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Limited joint mobility (LJM) of the hand in patients with diabetes mellitus: relation to chronic complications

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SUMMARY Limited joint mobility (LJM) of the hand was studied by visual examination in 361 diabetic outpatients aged 11 to 83 years, and 45 non-diabetic controls, without evidence of arthritis. LJM was evident in 58% of diabetic subjects and 4% of controls ($p<0.001$). LJM was noted in 131 (55%) of the 238 patients with insulin-dependent diabetes mellitus (IDDM) as opposed to 31 of the 41 patients (76%) with non-insulin-dependent diabetes mellitus (NIDDM). LJM occurred in 60 of the 82 diabetic subjects (73%) receiving insulin therapy who developed diabetes after the age of 35 years. LJM was significantly related to duration of diabetes in the patients with IDDM less than 40 years of age but was not associated with duration in the patients with NIDDM. A significant association of LJM and neuropathy was noted in patients less than 40 years of age with less than 20 years of diabetes. A significant association of LJM and retinopathy was also noted in those less than 40 years of age with less than 30 years of diabetes. There was no association of LJM and nephropathy regardless of age or duration of diabetes.

Key words: diabetes mellitus—complications, retinopathy, neuropathy, nephropathy, juvenile onset, adult onset.

Limited joint mobility (LJM) of the hand is a clinical finding noted in approximately 30% of children and adolescents with insulin-dependent diabetes mellitus (IDDM).[1–3] The frequency of this finding appears to be related to increasing age[3] and duration of diabetes mellitus.[1 2] Two studies have noted an increased risk for diabetic microvasculopathy in those with LJM.[4 5] Pathologic findings of increased collagen deposition, cross linking, and glycosylation have been described in the thickened skin of subjects with LJM.[4 6] Similar changes have been postulated to occur in the joint capsule and lungs.[6–8]

There are little data available on LJM in adult IDDM patients and in patients with non-insulin-dependent diabetes (NIDDM). Therefore we examined 406 subjects to assess the prevalence of LJM, its relation to age, age of onset (or diagnosis), duration of diabetes, and to certain chronic complications of diabetes such as retinopathy, neuropathy, and nephropathy.

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Subjects and methods

SUBJECTS

A total of 406 subjects with no history of arthritis or primary joint disease was studied. Group 1 (n=45) comprised non-diabetic employees of the Joslin Diabetes Center. Group 2 (n=361) included all diabetic patients who visited the William P Beetham Eye Unit at the Joslin Diabetes Center between May and August 1982 for either routine evaluation or treatment of eye disease. This group included 320 subjects treated with insulin and 41 subjects treated with either diet or oral hypoglycaemic agents. Of the 320 insulin-treated subjects, 238 had developed diabetes before the age of 35 years and 82 subjects developed diabetes at 35 years of age or older. In

contradistinction, all subjects in the non-insulin treated group developed diabetes after the age of 35 years. A summary of the demographic data is given in Table 1.

METHODS

All subjects were screened for the presence of LJM of the hand by trained observers after informed consent had been obtained. Subjects were asked to put their hands in the 'clapping position' and inability to oppose palmar surfaces in any interphalangeal joint was defined as positive. If there was doubt, subjects were asked to place their hands flat on a table with fingers spread. Failure of any joint to make contact was classified as LJM.

A questionnaire was then completed recording sex, age, and presence of diabetes mellitus. If diabetes was present, age at onset (or diagnosis) and duration, and current treatment modality were noted.

Subjects were considered to have clinically symptomatic neuropathy if they had a history of pain, paraesthesia, burning, or decreased sensation in any extremity. Nephropathy was noted in those with proteinuria or any prior abnormality in renal function tests.

Table 1 *Characteristics of subjects assessed for limited joint mobility (LJM)*

Study group	*Non-diabetic controls (n=45)*	*Diabetic outpatients (DM) (n=361)*
Age (years)		
mean±SD	47·8±12·0	46·2±17·8
range	19–69	11–83
Duration DM (years)		
mean±SD	—	19·8±11·2
range		0·5–63·1
Age onset DM (years)		
mean±SD	—	26·7±19·7
range		1–75
Sex		
male	25	174
female	20	187
total	45	361
Insulin usage		
yes	—	320*
no		41†
LJM		
No	2	209
%	4·4	57·9

*Two hundred and thirty-eight of these subjects were <35 years of age at diabetes onset.
†All subjects not on insulin therapy were >35 years of age at diabetes onset or diagnosis.

All subjects in group 2 (diabetic outpatients) underwent ophthalmologic evaluation through a dilated pupil by an examiner unaware of joint status. Retinopathy was classified, as none, background, preproliferative, or proliferative by the modified Airlie criteria.[9] If the degree of retinopathy differed in the two eyes, the eye with the worst disease was used for classification.

Data files were stored on a VAX 11/780 computer. Statistical analyses were performed on an IBM 4341 computer with the SAS (statistical analysis system) programming package.[10] χ^2 Analysis was used to determine the significance of associations of LJM with various clinical criteria. Relative risks and 95% confidence limits were calculated by standard methods.[11] In addition, positive and negative predictive values were calculated by the following formulae:

$$\text{Predictive value } (+) = \frac{\text{true positives}}{\text{true positives + false positives}} \times 100$$

$$\text{Predictive value } (-) = \frac{\text{true negatives}}{\text{true negatives + false negatives}} \times 100$$

Positive and negative predictive values reflect the importance of presence or absence of LJM for the prediction of associated clinical findings.

Results

LJM PREVALENCE AND DEMOGRAPHICS (Table 1)

LJM was noted in 4·4% of non-diabetic controls and in 57·9% of diabetic outpatients ($p<0·001$). There was no significant difference in LJM prevalence when those subjects on insulin therapy were compared with those on alternative regimens.

In the total group of diabetic outpatients LJM was noted in 51·3% of subjects less than 40 years of age, 56·1% of subjects age 40 to 59, and 70·4% of subjects age 60 years or greater. In the group less than 40 years of age and in those 40 to 59 years of age duration of diabetes was significantly related to the presence of LJM ($p<0·005$ and $p<0·001$, respectively) (Fig. 1). Age at diabetes onset or diagnosis did not influence LJM frequency in any group.

Those subjects with age at onset less than 35 years and requiring insulin therapy were then analysed further. In this subgroup of 238 subjects LJM was noted in 75 of 150 (50·0%) less than 40 years of age, 43 of 72 (59·7%) 40 to 59 years of age, and 13 of 16 (81·2%) 60 years of age or greater. The presence of LJM was significantly related to the duration of diabetes in the less than 40-year age group ($p<0·001$) but not in the two older age groups.

There were 41 subjects with age at diabetes diagnosis of 35 years or greater who were not on insulin therapy. In this group LJM was noted in three of 10 (30·0%) aged 35-59 years and in 28 of 31 (90·3%) 60 years or greater. There was no significant association of LJM with duration of diabetes in either age group.

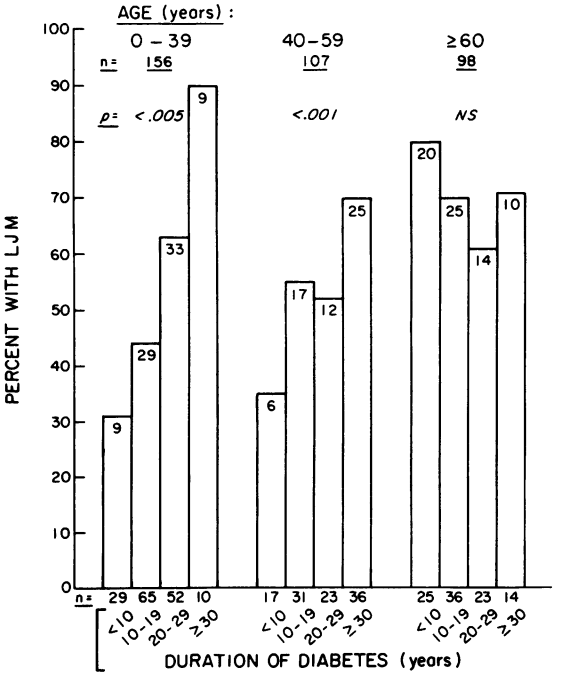

Fig. 1 *LJM v age and duration of diabetes mellitus (group 2, n=361). The number under the top limit of each bar shows the number of subjects at each age and duration of diabetes with LJM. The number under each bar shows the total number of subjects in each age and diabetes duration group. The total number of subjects in each age category is shown at the top of each group of vertical bars.*

LJM AND CHRONIC COMPLICATIONS

Neuropathy

Symptomatic neuropathy was documented in 84 (23·3%) subjects in the diabetic outpatient population of whom 59 (70·2%) showed LJM. In those with no evidence of neuropathy a smaller percentage had LJM, 149 of 276 (54·0%, p<0·02).

When these diabetic outpatients with neuropathy were stratified by age (Fig. 2a) LJM was noted in 21 of 30 (70·0%) in the less than 40 year age group, 20 of 31 (64·5%) in the 40–59 year age group, and 18 of 23 (78·3%) in the 60 year or greater age group. In contrast, LJM was noted in 59 of 126 (46·8%), 39 of 75 (52·0%) and 51 of 75 (68·0%) of those in the same age groups with no evidence of neuropathy. Thus LJM was significantly more frequent (p<0·03) in subjects under the age of 40 years with neuropathy than in those without neuropathy. There was no association of LJM and neuropathy in the two older age groups.

To determine whether duration of diabetes modulated the relationship between neuropathy and LJM, each age group was stratified into two groups, those with diabetes duration less than 20 years and those with 40 years or more of diabetes. An effect of duration of diabetes upon neuropathy was noted only in the less than 40 year age group. Those with 20 years or more of diabetes showed no association of LJM and neuropathy. In contradistinction, in those less than 40 years of age with less than 20 years of diabetes, 71% of the subjects with neuropathy had LJM, whereas only 35% of those without neuropathy showed LJM (p<0·02, Table 2). This represents a 4·3 relative risk (95% confidence limits are 1·3–14·2) for neuropathy in those with LJM. Table 2 also shows positive and negative predictive values for this group.

Nephropathy

In the diabetic outpatient group, there was no

Table 2 *LJM—associations with neuropathy and retinopathy in those <40 years of age*

	Duration of diabetes (years)	*Proportion with LJM*	*Percentage with LJM*	*p*	*Predictive values* (+)	*Predictive values* (−)	*Relative risk (95% confidence limits)*
Neuropathy present	<20	10/14	71	<0·02	26	93	4·3 (1·3–14·2)
absent	<20	28/80	35				
Retinopathy present	<30	62/110	56	<0·003	87	36	3·7 (1·6–8·5)
absent	<30	9/36	25				
Preproliferative and proliferative only	<30	50/84	60	<0·001	85	44	4·2 (1·8–9·8)

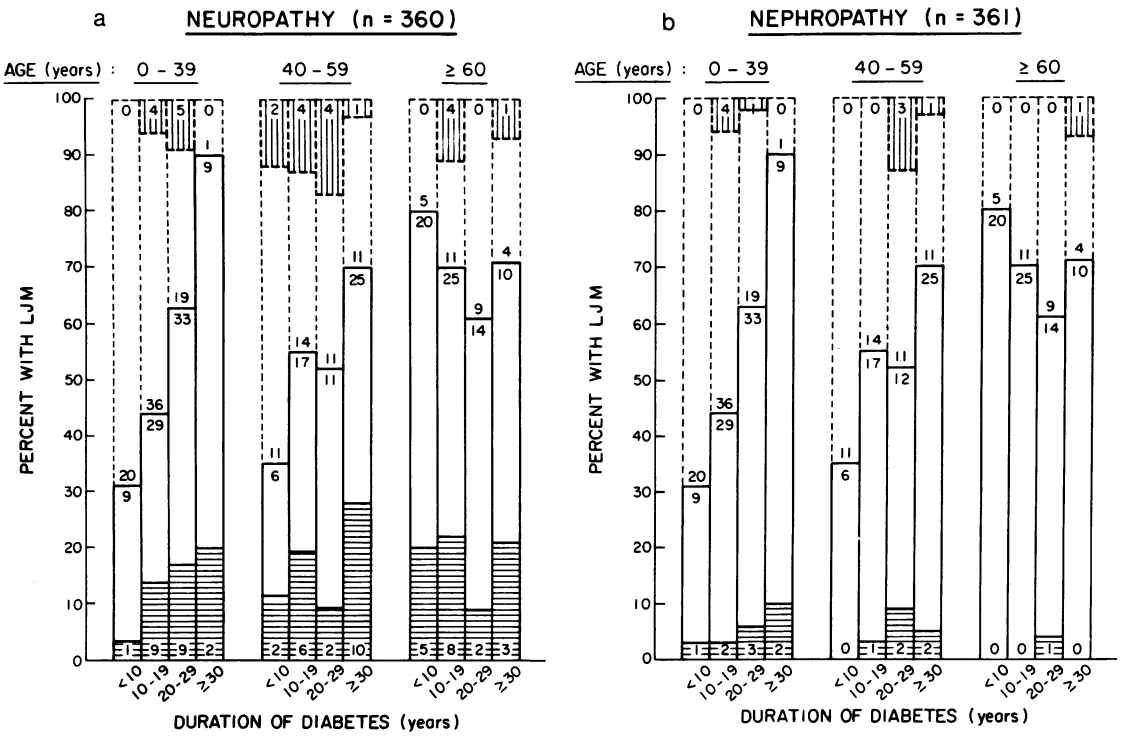

Fig. 2 *LJM* v *(a) neuropathy and (b) nephropathy. The solid bar (bottom) and dotted bar (top) show the proportion of subjects with and without LJM, respectively, in each age and duration of diabetes category. The actual number of subjects in each category is shown just below and above the solid bar. The shaded area within each bar represents those subjects with neuropathy (2a) and nephropathy (2b) in the LJM (bottom) or non-LJM (top) group. The actual number of subjects with neuropathy or nephropathy with and without LJM is shown at the bottom and top of each column, respectively.*

association of LJM with nephropathy regardless of age or duration of diabetes (Fig. 2b).

Retinopathy

Retinopathy was documented in 267 (74·6%) subjects in the diabetic outpatient population of whom 164 (61·4%) showed LJM. In those with no evidence of retinopathy, 45 of 91 (49·5%) had LJM ($p<0·03$).

When diabetic outpatients with retinopathy were stratified by age (Fig. 3a) LJM was noted in 71 of 120 (59·2%) patients aged less than 40 years, 50 of 82 (61·0%) age 40–59 years, and in 43 of 65 (66·2%) 60 years or older. In contrast, LJM was noted in 9 of 36 (25·0%), 10 of 24 (41·7%), and 26 of 31 (83·9%) in the same age groups with no evidence of retinopathy. Thus LJM was significantly more common ($p<0·005$) in subjects under 40 years of age with retinopathy than in those without retinopathy. There was no association of LJM and retinopathy in the older age groups, though there was a strong trend in the 40–59 year age group.

To determine whether duration of diabetes modulated the relationship between retinopathy and LJM each group was stratified into two groups, those with diabetes duration of less than 20 years and those with diabetes for 20 years or more. A significant effect of duration of diabetes was noted only in the less than 40 year age group; only those with less than 20 years of diabetes had a significant relation between the presence of retinopathy and LJM ($p<0·05$). The significant association of the presence of LJM and retinopathy was also seen in those less than 40 years of age with less than 30 years of diabetes (Table 2).

In this latter group 56% of subjects with retinopathy had LJM, whereas only 25% of subjects without retinopathy showed LJM ($p<0·003$). This represents a relative risk of 3·7 (95% confidence limits of 1·6–8·5) for retinopathy in those with LJM. Table 2 also shows positive and negative predictive values for this group.

When subjects with preproliferative or prolifer-

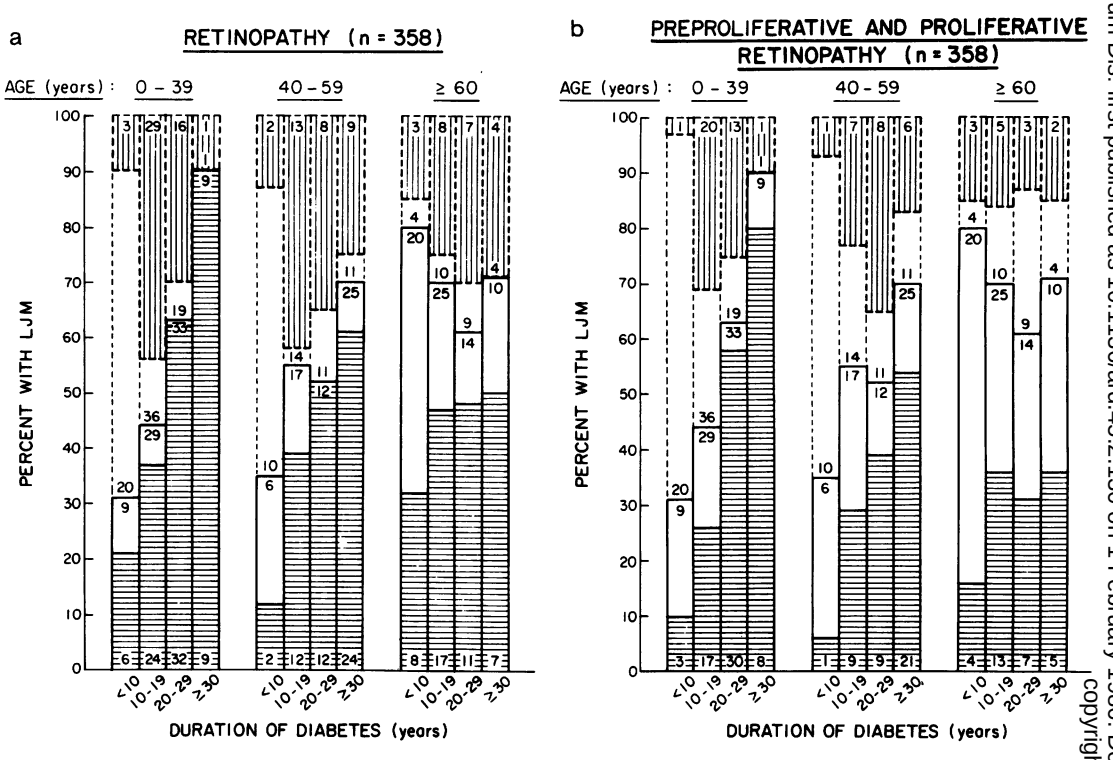

Fig. 3 *LJM* v *(a) all retinopathy and (b) preproliferative and proliferative retinopathy. The solid bar (bottom) and dotted bar (top) show the proportion of subjects with and without LJM, respectively, in each age and duration of diabetes category. The actual number of subjects in each category is shown just below and above the solid bar. The shaded area within each bar represents those subjects with retinopathy (3a) or preproliferative or proliferative retinopathy (3b) in the LJM (bottom) and non-LJM (top) group. The actual number of subjects with retinopathy or preproliferative or proliferative retinopathy and with and without LJM is shown at the bottom and top of each column, respectively.*

ative retinopathy were similarly studied, association with LJM was similar to that seen for all retinopathy (Fig. 3b and Table 2).

Discussion

A consistent association of LJM of the hand with diabetes mellitus has been confirmed in subjects with IDDM and in subjects with NIDDM. In our population LJM was present in 55% of subjects with IDDM and 76% of subjects with NIDDM. This compares with a prevalence of 51% and 39%, respectively in subjects with IDDM (n=215) and NIDDM (n=241) recently studied by Lawson *et al.*[5] We also found an increasing prevalence of LJM of the hand in the older age groups.

The decreasing association of LJM with duration of diabetes as age increases may be at least partially attributed to the cross-sectional nature of our study. Mortality of patients with diabetes increases significantly with increasing duration of diabetes [12] and with increasing age in those over 40 years old regardless of age at diabetes onset.[13 14] If, in fact, diabetic complications are associated with LJM of the hand, this selected population would tend to show a decreasing frequency of LJM with increasing age and duration of diabetes. This would leave fewer than expected subjects with LJM in older age groups. In addition, the increase in LJM unrelated to diabetes duration in the older age groups may in part be related to the difficulty in establishing age at diabetes onset in the NIDDM group. Perhaps many of those in the shorter duration categories may in fact have had glucose intolerance or mild NIDDM for a significant period of time before diagnosis of diabetes.

Most notable was the association of LJM of the hand with the presence of diabetic complications

We found LJM to be present in 64% of subjects with retinopathy as opposed to 45% of subjects with no evidence of eye disease. This compares with LJM prevalence of 55% in retinopathy and 26% in non-retinopathy populations in Lawson's study group which included both IDDM and NIDDM.[5] Rosenbloom *et al.*, examining only IDDM, found LJM in 80% of patients with retinopathy and in 35% of those without retinopathy.[4] When retinopathy was categorised by severity, we found an increasing association of LJM with worsening eye disease as previously described.[4 5] We also found a significant age and duration effect with the highest LJM/retinopathy association seen in subjects less than 40 years of age with less than 20 years of diabetes mellitus.

In addition to studying the associations of LJM and diabetic retinopathy, our study also examined relationships with diabetic neuropathy and nephropathy. We found a significantly increased frequency of clinically symptomatic neuropathy in subjects with LJM of the hand. This was particularly noteworthy in those subjects less than 40 years of age with less than 20 years of diabetes mellitus. In contradistinction, no association of LJM of the hand and nephropathy was noted in our diabetic population.

Although the association of LJM with diabetic complications is limited to clinical predictive value by the relatively long time span necessary for expression, the association with collagen defects in the skin and elsewhere underscores the potential utility of this finding. LJM of the hand may serve as a barometer of collagen alteration analogous to a 'long-term' glycosylated haemoglobin determination. Whether these collagen changes are related to metabolic milieu or are also a function of individual tissue sensitivity remains to be determined. The fact that the finding is easily demonstrable, however, may well provide the impetus for improved patient compliance with the treatment regimen and thus improved blood sugar control. Longitudinal studies are presently in progress to delineate the natural history of LJM and the relation of this finding to long and short-term indicators of glycaemic control.

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