and treatment rates increased and mean lipid levels decreased markedly over time. Those with diabetes were 26% less likely to have a lipid profile and 17% less likely to receive a lipid-lowering medication than their non-diabetic counterparts, and this disparity did not diminish over time. Among treated patients, mean non–HDL cholesterol (non–HDL-C) and LDL cholesterol (LDL-C) declined less rapidly over time for patients with than without diabetes.

CONCLUSIONS — Although impressive progress was made in the outpatient lipid management of CAD patients, lipid management for CAD patients with diabetes improved no more rapidly, and in some cases less rapidly, than for nondiabetic patients. Given their higher risk, more effort is needed to ensure that CAD patients with diabetes receive aggressive lipid management.

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The increased risk of cardiovascular events associated with diabetes is well established (1–6). In a recent report from a Finnish cohort, Haffner et al. (2) demonstrate that diabetic patients without a prior myocardial infarction (MI) had approximately the same 7-year incidence of MI (~20%) as nondiabetic patients with a prior MI (2). This finding is consistent with a recent report of patients hospitalized with unstable angina or non–Q-wave MI showing that the 2-year event rate for diabetic patients without prior coronary artery disease (CAD) was similar to that of nondiabetic patients with prior CAD (3). Another important finding from both studies, and one especially relevant for this report, is that the incidence of new MI among diabetic patients with a prior MI is more than twice that of patients with either prior MI or diabetes alone. Others have demonstrated that CAD patients with diabetes are more likely to die following an MI than their non-diabetic counterparts (4–6).

Thus, a multitude of clinical and epidemiological evidence indicates that individuals with both CAD and diabetes are at an exceptionally high risk for new cardiovascular events and mortality compared with those with either CAD or diabetes alone (1–10). Patients with combined CAD and diabetes represent one of the highest risk populations commonly seen by physicians in the outpatient setting.

Although at high risk for future cardiovascular events, individuals with CAD and diabetes are as likely as those without diabetes to benefit from 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, subsequently referred to as statins, as a treatment to lower cholesterol. The Scandinavian Simvastatin Survival Study (4S), the Cholesterol and Recurrent Events (CARE) trial, and the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) trial are consistent in their findings that CAD patients with diabetes experienced reductions in relative risk with statin treatment of similar magnitude to the risk reductions for CAD patients without diabetes (11–13).

The results from the Heart Protection Study further demonstrate the benefits of statin treatment in patients with diabetes only (14). Given their elevated risk and similar lipid management goals, one would expect CAD patients with diabetes to be treated at least as aggressively as those without diabetes. Nevertheless, CAD patients, in general, continue to receive less than optimal lipid management, and those with diabetes may be relatively under-treated compared with those without diabetes (15–19). Hopefully, widespread dissemination and
implementation of lipid management guidelines have resulted in improved outpatient lipid management over time (20, 21). However, few studies have examined trends in lipid management.

We describe trends in lipid testing, lipid treatment, and serum cholesterol levels in a national population of CAD patients seen in the outpatient setting between 1996 and 1998 to determine whether clinical and public health efforts have indeed brought about improved lipid management for this high risk population. We further compare testing and treatment trends to assess whether CAD patients with diabetes, compared with those without diabetes, were receiving increasingly more aggressive lipid management over time, consistent with their higher risks.

**RESEARCH DESIGN AND METHODS** — Lipid testing rates, lipid-lowering drug prescription rates, and mean serum lipid concentrations were determined for patients most recently seen by physicians over nine consecutive quarters (i.e., 3-month time intervals). This information was obtained from medical record review for CAD patients seen by physicians participating in Quality Assurance Program (QAP)-II. QAP was designed to characterize patients and their medication usage related to the treatment of CAD and/or heart failure in an outpatient setting. Data collection methods and the study population differed between the first and second phases of the program (QAP-I and -II), as described elsewhere (15,16). Only trends during the more recent QAP-II are considered in this report. All data were obtained from medical chart reviews performed by ACCESS Medical (Arlington Heights, IL). Identifying patient, physician, and practice information was removed by ACCESS before the release of the data for analysis to ensure confidentiality.

Physicians writing large numbers of prescriptions for cardiovascular medications were invited to participate in QAP. Medical records were reviewed in each participating practice for a random sample of patients with CAD or heart failure. Only patients with CAD (with or without heart failure) were included in this analysis. These were identified from documented *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes (410–414), medical history, and cardiac procedures. Similarly, diabetes and other comorbidities were identified from diagnosis codes (e.g., 250.0–250.9 for diabetes), medical history, specific medications (e.g., insulin or oral hypoglycemics for diabetes), and/or medical procedures (22).

Indicators of lipid management were determined for patients within strata of quarter based on the date that the patient was most recently seen by the physician. Excluded were patients most recently seen by the physician 2 years or more before the review date and patients seen only once by the physician. The most current lipid management information was identified from the most recent and/or earlier patient-physician encounters. Individual patients were not followed over time.

We focused on three indicators of lipid management in this study: 1) the occurrence of medical record documentation of LDL cholesterol (LDL-C), non-HDL cholesterol (non–HDL-C), and/or lipid profile (i.e., lipid testing rate); 2) the occurrence of medical record documentation of a lipid-lowering medication prescription (i.e., lipid treatment rate); and 3) the mean serum LDL-C and non–HDL-C concentrations.

Although LDL-C is a primary predictor of CAD risk, we also measured non–HDL-C (23). National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines recommend non–HDL-C as a secondary target when triglycerides are >200 mg/dl, as is frequently the case among individuals with diabetes (21). Lipid testing was determined by the presence in the medical record of total cholesterol and HDL-C concentrations measured on the same date (non–HDL-C testing) and by the presence of LDL-C values (LDL-C testing). Non–HDL-C was calculated as total cholesterol minus HDL-C where values were documented on the same date. A lipid profile was defined as the presence of documented total cholesterol, LDL-C, HDL-C, and triglyceride values determined on the same date.

Lipid treatment was determined by whether the patient was prescribed one or more of any commonly used lipid-lowering medication. Both statins and nonstatins were included. Discontinued medications were not included. Lipid testing rates, treatment rates, and mean serum cholesterol levels (when recorded) were determined for patients seen by physicians in each quarter or in aggregates of quarters in some cases.

Logistic regression was used to examine time trends in lipid testing and treatment for CAD patients with and without diabetes. Lipid testing and lipid treatment were dependent variables in separate models including time and diabetes status as independent variables. The regressions were performed first with an ordinal variable representing time in quarters and a dichotomous diabetes indicator in the model to test for trend over time. Subsequently, the interaction term quarter × diabetes was added to see if the trends differed by diabetes status. Our a priori significance level for the interaction was 0.20. All logistic regression models controlled for age, sex, medical practice specialty, and location as potential confounding or explanatory variables in relations between time and lipid testing and time and lipid treatment.

Linear regression was used to examine relations of serum lipid concentrations with time and diabetes status. LDL-C and non–HDL-C concentrations were considered separately as continuous dependent variables in linear regression models with time (quarters) and diabetes status as independent variables. Similar to the logistic regression models, we used interaction terms to test whether changes in LDL-C and non–HDL-C over time were different for CAD patients with diabetes compared with those without diabetes. We controlled for both age and sex in linear regression models as potential confounding or explanatory variables.

**RESULTS**

**Patients**

The dataset included 47,813 patients with CAD randomly selected within 295 medical practices throughout the U.S. These patients were seen by 1,540 participating physicians from the first quarter of 1996 through the first quarter of 1998. The fewest patients (2%) were seen in the first quarter of 1996, and the most (23%) were seen in the third quarter of 1997. Patient age ranged from 21 to 97 years and averaged ~68 years (Table 1). Patients were somewhat more likely to be men. A large proportion of these CAD patients, approximately a quarter, had diabetes. Although patients were seen at
medical practices throughout the U.S., most practices were located in the northeast and midwest. Over half of the patients were identified in participating cardiology practices. Patients with diabetes were slightly younger on average and more likely to be women compared with those without diabetes.

### Lipid testing and treatment trends

Approximately 52% of the patients had lipid profiles. LDL-C and non-HDL-C values were documented for 61 and 58%, respectively, of all patients over the course of the study. Crude lipid testing rates for lipid profiles, LDL-C, and non-HDL-C during three-quarter (9-month) intervals (Fig. 1) increased markedly over time. Quarterly lipid profile rates ranged from 37 to 57% for patients without diabetes and from 28 to 50% for those with diabetes. The quarterly rates ranged from 32 to 51% for nondiabetic patients and from 33 to 50% for those with diabetes.

After controlling for potentially confounding and explanatory variables in logistic regression analyses (Table 2), patients seen in the first quarter of 1997 and 1998 were, respectively, 1.6 (95% CI 1.3–1.9) and 2.5 (2.1–3.0) times more likely to have a documented lipid profile than patients seen in the first quarter of 1996. Similarly, patients seen in first quarter of 1997 and 1998 were, respectively, 1.4 (1.1–1.9) and 2.2 (1.7–3.0) times more likely to receive a lipid-lowering drug prescription than patients seen in the first quarter of 1996. The choice of the referent quarter in these models had no substantial affect on our results and conclusions. These results confirm that the overall improvements in lipid testing and treatment described in Fig. 1 are statistically significant. Consistent with previous reports (16), patients of advanced age were markedly less likely to receive lipid testing and lipid drugs compared with their younger counterparts. Despite their elevated risks, patients with diabetes were 26% (odds ratio 0.74, 95% CI 0.70–0.77) less likely to have a lipid profile and 17% (0.83, 0.78–0.89) less likely to have a lipid drug prescription than patients without diabetes.

Logistic regression analyses revealed no significant interactions involving time.

### Table 1—Population characteristics

<table>
<thead>
<tr>
<th>Overall</th>
<th>Without diabetes</th>
<th>With diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>47,813</td>
<td>36,967</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.5 ± 0.0</td>
<td>68.7 ± 0.1</td>
</tr>
<tr>
<td>Women (%)</td>
<td>37</td>
<td>35</td>
</tr>
<tr>
<td>Practice* location (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>Northeast</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>South</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>West</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Practice* specialty (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>54</td>
<td>55</td>
</tr>
<tr>
<td>Family medicine</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Multi-specialty</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

*Medical practice where chart review performed.

Figure 1—Trends in the percent with documented lipid tests or lipid drug prescription for CAD patients with and without diabetes.
and diabetes status with regard to lipid testing and treatment, and results in Table 2 are from models not including the interaction term. Thus, the under-testing and under-treatment of CAD patients with diabetes compared with those without diabetes did not diminish during these nine quarters of the late 1990s.

### Lipid concentration trends

Declines in mean serum non–HDL-C and LDL-C concentrations were contemporaneous with improvements in testing and treatment. Trends in non–HDL-C and LDL-C for patients given lipid medications are shown in Fig. 2. Although there was substantial variability over time in quarterly means, especially for patients with diabetes, CAD patients with diabetes generally had higher non–HDL-C levels than those without diabetes. In contrast, quarterly mean LDL-C levels were typically lower among treated patients with diabetes compared with those without. The fitted curves suggest that treated patients without diabetes experienced a greater decrease in non–HDL-C over time than those with diabetes. Thus, the diabetes-related gap in non–HDL-C levels appears not to have diminished over time. Mean LDL-C levels also appear to decline more rapidly for treated patients without diabetes than with diabetes. As a result, the difference in LDL-C levels by diabetes status virtually disappears over time.

After controlling for age, sex, and diabetes in linear regression models with quarter × diabetes interaction terms (Table 3), a significant non–HDL-C and LDL-C decline was noted for CAD patients prescribed lipid drugs. These models also show that among patients given lipid drugs, time trends in non–HDL-C and LDL-C levels differed by diabetes status. Diabetes status was not significantly associated with serum non–HDL-C concentrations in the presence of the interaction term in the regression model even though non–HDL-C levels were higher on average for patients with diabetes compared with those without diabetes. The diabetes term lost significance in models containing the interaction term because the effect of diabetes status on non–HDL-C concentrations was absent in some quarters. For those without diabetes, each quarter was associated with a 2.5 mg/dl decline in non–HDL-C and a 2.3 mg/dl decline in LDL-C (Table 3). Non–HDL-C for diabetic patients was predicted to be 1.3 mg/dl higher than that of nondiabetic patients in the last quarter of 1996. This gap was predicted to increase by 0.7 mg/dl per quarter. As a result, during the remaining eight quarters the predicted non–HDL-C difference between patients with and without diabetes increased by >5 mg/dl. Similarly, LDL-C levels for diabetic patients declined less rapidly than those for nondiabetic patients. However, since LDL-C levels were initially higher on average for those without diabetes, the absolute difference in mean LDL-C levels between patients with and without diabetes diminished and virtually disappeared.

**CONCLUSIONS** — To summarize, we have demonstrated remarkable improvements in the management of dyslipidemia among patients with CAD.

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**Table 2** — The association of time, diabetes, and age with lipid profiles and prescriptions of lipid-lowering drugs

<table>
<thead>
<tr>
<th>Lipid profile*</th>
<th>Lipid-lowering drug prescription†</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>44,959</td>
</tr>
<tr>
<td>First quarter 1996</td>
<td>23,467</td>
</tr>
<tr>
<td>First quarter 1997</td>
<td>1.0</td>
</tr>
<tr>
<td>First quarter 1998</td>
<td>1.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.7</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>2.2</td>
</tr>
<tr>
<td>21–44</td>
<td>3.1</td>
</tr>
<tr>
<td>45–54</td>
<td>4.5</td>
</tr>
<tr>
<td>55–64</td>
<td>6.2</td>
</tr>
<tr>
<td>65–74</td>
<td>6.6</td>
</tr>
<tr>
<td>75–84</td>
<td>7.7</td>
</tr>
<tr>
<td>≥85</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Data are OR (95% CI). *From logistic regression models controlling for quarter, diabetes history, age, sex, geographic region, and medical practice type. †From logistic regression models controlling for quarter, diabetes history, age, sex, geographic region, medical practice type, and serum non–HDL-C concentrations among patients with documented lipid profiles.
Table 3—Linear regression coefficients relating serum lipid concentrations to time and diabetes status among patients with lipid-lowering drug prescriptions*

<table>
<thead>
<tr>
<th></th>
<th>Non–HDL-C†</th>
<th>LDL-C†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quarter (n = 15,678)</td>
<td>–2.49 (&lt;0.0001)</td>
<td>–2.26 (&lt;0.0001)</td>
</tr>
<tr>
<td>Diabetes (n = 16,924)</td>
<td>0.61 (0.85)</td>
<td>–10.05 (0.0003)</td>
</tr>
<tr>
<td>Diabetes × quarter</td>
<td>0.68 (0.17)</td>
<td>0.94 (0.0224)</td>
</tr>
</tbody>
</table>

From linear regression models controlling for quarter (1–9), diabetes, age, sex, and the interaction between quarter and diabetes. †Serum concentration (mg/dl) of non–HDL-C or LDL-C.

Although LDL-C is recognized as a primary predictor of CAD, emerging evidence suggests that non–HDL-C is also a significant risk factor in the development of CAD. Drawing on a large sample of elderly men from Finland, Italy, and the Netherlands, Menotti et al. (24) found a significant relationship between non–HDL-C and all-cause mortality in the Finnish and Dutch populations. A study of >3,000 men and women participating in the third examination cycle of the Framingham Offspring study demonstrated that non–HDL-C levels were significantly associated with CAD (25). More recent work has also shown significant associations between high levels of non–HDL-C and the presence of extensive fatty streaks in both abdominal aortas, right coronary arteries, and left anterior descending arteries (26,27).

In addition to the clinical significance of non–HDL-C for all patients, non–HDL-C appears to be particularly important for patients with diabetes. Dyslipidemia in patients with diabetes is often marked by high triglyceride levels. Especially if not measured directly, LDL-C values for these patients may be unreliable and misleading (23). Therefore, NCEP ATP III guidelines recommend non–HDL-C as a secondary target of treatment when triglycerides exceed 200 mg/dl with a goal for non–HDL-C of <130 mg/dl (21). Our findings highlight the need for increased attention to serum non–HDL-C among patients with diabetes and CAD. Not only is the gap in non–HDL-C between CAD patients with and without diabetes diminishing over time, but the mean non–HDL-C level for diabetic patients remains well above the target of 130 mg/dl.

Educational efforts aimed at both clinicians and patients are clearly needed in order to convey the importance of lipid management in patients dually diagnosed with CAD and diabetes. Current initiatives by both the American Diabetes Association (ADA) and the National Diabetes Education Program (NDEP) recognize this need. In their ABC campaign, the NDEP is clearly communicating that patients with diabetes and the clinicians who treat them must pay equal attention to glycemic (“A” for A1C), blood pressure (“B”), and lipid (“C” for cholesterol) control (28). The message that the macrovascular risks associated with diabetes must be properly managed in this high-risk population is also prominent in the ADA–American College of Cardiology (ACC) Make the Link program (29).

While educational programs are necessary for correcting problems of under-treatment, studies demonstrate that education and knowledge alone will not suffice to improve treatment patterns. Recent studies about the treatment of diabetes and hypertension suggest that physician attitudes and beliefs about chronic conditions, the patients they treat, and the pharmacological therapies used are important components of practice patterns and treatment decisions (30,31). Given the urgency of treating dyslipidemia in patients with CAD and diabetes, future studies should explore potential attitudinal causes of poor lipid management among diabetic CAD patients. It is possible, for example, that both physicians and patients focus on achieving glycemic control before treating dyslipidemia. The asymptomatic nature of dyslipidemia may also make its treatment less of a priority for patients and physicians. In addition, diabetic patients may worry more about complications such as amputation and blindness than the macrovascular complications of diabetes. Resource constraints, such as lack of physician time, lack of a nurse educator, and inadequate educational materials or programs may further hinder efforts at improving patient care (17).

In considering the findings from this study, several limitations must be kept in mind. Since the data for this study were collected via chart review, there is a potential for incomplete medical information. Data regarding adverse effects and patient compliance are difficult to assess from medical records. Although significant contraindications and adverse effects are uncommon for most popular lipid-lowering drugs, these conditions may have resulted in the intentional withdrawal of these medications from a mi-

and diabetes receive aggressive lipid management consistent with their higher risk.

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References
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