Longitudinal Predictors of Reduced Mobility and Physical Disability in Patients With Type 2 Diabetes

The Fremantle Diabetes Study

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OBJECTIVE — The purpose of this study was to determine longitudinal predictors of impaired mobility and physical disability in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS — We studied patients with type 2 diabetes who participated in a prospective, community-based study. A wide range of baseline variables were examined to determine whether they predicted future difficulties with 1) mobility and 2) basic activities of daily living (ADLs) in patients free of ADLs difficulty at baseline. To study mobility impairment, subjects with baseline mobility problems were also excluded.

RESULTS — After an average 4.6 ± 2.3 and 4.8 ± 2.3 years of follow-up in 818 and 934 patients, respectively, 28.5% of subjects had developed new mobility impairment and 18.1% had developed new ADL disability. In Cox proportional hazards models, the risk of mobility impairment was significantly increased by older age (6%/year), peripheral neuropathy (40% increase), stroke history (123%), insulin treatment (117%), albuminuria, and arthritis (82%); taking exercise and being married lowered the risk (by 39 and 32%, respectively). The risk of new ADL disability was increased by baseline mobility problems (222% increase), stroke (92%), claudication (67%), and depression (41%) and was also influenced by age, smoking, lack of exercise, nonfluency in English, and indigenous Australian ethnicity.

CONCLUSIONS — Both mobility impairment and ADL disability in type 2 diabetes have multiple causes that are due to diabetes complications and common comorbidities. The specific causes of each functional problem are largely distinct, and different approaches may be required to prevent their onset or progression.

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Abbreviations: ADL, activity of daily living; CHD, coronary heart disease; CVD, cerebrovascular disease; FDS, Fremantle Diabetes Study; GHS, General Health Status

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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FDS was a prospective observational study of a representative sample of patients from a postcode-defined community of 120,097 people in Fremantle, Western Australia. The FDS protocol was approved by the human rights committee of Fremantle Hospital, and all subjects gave informed consent before participation. All people with diabetes living in the region were eligible to participate. Identification and recruitment methods, sample characteristics including classification of diabetes, and details of nonrecruited patients have been described elsewhere (16–18).

We identified 2,258 individuals with diabetes between 1993 and 1996 and recruited 1,426 (63%) to the FDS. Based on contemporaneous national data, this number was consistent with the proportion expected to have diabetes. Type 2 diabetes was defined clinically, after excluding secondary diabetes, as that treated with diet and/or oral hypoglycemic agents irrespective of age at diagnosis, 2) in patients aged ≥60 years at diagnosis whatever the treatment history, and 3) diagnosed between 40 and 60 years of age, treated with insulin at study entry but not at diagnosis, and associated with a BMI >30 kg/m². The FDS cohort included 1,294 (91%) type 2 diabetic subjects (mean age 64.1 ± 11.3 years, range 14.9–96.9).

The present study excluded subjects who did not return for follow-up assessment (259 subjects) and those with baseline disability. Two overlapping subgroups were studied: 1) 818 subjects who were free of mobility impairment and independent in ADLs at baseline (group 1) and 2) 934 subjects who were free of ADL problems at baseline (i.e., not excluding impaired mobility) (group 2). All subjects had at least partial follow-up, and attrition from the study by close-out (1 November 2001) was due to death (170 subjects from group 1 and 202 from group 2), moving from the study area (73 and 82 subjects, respectively), withdrawal (190 and 220 subjects, respectively), and unknown reasons (17 and 19, respectively).

Clinical assessment

At each patient's first and subsequent annual FDS visits, a comprehensive history was taken and a physical examination was performed. Detailed demographic and socioeconomic data were recorded, as was information relating to diabetes and its complications and all other comorbid conditions. Patients reported whether they had participated in physical exercise in the 2 weeks before the assessment. Each patient provided fasting blood and urine samples for automated biochemical analyses including the urinary albumin-to-creatinine ratio (17).

Peripheral sensory neuropathy was defined using the clinical portion of the Michigan Neuropathy Screening Instrument (19). Retinopathy was defined if any grade of retinopathy, including maculopathy, was detected by direct and/or indirect ophthalmoscopy in one or both eyes and/or more detailed data in patients assessed for photocoagulation. Visual acuity was assessed using Snellen charts and classified as normal (≥6/12 in the best corrected eye), impaired (<6/12 best corrected with pinhole or glasses but ≥6/120 in both eyes), or blind (in one or both eyes <6/120).

Self-reported stroke and transient ischemic attack were amalgamated with prior hospitalizations to define baseline cerebrovascular disease (CVD) status (20). Patients were classified as having CHD if there was a self-reported/hospital history of myocardial infarction, angina, coronary artery bypass grafting, angioplasty, and/or definite myocardial infarction on Minnesota coding of a resting 12-lead electrocardiogram (codes 1-1 and 1-2) (18). The ankle-to-brachial index was obtained by using brachial and ankle (with Doppler detection) systolic blood pressures and peripheral vascular disease was defined as ankle-to-brachial index ≤0.90.

Assessment of depression, mobility, and ADLs

All subjects completed the General Health Status (GHS) questionnaire (21), which addresses the five health domains of physical activity, self-care, pain, mental health, and autonomy. The assessment of depression was based on self-reporting of mood symptoms contained in the GHS. Subjects rated the presence and extent of feeling sad/depressed, anxious/worried, uncertain about the future, anger/resentment, guilt, loneliness, loss of self-confidence, difficulty sleeping, lack of energy, and inability to concentrate over the previous 2 weeks. A 10-cm visual-analog scale from “No distress at all” to “Extreme distress” was used for each variable.

Because this methodology has not previously been validated for the assessment of depression, we recruited a separate convenience sample of 51 patients (mean age 67.7 ± 6.0 years; 60.8% males) with type 2 diabetes drawn from other research studies. A trained researcher rated the subjects for the presence of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) depression syndromes using the Mini International Neuropsychiatric Interview that has been validated for making the major Axis I DSM-IV depression diagnoses (22). We decided a priori that GHS depression symptoms were present if a rating of ≥5 cm was chosen on the visual-analog scale and then determined whether the presence of ≥1, ≥2 or ≥3 GHS symptoms predicted DSM-IV depression. Twelve of the patients had clinical depression (six major depression, three minor depression, and three dysthymia). The presence of ≥2 GHS symptoms proved to be the best predictor of clinical depression (sensitivity 83.3% [95% CI 50.9–97.1], specificity 94.8% [81.4–99.1], positive predictive value 83.3% [50.9–97.1], and negative predictive value 94.8% [81.4–99.1]) and was used to identify baseline depression in the present FDS patients.

The GHS assesses four ADLs and mobility separately. Subjects were asked: “Do you have difficulty with any of the activities listed below? If you do, do you also need help from someone else to do them?” They self-rated their ability on the following: “Washing yourself,” “Dressing yourself,” “Eating and drinking,” and “Using the toilet,” by choosing from three degrees of difficulty: 1, no difficulty at all; 2, some difficulty but cope on my own; or 3, such difficulty that I need someone’s help. Because subjects who report difficulty but who can carry out ADLs independently have an increased risk for future ADL dependency (23), we dichotomized the data into no difficulty or any difficulty with ADLs to facilitate analysis.

The subjects selected one of six statements that best described their mobility: 1) I can move around indoors and outdoors on my own with no difficulty but I have to use a walking aid (e.g., stick, frame, crutch, wheelchair, etc.); 2) I can move around indoors and outdoors on my own with a little difficulty but with no aids or help; 3) I can get about indoors but outdoors on my own but I have to use a walking aid (e.g., stick, frame, crutch, wheelchair, etc.); 4) I can move around the house without anyone’s help, but I need someone’s help to get outdoors; 5) I spend nearly all my time confined to a chair (other than wheelchair); or 6) I spend nearly all my time in bed. We dichotomized the data into nor-
Predictors of mobility impairment

The 818 group 1 patients had a mean ± SD age of 62.5 ± 10.2 years, a median duration of diabetes of 3.0 years (interquartile range 0.8–8.0), and 50.0% were males. After an average of 4.6 ± 2.3 years follow-up, 28.5% had developed problems with mobility (77.7% reported having a little difficulty, 16.7% moved around with an aide, 4.3% needed help of another to go outdoors, and 1.3% reported being bed/chair fast). In univariate analyses, a large number of baseline variables were significantly associated with the subsequent development of mobility impairment (Table 1). Nonsignificant variables not displayed in Table 1 included fasting glucose, HbA1c (A1C), diastolic blood pressure, cholesterol, triglycerides, lipid-lowering therapy, lower-limb amputation, mental illness, and taking antidepressants (all P > 0.20).

In a time-dependent Cox proportional hazards model including ln(time) and mobility status, the interaction between these variables was significant (P < 0.001). This indicated that the proportional hazards assumption may be invalid. However, the log(−log[survival]) curves were parallel, and inspection of the residual β values versus time plots for all significant covariates revealed no outliers. Therefore, we concluded that the nonproportionality made no difference to the interpretation of the data (24). In the Cox model, older age, CVD, treatment with insulin, microalbuminuria, peripheral neuropathy, arthritis, current smoking, unmarried status, and not taking exercise remained independently associated with the development of mobility impairment (Table 2). When insulin treatment was removed from the Cox model, retinopathy and nonfluency in English became significant.

Predictors of ADL disability

The 934 group 2 patients had a mean ± SD age of 63.5 ± 10.4 years, a median duration of diabetes of 3.0 years (interquartile range 0.8–8.0), and 49.7% were men. After an average of 4.8 ± 2.3 years follow-up, 169 (18.1%) reported having any difficulty with any ADL (152 reported having some difficulty with at least one ADL and 17 reported requiring another’s help for at least one ADL). A large number of baseline variables correlated significantly in univariate analyses with the development of ADL disability (Table 1). Nonsignificant variables not displayed in the table included fasting glucose, A1C, diastolic blood pressure, cholesterol, triglycerides, lipid-lowering therapy, lower-limb amputation, mental illness, and taking antipsychotic medications (all P > 0.20).

In Cox proportional hazards modeling, age, CVD, not taking exercise, smoking status, claudication, mobility problems, depression, nonfluency in English, and indigenous Australian ethnicity independently predicted the development of ADL disability (Table 2). The cumulative survival curves for patients remaining free of ADL disability in patients with and without baseline mobility problems are shown in Fig. 1 (P < 0.0001, log-rank test).

CONCLUSIONS — In the present prospective community-based study of patients with type 2 diabetes, almost one-third of the subjects with normal mobility at baseline developed some degree of mobility impairment after an average of 4.6 years, and close to one-fifth developed new difficulties with basic ADLs within the same time frame. The majority of subjects developed relatively minor physical deficits. For example, nearly 80% of those reporting mobility problems did not require a walking aide, and few subjects became fully dependent on another person for assistance with ADLs. Nevertheless, even minor impairments in mobility predicted future functional decline in the general population (14), and consistent with this observation, those of our subjects who reported difficulty with mobility at baseline had more than three times the risk of subsequently developing ADL disability.

As in previous reports (5,6), the development of new mobility impairment and ADL disability was multifactorial and largely explained by diabetes complications, common comorbid conditions, cardiovascular risk factors, and several social factors. However, although there were similarities in the etiological factors involved in the two disabling processes, there were also differences that may be useful in understanding disablement in diabetes. Patients who developed mobility impairment were more likely to have peripheral neuropathy and a history of stroke and arthritis at baseline, conditions known to affect lower-limb function and to cause gait disorders (12,25,26). Why baseline insulin therapy and microalbuminuria predicted mobility impairment is less clear, but removal of insulin treatment from the Cox model caused retinopathy to enter as an additional predictor, suggesting that microangiopathy may directly or indirectly affect lower-limb function. ADL disability also had multiple causes, with the strongest predictive variable being baseline mobility impairment. The other disease-related risk factors for ADL disability, namely stroke, peripheral vascular disease, and depression, are known causes of disability in the general population (12,27) and all, including depression, occur with an increased frequency in type 2 diabetes (28). Presumably one or more such conditions progressed to cause further functional limitation and ultimately disability (29).

Our definition of ADL disability did not include mobility assessment unlike many ADL assessment tools. This important distinction may explain why other
studies have found common determi-
nants (12) when we found different etio-
logical factors for mobility impairment
and ADL disability. The stepwise analyti-
cal approach we used relies on statistical
significance irrespective of the strength of
associations in two unequal groups,
which might have influenced the results.
Nevertheless, the model predictors had
sizeable effects and the group sizes were
large.

The increased risk of mobility impair-
ment and disability in our patients was
explained by the complications of dia-
betes in combination with several common
age-related disorders, but we found no
role for hyperglycemia or CHD. These
findings are inconsistent with other lon-
gitudinal studies (5,6), but there are im-
portant differences in study design and
the numbers of assessed variables. We
considered predictors of disability within
a diabetic cohort rather than comparing
diabetic with nondiabetic subjects (5,6).
In addition, the two previous studies had
limited data on diabetes diagnosis, glycem-
ic control, and micro- and macrovascu-
lar complications.
Table 2—Baseline variables that independently predicted time to progression to mobility impairment and ADL difficulty in patients with type 2 diabetes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mobility Hazard ratio</th>
<th>P value</th>
<th>ADL Hazard ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.06 (1.04–1.08)</td>
<td>&lt;0.001</td>
<td>1.05 (1.03–1.07)</td>
<td>&lt;0.001</td>
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<td>CVD</td>
<td></td>
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<td>No</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>2.23 (1.51–3.33)</td>
<td>&lt;0.001</td>
<td>1.92 (1.27–2.91)</td>
<td>0.002</td>
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<td>Any exercise</td>
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<td></td>
<td></td>
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<tr>
<td>No</td>
<td>1</td>
<td></td>
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<tr>
<td>Yes</td>
<td>0.61 (0.45–0.83)</td>
<td>0.002</td>
<td>0.53 (0.38–0.73)</td>
<td>&lt;0.001</td>
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<td>Current smoker</td>
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<td>No</td>
<td>1</td>
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<tr>
<td>Yes</td>
<td>1.64 (1.12–2.40)</td>
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<td>Ex-smoker</td>
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<td>No</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>Yes</td>
<td>1.55 (1.13–2.14)</td>
<td>0.007</td>
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<td>Insulin treatment</td>
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<td>No</td>
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<tr>
<td>Yes</td>
<td>2.17 (1.49–3.18)</td>
<td>&lt;0.001</td>
<td>0.61 (0.45–0.83)</td>
<td>0.002</td>
</tr>
<tr>
<td>In(ACR) (mg/mmol)*</td>
<td>1.15 (1.04–1.26)</td>
<td>0.006</td>
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<td>Neuropathy</td>
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<tr>
<td>Yes</td>
<td>1.40 (1.04–1.88)</td>
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<td>Arthritis</td>
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<tr>
<td>Yes</td>
<td>1.82 (1.37–2.42)</td>
<td>&lt;0.001</td>
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<td>Married</td>
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<tr>
<td>Yes</td>
<td>0.68 (0.51–0.92)</td>
<td>0.01</td>
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<td>Claudication</td>
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<tr>
<td>Yes</td>
<td>1.67 (1.13–2.46)</td>
<td>0.010</td>
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<tr>
<td>Mobility problems</td>
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<td>No</td>
<td>NA</td>
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<tr>
<td>Yes</td>
<td>3.22 (2.28–4.57)</td>
<td>&lt;0.001</td>
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<tr>
<td>Yes</td>
<td>1.41 (1.02–1.95)</td>
<td>0.038</td>
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<tr>
<td>Nonfluent in English</td>
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<td>No</td>
<td>1</td>
<td></td>
<td>2.83 (1.96–4.08)</td>
<td>&lt;0.001</td>
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<td>Yes</td>
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<tr>
<td>Indigenous Australian</td>
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<tr>
<td>Yes</td>
<td>4.33 (1.04–18.08)</td>
<td>0.044</td>
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</table>

Data are hazard ratio (95% CI). ACR, albumin-to-creatinine ratio; NA, not applicable. *A 2.72-fold increase in ACR corresponds to an increase of 1 in ln(ACR).

CHD has been an important factor in other studies of disability (12). Age adjustment alone attenuated, at least in part, the univariate association seen in the present study (data not shown). Our method of assessing CHD and CVD was rigorous; patient self-reports being supplemented with hospital records and electrocardiographic data for confirmation and to diagnose silent ischemia (18). The instrument we used may be relevant because the GHS relies on self-reports, and we had no objective measures of physical function. Self-reported data can also be compromised by cognitive difficulties, although we used attendant relatives as additional sources of information where necessary.

Diabetic peripheral neuropathy affects mobility through altered balance and posture (25,26), but the nature of an association between mobility and the other microvascular complications is less clear. Age-related muscle loss is a powerful risk factor for disability (30), especially in patients with renal disease (31). It is possible that progression of neuropathy and nephropathy in our patients contributed to a reduction in muscle mass with a consequent impact on mobility. The contribution of retinopathy to this process in the absence of differences in visual acuity is difficult to explain and may reflect the strong intercorrelation between microvascular complications.

Our finding that lifestyle and social and cultural factors were important determinants of the risk of mobility impairment and ADL disability indicates potential areas for disability prevention in diabetic populations, especially in regard to smoking and exercise. Two groups had a heightened risk for becoming disabled, specifically migrants with limited fluency in English and indigenous Australians. Although the number of indigenous Australians in this study was small and the confidence intervals for the estimates wide, these data are consistent with studies demonstrating a high disability burden in indigenous Australians (32). The majority of people who were nonfluent in English in our study are elderly migrants of Southern European origin, principally Italian and Portuguese. The literature on disability has attributed racial differences to economic factors (12). We have previously reported that non–English-speaking diabetic migrants in Fremantle are less likely to receive diabetes education or to perform self-monitoring of blood glucose (33), indicating that access to health care could be important.

The strengths of the present study include the representative nature of the cohort, the detailed nature of the assessment of a large number of important diabetes-related variables, the large sample size including men, and the duration of follow-up. The main limitations were the reliance on self-report for the assessments of disability, mobility, and arthritis and the lack of data on cognitive function. We also have no knowledge of the mode of development of functional limitation in these patients, which can occur transiently, progressively, or in a catastrophic fashion.

Our data extend the results of previous studies of disability in older people with diabetes and provide a conceptual framework that may help to clarify the causal pathways leading to disability (34). For instance, studying the causes of the progression from preclinical to clinical...
mobility problems in diabetes may be critical in understanding the overall disablement process. In the clinical sphere, it is important to assess patients with type 2 diabetes for early limitations in mobility to consider appropriate preventive activities and avert a decline to physical disability.

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References
26. Resnick HE, Stansberry KB, Harris TB,


