Reduced Prevalence of Limited Joint Mobility in Type 1 Diabetes in a U.K. Clinic Population Over a 20-Year Period

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OBJECTIVE — Limited joint mobility (LJM), one of the earliest clinically apparent long-term complications of type 1 diabetes, is a risk marker for subsequent microvascular complications. We hypothesize that the prevalence of LJM may have decreased during the past two decades due to improved standards of glycemic control.

RESEARCH DESIGN AND METHODS — A single observer performed a survey in 204 consecutive patients with type 1 diabetes (106 men and 98 women, age 27 ± 1 years, HbA_{1c} 8.3 ± 0.1%, duration of diabetes 14.5 ± 0.8 years, insulin dose 63 ± 2 units/day). We used the same examination method and criteria for assessment of LJM as used by us in an earlier study in 1981–1982.

RESULTS — The prevalence of LJM has fallen from 43 to 23% between the 1980s and 2002 ($P < 0.0001$). The relative risk for LJM in 2002 compared with the 1981–1982 cohort was 0.53 ($0.40 < RR < 0.72$, $P < 0.0001$). The prevalence of LJM was increased with longer duration of diabetes (<10 years, 13%; 10–20 years, 19%; 20–29 years, 30%; >30 years, 65%; $P < 0.001$). The relative risk for those with a mean HbA_{1c} <7% in 2002 was 0.3 ($0.1 < RR < 1.2$, $P = 0.05$) when compared with those with mean HbA_{1c} >7%.

CONCLUSIONS — The present study confirms the hypothesis that the prevalence of LJM is lower than 20 years ago and that improved standards of glycemic control and diabetes care may have contributed to this occurrence. Joint limitation in type 1 diabetes is strongly associated with duration of diabetes. The presence of LJM remains a common and important clinical marker for subsequent microvascular disease and can be a useful clinical tool for identification of patients at increased risk.

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Limited joint mobility (LJM), one of the earliest and most common clinical complications in type 1 diabetes, was first described by Rosenbloom in 1974 (1,2). LJM is characterized by stiffness and thickening of the periarticular connective tissue, beginning in the hand at the fifth interphalangeal joints and extending radially. It is useful to recognize this complication of type 1 diabetes because of its association with the development of microvascular complications (3).

The prevalence of LJM in type 1 diabetes quoted in several studies of pediatric and adult diabetes clinics ranges from 9 to 58% (3–5). This variability depends largely upon the population studied and the way in which joint mobility is measured (6). In a previous survey of our clinic population in Belfast published in the 1980s, the prevalence of LJM was 43% (7). Many of the LJM studies were conducted before the introduction of current standards for intensive diabetes care (8). A recent survey of pediatric patients with type 1 diabetes attending diabetic camps in Florida demonstrated a reduced prevalence of LJM between 1976 and 1998 (9). This change was attributed to more intensive glucose control during the past two decades, since there is some evidence that long-term glycemic control influences the onset of this condition (9,10).

The current study was designed to compare the frequency of LJM in our own U.K. clinic population across two decades. We performed a survey of patients with type 1 diabetes attending our clinics in 2002 and compared this to observations made in the same clinic in 1981–1982 (7,11). We hypothesized that the prevalence of LJM would be less in 2002, in line with improved standards for glycemic control in the intervening years.

RESEARCH DESIGN AND METHODS

— Patients were prospectively recruited from the diabetes clinics of the Royal Victoria Hospital and the Royal Belfast Hospital for Sick Children, Belfast, U.K. The hospital operates within a managed public health care system and is a tertiary referral center with a diabetes clinic that serves a predominantly Caucasian population within the south and west Belfast area. The population has remained stable in terms of both size and socioeconomic status across the duration of the two surveys.

The diagnosis of type 1 diabetes was based on the onset of the classic symp-

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Abbreviations: LJM, limited joint mobility.

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

Table 1—*Clinical characteristics of the 2002 survey of LJM in patients with type 1 diabetes in a U.K. clinic population*

Sex (M/F)	106/98
Current age (years)	27.1 ± 1.1 (4–79)*
Duration of diabetes (years)	14.5 ± 0.8 (0.1–60)†
Dose of insulin (units/day)	63.3 ± 2.2 (9–160)
Weight (kg)	69.6 ± 1.2 (25–126)
BMI (kg/m^2)	25.7 ± 0.4 (16–48)
HbA_{1c} (%)‡	8.3 ± 0.1 (5–13)
Blood pressure (mmHg)	120/74 ± 1/1 (80/50–167/100)
ACR (mg/mmol)	4.4 ± 1.5 (0.2–192)
Serum creatinine (μmol/l)	68.7 ± 2.2 (27–384)
Total cholesterol (mmol/l)	4.8 ± 0.1 (2.7–8.1)

Data are means ± SE (range) (n=204). Age range for 1981–1982 series: *4–79 years; †3–53 years (102 men/102 women). ‡Mean of three consecutive readings. ACR, albumin-to-creatinine ratio.

toms of thirst, polyuria, and weight loss before the age of 40 years, in association with ketonuria and subsequent dependence on insulin. Patients were excluded if they gave a history of hand injury, Dupytren's contracture, or arthritis. The study was a cross-sectional design with consecutive patients attending routine outpatient follow-up, recruited and assessed by a single observer (J.R.L.).

Joint mobility was assessed in both the 1981–1982 and 2002 series by the method and classification of Grgic et al. (2). The patient was asked to place both hands, palms down, on a table top with the fingers fanned out and were viewed by the examiner at table level. In stage 0, the entire palmer surface of the fingers makes contact with the table top. In stage 1, one finger only is affected, usually the fifth proximal interphalangeal joint of one or both hands. In stage 2, two or more fingers of both hands are affected, usually the fourth and fifth proximal interphalangeal joints. In stage 3, there is involvement of all the fingers of both hands and limitation of movement in some larger joint(s), usually the wrists or elbows (2).

Each consecutive patient was assessed for evidence of LJM, and a record was taken of results for glycemic control as measured by HbA_{1c} (current and mean of last three visits over the previous 12 months), current blood pressure, serum creatinine, and spot urine for microalbumin. Retinopathy status was determined by the most recent opthalmological assessment by an experienced operator within the primary team.

HbA_{1c} was measured in EDTA whole blood by ion-exchange high-performance liquid chromatography using the Menari HA-8140 (Biomen, Berkshire, U.K.). Serum creatinine was determined using a Johnson and Johnson Vitros 950 analyzer using a multilayered dry-slide technique with measurement of the enzyme aminohydrolase. Serum cholesterol was measured using a dry multilayered technique on the Johnson and Johnson Vitros 950 analyzer. Microalbuminuria, expressed as albumin-to-creatinine ratio (normal <3.0 mg/mmol), was measured on random urine specimens using an immunoturbimetric method on a Cobas Fara centrifugal analyzer (Roche Diagnostics, East Sussex, U.K.)

Statistical analyses

All data are expressed as means ± SE or as 95% CIs. Differences in the frequency of LJM between the 1981–1982 cohort and the current survey were assessed using χ^2 testing. Differences in continuous variables between affected and unaffected individuals in the 2002 group were assessed by unpaired Student's t tests. Yate's continuity corrected test was used to compare grades of LJM between the two surveys. Due to small numbers in the most severe category, data from groups with LJM grades 2 and 3 were combined for the purposes of the analysis. Testing was performed using SPSS version 12 for Windows (SPSS, Chicago, IL) and GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego, CA).

RESULTS — A total of 204 patients (aged 27 ± 1 years, 106 men and 98 women) with type 1 diabetes were examined. Characteristics of patients in the current survey are shown in Table 1. Full demographic details of the 1981–1982 cohort were not available; however, the 2002 cohort had a similar age range (4–79 years) to the patients from the 1985 cohort (7–71 years). The groups from both surveys were well matched for sex distribution (P = NS). In contrast to the 2002 cohort, the 1981–1982 cohort had a longer duration of diabetes (19.7 ± 0.3 vs. 14.5 ± 0.8 years, $P < 0.001$). Patients who comprised the current survey had moderate glycemic and blood pressure control (HbA_{1c} 8.3 ± 0.1%, n = 201; blood pressure 120/74 ± 1/1 mmHg, n = 191). Serum creatinine was 69 ± 2 μmol/l (n = 192), and total cholesterol was 4.8 ± 0.1 mmol/l (n = 161). Fourteen percent (of a total number of 180 available random spot urine collections) had microalbuminuria as defined by an albumin-to-creatinine ratio of >3.0 mg/mmol.

The prevalence of LJM in the current survey was 23% (n = 47 of 204) compared with 43% (88 of 204) in the 1980s ($P < 0.0001$). The relative risk of LJM for patients in 2002 was 0.53 ($0.4 < RR < 0.7$, $P < 0.0001$) compared with the 1981–1982 cohort (7). The relative risk for patients with a mean HbA_{1c} of <7% over the previous three clinic visits in 2002 was 0.3 ($0.1 < RR < 1.2$, $P = 0.05$) compared with those with poorer glycemic control.

The distribution of severity of LJM changed between the 1980s (grade 1, 15.9%; grade 2, 79.5%; grade 3, 4.6%) and 2002 (grade 1, 43%; grade 2, 57%; $\chi^2 = 4.83$, $P < 0.05$). There were no cases identified with severe joint limitation in the 2002 cohort. LJM in 2002 was significantly associated with duration of diabetes (<10 years, 13%; 10–20 years, 19%; 20–29 years, 30%; >30 years, 65%; $P < 0.001$) (Fig. 1). LJM was also associated with the presence of other microvascular complications, including retinopathy and nephropathy. An increased number of

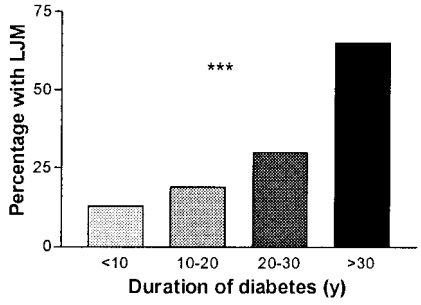

Figure 1—*Association between duration of diabetes and the prevalence of LJM in 2002. ***P < 0.001.*

Figure 2—*The "prayer sign" caused by the failure of opposition of the palmer surfaces of the hands due to joint limitation, is a useful clinical sign for identification of patients with limited joint mobility. (Reproduced by permission of BMJ publishing. From Smith LL, Burnet SP, McNeil JD.* Br J Sports Med *37:30–35, 2003. Copyright 2003 BMJ publishing.)*

cases with joint limitation had evidence of retinopathy compared with those with normal joint mobility (49 vs. 18%, $P < 0.001$). Twenty-nine percent of cases with LJM had albumin-to-creatinine ratio >3.0 mg/mmol compared with 10% of cases surveyed with normal hand mobility ($P < 0.01$). The albumin-to-creatinine ratio for affected patients was 0.8 mg/mmol (0.55–3.63) [median (interquartile range)] compared with 0.62 mg/mmol (0.43–1.37) for those with normal hand mobility ($P = 0.008$).

Stepwise logistic regression analysis was then used with backward elimination of least significant variables. The initial model included age, sex, duration of diabetes, systolic and diastolic blood pressure, HbA_{1c}, cholesterol, and log(serum creatinine). Duration of diabetes was identified as a significant variable within the model contributing to the presence of LJM (B 0.097, $P < 0.001$).

CONCLUSIONS — A number of locomotor system complications, including Dupuytren's contracture, stiff hand, carpal tunnel syndrome, and limited joint mobility, are associated with diabetes (3,12–14) (Fig. 2). LJM is defined as a painless limitation of the finger joints often associated with thick, tight, and waxy skin, which can also affect large joints occurring in patients with diabetes (3).

The exact etiology of LJM is unknown, although there is evidence of soft tissue accumulation of advanced glycation end products in tissues, which may cause stiffening (15). The importance of LJM relates to its association with the presence of retinopathy (16–18) and nephropathy (18,19) in type 1 diabetes and macrovascular disease in type 2 diabetes (20). There has been debate as to whether LJM might predict subsequent complications of diabetes based on results from early cross-sectional analyses. In fact, we conducted one of the few prospective cohort studies of LJM in 44 diabetic patients without microvascular complications at study entry in order to determine its predictive value (21). After 10 years, the presence of LJM at entry did not effectively predict the onset of retinopathy or nephropathy. Our observations have since been confirmed by a more recent series (5).

Our survey demonstrates an almost twofold reduction in the prevalence of LJM between the 1980s and 2002, which is in agreement with our initial hypothesis. Our findings concur with a recent study by Infante et al. (9), who demonstrated a fourfold reduction in the frequency of LJM in children attending diabetes camps in Florida between 1976–1978 and 1998. While Infante et al. used similar methods for detection of LJM, they studied children aged 7–18 years attending diabetes camps. The lower magnitude of differences between surveys in our study may be partly the result of an older patient population with a longer duration of diabetes. In agreement with our series, Infante et al. also found a reduction in the distribution of cases with moderate to severe joint limitation. They hypothesized that the reduction in prevalence and severity was most likely accounted for by improved glycemic control. Indeed, there is a theoretical basis for reduction in skin glycation with improved glycemic control (22).

In line with modern standards for glycemic control, we anticipated a reduction in the prevalence of limited joint mobility attributable to improvements in glycemic control and clinical care across the two decades (8). The current survey failed to demonstrate a close correlation between contemporaneous glycemic control and LJM, consistent with results from earlier cross-sectional studies (5). Although the severity of LJM did not correlate with HbA_{1c} in a linear manner, we found a trend toward reduced prevalence of LJM in patients with an HbA_{1c} <7%. The results just failed to reach statistical significance ($P = 0.05$). Not withstanding our current observations, Rosenbloom et al. (10) recently described a relationship between LJM and longer-term glycemic control in a prospective case-control study across 6 years for the first time, suggesting that this issue merits further investigation.

Our study had several limitations. A direct comparison of glycemic control between our consecutive surveys is limited due to differences between analytical techniques used for measurement of HbA_{1c}. Furthermore, although the surveys were well matched for age and sex distribution, one of the major limitations of our analysis is that the groups were not matched for duration of diabetes. A significant observation from both surveys was that LJM was strongly associated with duration of diabetes. Consequently, some of the variation in prevalence across the two decades may have been accounted for by differences in duration of disease (23). This finding reflects our strong desire to avoid selection bias during the most recent survey by assessing representative consecutive patients attending our joint clinics. It is notable that our main observation of a reduced prevalence of LJM is consistent with other large series and that the primary difference is the magnitude of change (9). Further support for a reduced prevalence across the two decades comes from a comparison with a preliminary study of the prevalence of LJM from our clinic in 1981–1982, which was well matched with the 2002 survey for both duration of diabetes and insulin dose (11). A further potential bias within the 2002 analysis was that a different examiner (J.R.L.) undertook the clinical assessment, data collection, and analysis. However the published method for assessment of LJM is standardized and was carefully followed. Furthermore, the continuity of the present analysis was ensured by involvement of the lead author from the 1981–1982 cohort (L.K.) during the study design, implementation, and analysis.

In summary, the present study confirms the hypothesis that the prevalence of LJM has fallen across two decades in a representative U.K. population with type 1 diabetes. The reduced prevalence of LJM may be related to improved standards of glycemic control or changes in diabetes care; however, further studies are required to support this relationship.

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