Comorbidity and Glycemic Control in Patients With Type 2 Diabetes

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Background: It is commonly believed that good glycemic control is hard to achieve in patients with diabetes mellitus and concurrent chronic illnesses.

Objective: To determine the impact of comorbidity on glycemic control at presentation and subsequent follow-up in patients with type 2 diabetes.

Methods: We studied 654 consecutive patients who presented to a diabetes clinic in 1997. Comorbidity was rated using the Chronic Disease Score (CDS) index, which is a validated, weighted score that takes into account the patient's age, sex, and classes of medications. Univariate and multivariate linear regressions were used to determine the contribution of age, body mass index (calculated as weight in kilograms divided by the square of height in meters), diabetes duration, type of therapy, and CDS to initial hemoglobin A1c (HbA1c) level. A similar analysis was performed for the 169 patients with follow-up HbA1c levels 6 months after presentation.

Results: Patients were 90% African American, and 66% female, with average age of 53 years. Average diabetes duration was 5 years; body mass index, 33; HbA1c level, 8.8%; and CDS, 1121 (range, 232-7953). At presentation, patients with higher CDSs tended to be older and to have a lower HbA1c level, but multivariate linear regression showed that receiving pharmacological therapy, younger age, and having a lower C-peptide level were the only significant contributors to HbA1c level. In the 169 follow-up patients, presenting characteristics were not significantly different from those of the full cohort: average initial HbA1c level was 8.8%; CDS, 1073. Their HbA1c level at 6 months averaged 7.5% and the CDS had no significant impact on their follow-up HbA1c level.

Conclusion: Comorbidity does not appear to limit achievement of good glycemic control in patients with type 2 diabetes.

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RESEARCH DESIGN AND METHODS

STUDY DESIGN

The Grady Health System Diabetes Clinic serves a predominantly African American population with type 2 diabetes, with high rates of comorbidity and diabetes-related complications.16,27 Four clinic visits are scheduled within the first 2 months after presentation, when therapy for patients with type 2 diabetes is focused on dietary approaches to glycemic control. If satisfactory metabolic control cannot be achieved during the first 2 months, then pharmacological therapy is initiated or intensified at subsequent visits. The goal for glycemic control is an HbA1c level of below 7.0%.

We studied 654 consecutive patients with type 2 diabetes who presented to the Diabetes Clinic in 1997. As described previously, patients were identified as having type 2 diabetes based on published accepted clinical criteria.16 A computerized patient registry, maintained at the Diabetes Clinic, provided data on patient characteristics, medications, and laboratory values. Medication lists are derived from clinic pharmacy records and patient self-report.

A variety of scales have been used in the literature to measure the chronic disease status of individual patients.11,12,26 These instruments may rely on data obtained from review of patients’ medical records, survey of patients’ self-report of different conditions, and analysis of insurance claims, discharge diagnoses, or outpatient pharmacy data. Although each approach has inherent limitations, we chose a scale derived largely from pharmacy data based on ease of use, ready availability to most practitioners, and nonintensive need for personnel resources. Patient comorbidity was quantitated using the Chronic Disease Score (CDS) developed by Von Korff and colleagues25 and revised by Clark et al26 at the Center for Health Studies, Group Health Cooperative of Puget Sound, Puget Sound, Wash. The CDS is based largely on the medications used by individual patients, information that was easily obtained from the Diabetes Clinic registry. The original CDS was developed using expert physicians’ rating of severity of diseases corresponding to various medications. We used the revised CDS,26 which corresponds to projected total health care costs. The revised CDS is a weighted index that takes into account the patient’s age and sex and diagnoses as derived from the classes of medications that are used. The weights are disease specific and are derived from regression models analyzing the effect of specific chronic conditions on total health care costs, as derived from the database of the Group Health Cooperative of Puget Sound. A person’s CDS is the sum of the weights corresponding to the different medication classes, regardless of how many different medications he or she is taking within a given class. For example, a 40-year-old man with uncomplicated diabetes would have a score of 232, whereas a 40-year-old man being treated for diabetes, hypertension, and cardiac and vascular disease would have a score of 3018. The revised CDS has been shown to correlate with health care costs, hospitalization, and mortality.26

Of the initial 654 patients who presented for the first time to the Diabetes Clinic in 1997, 169 patients had another HbA1c level measurement 6 months later. A post hoc analysis was performed to study the contribution of the CDS to the follow-up HbA1c level in this subset. Plasma glucose level was measured using a glucose oxidase method (APEC, Inc, Danvers, Mass). Hemoglobin A1c levels were measured by means of a turbidimetric immunoinhibition assay (Roche, Basel, Switzerland) (reference range, 3.5%-6.0%). Levels of C peptide were measured by means of an immunochromatimunoassay (LabCorp, Burlington, NC) (reference range, 0.3-1.3 nmol/L).

STATISTICS

We used CH² and Mann-Whitney tests to evaluate differences in baseline characteristics. Univariate linear regression was used to measure associations between continuous variables. Multivariate linear regression was used to determine the relative influence of age, sex, body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters), C peptide levels, duration of diabetes, type of diabetes therapy, and CDS on HbA1c levels. A P value of less than .05 was considered significant. We used commercially available software (SPSS, Version 9.0; SPSS, Inc, Chicago, Ill) for the analyses.

RESULTS

Patient characteristics at first presentation to the Diabetes Clinic are shown in Table 1. The 654 patients were predominantly African American, middle-aged, and obese. The average HbA1c level was 8.8%, and the average CDS was 1121, with a median of 731 (range, 232-7954). At presentation, 20% of patients were being treated with diet alone, 48% with oral agents, and 32% with insulin alone.
or in combination with oral agents. Although patients in these management groups had different average HbA1c levels (7.6% ± 0.2% for diet, 8.8% ± 0.1% for oral agents alone, and 9.0% ± 0.2% for insulin; P < .001 for each group compared with the other groups), their average CDSs were comparable (1129, 1127, and 1108, respectively). Hyperkalemia was the most common pharmacologically treated comorbid condition, with 53% of patients using antihypertensive medications. Patients were using medications for pain in 13% of cases, for hyperlipidemia in 10%, for cardiac disease in 7%, and for peripheral vascular disease in 3%. Other conditions included peptic ulcer disease, gout, glaucoma, arthritis, thyroid disease, tuberculosis, human immunodeficiency virus infection, cancer, seizure disorder, and respiratory, renal, hepatic, and psychiatric illnesses.

As expected, there was a direct correlation between age and CDS (r = 0.34; P < .001). Although there was an inverse correlation between CDS and HbA1c level (r = −0.13; P = .001), there was also a slightly stronger inverse correlation between age and HbA1c level at presentation (r = −0.20; P < .001). When patients were grouped according to quintiles of the CDS, it appeared that patients with higher CDSs had a tendency to be older and to have lower HbA1c levels (Figure 1). Using multivariate linear regression to account for any codependent effects of age, sex, diabetes duration, BMI, C-peptide level, and current therapy, we found that only age, C-peptide level, and type of therapy contributed significantly to HbA1c levels; after such corrections, the CDS did not contribute to HbA1c levels at presentation (Table 2). However, treatment with oral agents or insulin, younger age, or having a lower C-peptide level predisposed patients to have a higher HbA1c level at presentation.

A post hoc analysis was performed for those 169 patients who had an HbA1c level available in the database 6 months after their initial presentation. The follow-up subset had characteristics that were similar to those of the original sample (Table 1). To verify that a selection bias did not contribute to the grouping of patients in the follow-up subset, we compared their characteristics with those of patients in the initial cohort who did not have a 6-month follow-up visit. There was no significant difference in age, sex distribution, race, diabetes duration, BMI, or initial HbA1c level between patients who did and did not have a 6-month follow-up visit. Average CDS was 1073 for follow-up patients (median, 753). In the entire subset, average HbA1c level improved from 8.8% at baseline to 7.5% after 6 months of care (P < .001). Figure 2 shows that follow-up HbA1c levels also improved in each of the 5 quintiles of the CDS (although not significantly because of small numbers of patients in individual quintiles). Although the CDS exhibited a weak inverse correlation with follow-up HbA1c levels (r = −0.15; P = .05), multivariate linear regression revealed that only age and diabetes duration were significant contributors. Better follow-up HbA1c levels were achieved in older patients and in patients with shorter duration of diabetes (Table 3). Type of therapy at presentation had no significant impact on HbA1c level at follow-up.

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients at Presentation (n = 654)</th>
<th>Patients With 6-mo Follow-up (n = 169)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>53 ± 1</td>
<td>53 ± 1</td>
</tr>
<tr>
<td>% female</td>
<td>66</td>
<td>64</td>
</tr>
<tr>
<td>% African American</td>
<td>90</td>
<td>89</td>
</tr>
<tr>
<td>Diabetes duration, y</td>
<td>5.0 ± 0.3</td>
<td>5.1 ± 0.6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>32.7 ± 0.3</td>
<td>32.8 ± 0.6</td>
</tr>
<tr>
<td>C peptide level, mmol/L</td>
<td>0.86 ± 0.1</td>
<td>0.83 ± 0.1</td>
</tr>
<tr>
<td>Fasting glucose level, mmol/L (mg/dL)</td>
<td>10.3 ± 0.2 (186 ± 4)</td>
<td>10.1 ± 0.4 (182 ± 7)</td>
</tr>
<tr>
<td>HbA1c level at baseline, %</td>
<td>8.8 ± 0.1</td>
<td>8.8 ± 0.1</td>
</tr>
<tr>
<td>CDS†</td>
<td>1121 ± 40</td>
<td>1073 ± 69</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are given as mean ± SE. BMI indicates body mass index; HbA1c, hemoglobin A1c; and CDS, Chronic Disease Score. †Scoring is explained in the “Study Design” subsection of the “Research Design and Methods” section.

### Table 2. Multivariate Linear Regression Table Showing Contribution of Selected Variables to HbA1c Level at Presentation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standardized Coefficient</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>9.94</td>
<td>. . .</td>
</tr>
<tr>
<td>Age, y</td>
<td>−0.15</td>
<td>.001</td>
</tr>
<tr>
<td>Sex†</td>
<td>0.004</td>
<td>.91</td>
</tr>
<tr>
<td>Treatment with oral agent‡</td>
<td>0.21</td>
<td>.001</td>
</tr>
<tr>
<td>Treatment with insulin§</td>
<td>0.28</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes duration, y</td>
<td>0.02</td>
<td>.65</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>0.01</td>
<td>.86</td>
</tr>
<tr>
<td>C peptide level, mmol/L</td>
<td>−0.26</td>
<td>.04</td>
</tr>
<tr>
<td>CDS§</td>
<td>−0.07</td>
<td>.07</td>
</tr>
</tbody>
</table>

*Abbreviations are explained in the first footnote to Table 1. †In the calculation of linear regression, not receiving insulin equals 0, being female equals 1. ‡In the calculation of linear regression, not receiving an oral agent equals 0, receiving an oral agent equals 1. §In the calculation of linear regression, not receiving insulin equals 0, receiving insulin equals 1. ††Scoring is explained in the “Study Design” subsection of the “Research Design and Methods” section.

The increasing prevalence of chronic health problems has become a leading public health issue. Among chronic...
illnesses, diabetes mellitus constitutes a major health care burden, in view of its associated morbidity, mortality, and costs. In patients with diabetes, the presence of complications such as cardiovascular and renal disease increases costs, but better glycemic control is associated with less frequent hospitalizations. To our knowledge, this is the first report that examines the relation of chronic illness to glycemic control in patients with type 2 diabetes. On initial examination, we were surprised to find that patients with higher comorbidity tend to have better glycemic control at first presentation. However, after correcting for age and other factors, the contribution of comorbidity to glycemic control was no longer significant. This finding is supported by the independent observation that older patients in the Diabetes Clinic tend to have better glycemic control.

The reasons for the relationship between age and HbA1c level are unclear. It is possible that patients with higher HbA1c levels died younger because of diabetes-related vascular complications, and/or that older patients are more adherent to recommendations for meal planning and more compliant with pharmacological regimens compared with younger patients. Glasgow et al reported that older people with diabetes had significantly better scores than younger patients on an instrument that measured barriers to testing of glucose levels, regular physical activity, healthy low-fat eating, and compliance with medications. Additional studies have shown that older patients tend to keep their follow-up appointments more regularly than younger patients, and that patients who keep their follow-up appointments tend to achieve better glycemic control.

Although average HbA1c levels improved during 6 months of follow-up care, we found no evidence of a negative impact of comorbidity. Although there might be a selection bias in patients who made follow-up visits compared with those who did not, there was no difference in average CDS, or in other characteristics, between patients who had 6-month follow-up HbA1c levels available and those who did not. The only significant factors that contributed to follow-up HbA1c level measurement in our analysis were age and diabetes duration. Longer duration of diabetes is known to be associated with poor control, possibly because of progressive impairment of insulin secretion due to beta cell failure, compounding the adverse effects of insulin resistance.

Our analysis also showed that receiving pharmacological therapy for diabetes was associated with a higher HbA1c level at presentation. This is not surprising, because patients with more severe hyperglycemia are more likely to have been prescribed insulin or oral agents by their primary care providers compared with patients with milder hyperglycemia. The finding is also consistent with results from the Third National Health and Nutrition Examination Survey, which revealed that patients with diabetes who were treated with diet alone had an HbA1c level of 6.4%, compared with those treated with oral agents or insulin, who had HbA1c levels of 8.0% and 8.3%, respectively.

There is relatively little information about the effect of comorbidity on glycemic control. Hellman et al studied the effect of intensive glycemic control on renal failure and death in patients with diabetes. In their studies, patients with type 2 diabetes and elevated comorbidity scores had the same median glycated hemoglobin levels as patients with low scores. This finding is consistent with our observations. Our results also shed some light on an earlier report by Glynn et al that found a lower rate of drug treatment in patients with older age and higher comorbidity. The authors speculated that concern about adverse effects or reduced treatment benefits may have been reasons for the observed lower rate of drug therapy but did not present data on the level of glycemic control in their study population. Extrapolating from our results, it is conceivable that older patients with higher comorbidity may have had better glycemic control than younger and healthier patients, with less need for pharmacological therapy.

Limitations of our study include the reliance on retrospective analyses and lack of information about hypoglycemia, a potential concern for providers who are deciding whether to intensify therapy for diabetes. Although the incidence of severe hypoglycemia in type 2 diabetes is low, hypoglycemia may be more common in acutely or chronically ill patients. A recent study found an overall...
incidence of severe hypoglycemia of 2 episodes per 100 person-years in elderly persons with diabetes treated with insulin or sulfonylureas, but hypoglycemia appeared to occur disproportionately more often in the oldest old, frail, and frequently hospitalized patients.36 These are the same patients with the least tolerance of hypoglycemia, and for whom attempts at tight glycemic control would generally be least justified. A preliminary analysis of hypoglycemia in our clinic suggests that it is more common in younger compared with older patients.43 Our study was also conducted in a population of relatively obese African American patients in whom the type and severity of comorbid illnesses may be different from what would be expected in a more diverse population sample. Patients in our clinic may also face barriers to care that are commonly present in the inner city, such as limited access to health services, poverty, and poor functional health literacy.46 Any influence of these barriers on diabetes care outcomes might confound a potential effect of comorbidity. In addition, since our studies were conducted in a specialty diabetes clinic that emphasizes comprehensive care, the findings may not apply to health care delivery sites that are focused primarily on responding to acute patient complaints rather than management of chronic diseases. In such settings, the necessity for delivery of short-term care might limit time and resources available for optimal diabetes management, especially in patients with competing comorbidity conditions. Our conclusions also may not apply to acutely ill or hospitalized patients, since our study was restricted to scheduled outpatient visits.

Measures of disease status are being used increasingly for risk adjustment and to characterize case mix in study populations.22-24 The use of the CDS as a measure of comorbidity is appealing because it is simple and easy to use, is inexpensive, and relies on information that is readily available, especially in settings where pharmacy data are automated. Moreover, the CDS has been shown to correlate with health care outcomes.20 However, the CDS has its limitations. Since the CDS is a relative measure, it has generally not been used to characterize the state of health of individual patients. Because the CDS relies on a patient’s medication list to evaluate morbidity, illnesses that are not treated with drugs would also be missed. Similarly, patients who decline to take a prescribed medication for a particular illness or do not have their prescriptions filled would have their disease burden underestimated. In addition, relying on pharmacy data may focus attention more on medication-treated risk factors such as hypertension and hyperlipidemia, and on symptomatic complaints such as musculoskeletal pains, than on conditions of impaired functional status and severity of individual illnesses. Thus, the impact of having had a lower extremity amputation might be underemphasized, and the status of a patient with unstable angina might be graded similarly to that of a patient with stable coronary artery disease, as long as both patients are being treated with cardiac medications. These limitations should be considered when the CDS is used to compare global comorbidity between 2 populations or to sort patients in a particular population according to increasing relative comorbidity as derived from drug use.

In a specialty diabetes clinic caring for a predominantly African American patient population, chronic comorbidity conditions do not necessarily predispose patients to poor glycemic control. As the US population grows and ages, the number of individuals with diabetes and other chronic diseases is expected to increase. We believe that intensive diabetes management in these patients should still be pursued as long as therapeutic goals are consistent with life expectancy and problems with hypoglycemia can be avoided.

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REFERENCES


