Prevalence and pattern of hand soft-tissue changes in type 2 diabetes mellitus

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Abstract

Aims and objectives. – Hand soft-tissue changes are well described in patients with T1DM, but not in T2DM patients. For this reason, this study aimed at examining the prevalence and pattern of hand soft-tissue changes in patients with T2DM.

Methods. – A total of 206 consecutive patients with T2DM and 203 age-, gender- and occupation-matched healthy controls were examined by two individual observers, and then underwent the appropriate investigations.

Results. – The 132 (64%) patients with T2DM included 187 hands compared with 96 (23.6%) healthy controls including 133 hands (P = 0.01 for both). Dupuytren’s contracture (DC) (42 vs. 29.3%, respectively; P = 0.01), limited joint mobility (LJM) (39 vs. 28.5%, respectively; P = 0.01) and carpal tunnel syndrome (CTS) (5.3 vs. 1%, respectively; P = 0.01) were significantly higher in T2DM patients than in the controls, but not stenosing flexor tenosynovitis (FTS, ‘trigger finger’). Indeed, none of the patients or controls had FTS. In patients with T2DM, DC showed a radial shift, and was more horizontal and severe than in the controls. These hand soft-tissue changes correlated significantly with age (P = 0.0001), duration of diabetes (P = 0.0001) and the presence of microangiopathy (P = 0.001).

Conclusion. – Hand changes are more prevalent and severe in patients with T2DM, and are correlated with age, duration of diabetes and microvascular complications.

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Keywords: Diabetes mellitus; Type 2 diabetes; Dupuytren's contracture; Carpal tunnel syndrome; Flexor tenosynovitis; Limited joint mobility; Hand; Soft tissues changes; Complications

Résumé

Prévalence et présentation clinique des anomalies des parties molles de la main chez les diabétiques de type 2.

Buts et objectifs. – Si les altérations des parties molles sont bien décrites chez des les diabétiques de type 1 (DT1), peu d’études ont été consacrées à cette question dans le DT2. Le but de cette étude était d’examiner la prévalence et les caractéristiques des anomalies des parties molles de la main dans le DT2.

Méthodes. – Deux-cent six patients consécutifs atteints de DT2 et 203 témoins appariés selon l’âge, le sexe et la profession ont été examinés par deux investigators et ont subi les explorations appropriées.

Résultats. – Cent trente-deux patients (64%) atteints de DT2 (187 mains) et 96 témoins (23.6%) (133 mains) ont participé à l’étude. Les fréquences des maladies de Dupuytren (42 vs 29.3 %, P = 0.01), des réductions de la mobilité articulaire (LJM) (39 vs 28.5 %, P = 0.01) et des syndromes du canal carpien (CTS) (5.3 vs 1 % ; P = 0.01) étaient significativement plus élevées chez les DT2 que chez les témoins. Aucun patient ni témoin n’avait de ténosynovite des fléchisseurs (« doigt à ressort »). La maladie de Dupuytren chez les DT2 était plus horizontale, avec plus fréquemment un déport radial et plus sévère que chez les témoins. Ces anomalies étaient en corrélation avec l’âge (P = 0.0001), la durée du diabète (P = 0.001) et la présence de complications microvasculaires (P = 0.001).

Conclusion. – Les anomalies des parties molles de la main sont plus fréquentes et plus graves chez les patients atteints de DT2, en corrélation avec l’âge, la durée du diabète et l’existence de complications microvasculaires.

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Mots clés : Diabète sucré ; Diabète de type 2 ; Parties molles ; Main ; Complications ; Maladie de Dupuytren ; Syndrome du canal carpien ; Ténosynovite des fléchisseurs ; Mobilité articulaire réduite

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1. Introduction

Diabetes is a constellation of metabolic abnormalities characterized by chronic and persistent hyperglycaemia that eventually results in micro- and macrovascular complications. These complications are well characterized, and their association with glycaemia – especially microangiopathic complications – is well defined. However, one less well-known and often neglected complication is soft-tissue involvement in the hands, as this causes relatively minor limitations to diabetic patients [1–3]. Because of the longer life expectancy that these patients now enjoy due to advances in treatment and prevention of life-threatening complications, hand problems have only just begun to surface more frequently. The original description of hand changes associated with diabetes included Dupuytren’s contracture (DC), limited joint mobility (LJM), carpal tunnel syndrome (CTS) and flexor tenosynovitis (FTS) [4–6]. Numerous studies in patients with type 1 diabetes mellitus (T1DM) have shown the high prevalence of hand changes, their varied patterns and poor response to treatment [6–12]. The observed spectrum of hand-related complications is also changing due to improved glycaemic control, with the result that the most severe forms of diabetic cheiroarthropathy, such as the ‘stiff hand syndrome’ reported in patients with long-standing T1DM, are rarely seen nowadays [13].

The presence of hand soft-tissue changes is correlated with the cumulative glycaemic burden and microvascular complications [11,12]. This means that the detection of such changes is a warning sign of diabetic complications. However, there is a dearth of studies in the literature regarding hand changes in patients with type 2 diabetes (T2DM), and what studies there are have examined only a small number of patients and mostly without a control group. Therefore, the present study aimed to assess hand soft-tissue changes in patients with T2DM and their correlation with other patient characteristics.

2. Patients and methods

A total of 206 consecutive patients with T2DM and 203 age-, gender- and occupation-matched non-diabetic controls were examined for hand changes. Non-diabetic controls included hospital staff and the people accompanying the patients. The study was carried out at the diabetes clinic of Nehru Hospital, Postgraduate Institute of Medical Education and Research (PGIMER), in Chandigarh, and was approved by the Institute’s ethics committee. Subjects with known connective-tissue disorders, hypothyroidism, chronic liver disease and a history of antiepileptic drug use were excluded.

All findings were objectively recorded according to the following definitions. DC was graded as nodules, cords or bands, tethering of skin and contractures, and marked on a hand diagram according to the ray area involved; it was also further subclassified into mild (nodules only) and severe (all other changes, from cords to contractures). A vertical pattern was defined as extension of DC changes parallel to the longitudinal axis of the hand, while a horizontal pattern was defined as a contractual pattern extending across the ray areas, perpendicular to the longitudinal axis of hand. LJM was assessed by the prayer sign and table test, and further staged using the Brink–Starkman classification system [14]: stage 0, no abnormality; stage I, skin thickening with no contractures; stage II, bilateral fifth-finger contractures; stage III, other fingers involved bilaterally; stage IV, bilateral finger and wrist involvement; and stage V, bilateral finger, wrist and other joint involvement (stages I–II of the prayer sign correspond to stages II–III of the Brink–Starkman classification). CTS was diagnosed as a clinical-symptom score of one or more, and was confirmed by a nerve conduction velocity (NCV) test, while FTS was diagnosed by the presence of pain, swelling and tenderness along the flexor tendons, with stenosing FTS (commonly known as ‘trigger finger’) determined by a history of fingers locked in flexion, followed by their release with a snapping sound. If positive, an attempt was made to reproduce the sign. Also, finger flexor tendons were palpated for nodules.

These observations were confirmed by a second examiner (P.D.) and, in cases of discrepancies, were resolved by a third examiner (A.B.). Microvascular complications, including retinopathy, were assessed by fundus examination, neuropathy by a vibration perception threshold (VPT) of greater than 25 mV and nephropathy by Mical-Test strips and/or 24-h urinary protein as required, while glycaemic control was assessed by HbA1c, as estimated by high-performance liquid chromatography (HPLC), using a Bio-Rad D-10 haemoglobin analyzer.

The non-diabetic controls underwent blood glucose examination after an 8- to 10-h overnight fast, and only those with a fasting plasma glucose (FPG) of less than 100 mg/dL were recruited for the study. Smoking was quantified as pack-years in those who smoked at least 400 cigarettes (40 packs), and alcohol intake was quantified as g/week in those who drank at least 30 g/day, in the course of 1 year.

2.1. Statistical analysis

The appropriateness of the match between patients and controls is shown in Table 1, along with other baseline characteristics. The standard errors of mean (SEM) of these characteristics...
were computed, as well as the frequencies of discrete variables and values of continuous variables. Ordinal data were analyzed using cross-tabulation, and significance ($P$ value) was calculated using either Pearson’s or Fischer’s exact test and the Chi$^2$ test, depending on the size of the data analyzed. Continuous variables that were non-parametric (abnormally distributed) were analyzed using the Kruskal–Wallis test. Finally, a multivariate analysis was carried out for those characteristics that were significantly correlated with a given hand change on the separate univariate analysis.

3. Results

3.1. Demographic characteristics

A total of 212 T2DM patients and 218 non-diabetic controls were initially recruited into the study. Of the patients, six were excluded because of chronic liver disease, hypothyroidism and other known connective-tissue disorders. Of the controls, 15 were excluded because of abnormal blood glucose profiles. Thus, 206 cases (98 men) and 203 controls (106 men) were ultimately included in the present analysis. Patients’ mean (± SD) age was 53.0 ± 8.2 years, while that of the controls was 52.04 ± 8.3 years. Other baseline characteristics (Table 1) were not statistically different between patients and controls, except for larger waist circumference and greater prevalence of hypertension among patients. The mean duration of diabetes was 8.5 ± 2.5 (range: 3–30) years. The majority of patients ($n = 116$) were treated with oral hypoglycaemic agents (OHAs), while 24 received insulin only; 46 were treated by both insulin and OHAs, and 20 were using only lifestyle modifications. Retinopathy was present in 37.5% of patients, nephropathy in 21.8% and neuropathy in 59%. The mean HbA1c of the patients was 8.9 ± 1.7%. The inter-observer correlation coefficient for patients and controls was 0.92 and 0.9, respectively, for all hand changes.

A total of 132 (64%) patients with T2DM had 187 hands involved in diabetes-related changes compared with 96 (23.6%) non-diabetic controls involving 133 hands ($P = 0.01$ for both the number of subjects and number of hands involved). The prevalence of hand soft-tissue changes in patients and controls is shown in Fig. 1. All these changes, except for FTS, were significantly higher ($P = 0.01$) in the diabetics than in the controls.

3.2. Dupuytren’s contracture

Altogether, 173 (42%) hands of the T2DM patients had DC compared with 119 hands (29.3%) of the controls ($P = 0.02$), and men were affected twice as frequently as women among the controls (74 vs. 36%, respectively). However, in the diabetics, there was no difference between men and women (52 and 48%, respectively). Patients with severe contractures had all precontractural lesions (specifically, nodules, cords or bands and tethering of skin). Horizontal-pattern DC (Fig. 2a) was statistically more frequent in patients than in controls (15 vs. 6%, respectively; $P = 0.03$), whereas vertical-pattern DC (Fig. 2b) was not statistically different between patients and controls ($P = 0.09$). The middle- and ring-finger ray areas were most commonly involved in both patients and controls. However, involvement of the index ($P = 0.0001$) and middle-finger ($P = 0.03$) ray areas was more common in patients than in controls, whereas it did not differ for the ring- and little-finger ray areas (Fig. 3). Severe forms of DC (those with lesions other than nodules) were considerably more common in T2DM patients than in controls (24.3 vs. 7.1%, respectively; $P = 0.0001$). On multivariate analysis, age ($P = 0.002$), alcohol intake ($P = 0.01$), retinopathy ($P = 0.02$) and neuropathy ($P = 0.02$) were all strongly correlated with DC.

3.3. Limited joint mobility

LJM was observed in 80 (39%) patients with T2DM and in 58 (28.5%) non-diabetic subjects on assessment by prayer sign ($P = 0.01$). When assessed by table test, the prevalence of LJM decreased to 11 and 6% in patients and controls, respectively ($P = 0.05$). Women were more commonly affected than men among both T2DM patients and controls, with a ratio of approximately 2 to 1 (women to men). In addition, patients with T2DM had more severe forms (stage II or higher by Brink–Starkman classification) of LJM compared with the controls, although this was not statistically significant ($P = 0.07$). However, none of the patients with LJM had ‘stiff hand syndrome’. On multivariate analysis, age ($P = 0.01$), duration of diabetes ($P = 0.008$) and occupation ($P = 0.03$) were correlated with the presence of LJM.

3.4. Carpal tunnel syndrome

Symptoms suggestive of CTS—predominantly paraesthesia and numbness of the fingers and hand—were observed in 10% of patients and 4.2% of controls (statistically significant at $P = 0.03$) but, when these participants underwent NCV examination, 5.3% of patients and 1% of controls were found to have CTS (statistically significant at $P = 0.01$). The majority of patients with CTS had bilateral disease, although it was relatively more severe in one hand than in the other. On multivariate analysis, CTS correlated with the presence of sensory neuropathy ($P = 0.05$).
3.5. Flexor tenosynovitis

None of the T2DM patients or controls had acute FTS. However, chronic stenosing FTS (so-called trigger finger) was observed in seven (3.2%) patients and three (1.5%) controls (not statistically significant at \( P = 0.12 \)). In all these cases, FTS was unilateral and unidigital, and all had a history of the locking phenomenon, with reproducibility of the snapping release, whereas a palpable flexor-tendon-based nodule was detected in only one patient with diabetes. Both CTS and trigger finger were found exclusively in women in the controls (100%) whereas, in the T2DM cases, 15–25% of these hand abnormalities were present in men. On multivariate analysis, increasing age \( (P = 0.05) \), female gender \( (P = 0.03) \), retinopathy \( (P = 0.0001) \) and proteinuria \( (P = 0.04) \) were correlated with FTS.

3.6. Coexistence of hand changes

One hand change was found in 36% of the controls and 38.8% of patients with T2DM (DC was the most common change, followed by LJM), which was not statistically significant \( (P = 0.90) \). In contrast, 22.3% of patients and 10.7% of controls had two hand changes, which was statistically significant \( (P = 0.001) \). No one had all four types of hand changes, although 2.4% of patients and 0% of controls had three hand changes. In addition, 14.5% of patients and only 3.3% of controls had both DC and LJM, which was statistically significant \( (P = 0.001) \). Furthermore, the number of hand changes were also correlated significantly with age \( (P = 0.0001) \), duration of diabetes \( (P = 0.001) \) and presence of microangiopathy \( (P = 0.03) \).

4. Discussion

The hand changes in patients with T2DM were more prevalent and more severe compared with non-diabetic controls, and were correlated with age, duration of diabetes and microvascular complications. The reported prevalence of DC among patients with diabetes varies from 14 to 42% [1–3], and both the prevalence and radial shift of DC seen in the diabetics in our study were consistent with those of previous studies [13,15–18]. Although the vertical pattern of DC was the more common form in both patients and controls, the horizontal pattern was also seen significantly more frequently in T2DM patients, a finding that has not been reported before. Nevertheless, the clinical significance of the two different patterns is as yet not clear. Moreover, severe forms of DC were considerably more commonly seen in the T2DM patients than in the non-diabetic controls. This suggests that the disease not only increases the prevalence, but also the severity, of DC. Also, the contributions of smoking, alcohol and occupation to DC were confirmed in our study, and were similar to observations made by others [19].

In addition, the present study confirmed the higher prevalence of LJM among patients with T2DM [20]. However, as a good number of the non-diabetic controls also had LJM, which correlated with occupation, it reinforces the fact that the condition is not specific to diabetes [21–23]. Also, the most severe form of LJM—‘stiff hand syndrome’—was not seen in our study participants. Of the two tests to identify LJM, the prayer sign was relatively more sensitive than the table test. In the prayer-sign test, where the palms of the hands are placed against each other, the early lesions in either hand are magnified compared with when each hand is placed separately on a table for the table test. This fact was based on the observation that only 25% of those with grade 1 deformity by prayer sign (Brink–Starkman stage II) also had a positive table test, an observation that has never been described previously. Assessment of LJM is particularly difficult in patients with DC, and can only be considered when the wrist or other large joints are involved. Also, as with the findings of previous studies, age, duration of diabetes and occupation [18,20,24], but not microvascular complications [25], correlated with LJM.

A greater prevalence of CTS was observed in patients with T2DM than in the controls in the present study, yet the overall
prevalence in both patients and controls was lower compared with earlier studies [1–3,26]. This could be because we carried out an NCV test only in those who had symptoms of CTS, while many T2DM patients with CTS may be asymptomatic [27,28].

Also, in the present study, the prevalence of trigger finger did not differ between patients and controls, and the overall prevalence was low in both the groups. Of those who had trigger finger, there was a significant correlation with retinopathy and nephropathy, as has also been shown in previous studies [16–18,20]. However, neither the patients nor controls in our study had acute forms of FTS.

Our present study showed associations between hand soft-tissue changes in T2DM patients with increasing age, duration of diabetes and presence of microangiopathic complications. These characteristics emphasize the fact that diabetes plays a definite role in the pathogenesis of such hand changes. Also, the fact that age had a strong correlation with the hand changes is consistent with the greater prevalence of such changes among T2DM patients and their age-matched controls than in T1DM patients.

Correlation with microvascular complications but not with HbA1c, as observed in our present study, was similar to the results of previous studies [16–18,20]. This may be explained by the fact that cumulative hyperglycaemia is required to produce these hand changes, while a single cross-sectional HbA1c estimate only represents the glycaemic control over the previous 3 months. The clinical implication of these observations is that a diabetic patient with normal HbA1c may still have hand changes and microangiopathic complications, and that these hand changes can limit the patient's manual dexterity.

The pathogenesis of hand soft-tissue changes has been extensively studied, and found to correlate with the cumulative glycaemic burden with advancing disease and microangiopathic complications [24,25]. Accumulation of advanced glycosylation end-products (AGEs) leads to abnormal cross-linkages of collagen fibres, thereby manifesting as skin thickening, and the formation of nodules and contractures [29]. Other contributing factors include abnormal expression of peptides that regulate growth factors such as transforming growth factor-beta (TGF-β), basic fibroblast growth factor (bFGF), and cytokines such as interleukin (IL)-1α and IL-1β, which may also lead to unregulated and abnormal proliferation of collagen [30]. On histology, there are abnormal fibroblast proliferation and matrix production, the appearance of myofibroblasts containing abnormal amount of actin [31], an increased ratio of type III to type I collagen in extracellular matrix [32], and an increase in both matrix proteoglycans [33] and free radicals in the affected tissue [34].

The strengths of the present study include a good number of patients with T2DM along with their matched controls who were assessed for hand soft-tissue changes as well as other diabetic complications. The limitations include a lack of objective assessment of functional impairment by measuring hand strength to grade the disability caused by these hand changes. Evaluation of CTS by NCV, considered the gold-standard diagnostic test, was performed only in those who had a positive clinical score, which is likely to have underestimated the true prevalence of CTS in both our patients and controls. Also, the lack of baseline data for
our population to allow comparative projections of these changes with increasing duration of diabetes is an inevitable weakness of cross-sectional studies. Furthermore, although patients with IFG were excluded from the control population, other parameters of the metabolic syndrome (MetS), which were not assessed, may also have modified the associations between these hand changes, as the MetS is the *forme fruste* of diabetes.

5. Conclusion

In the present study, hand soft-tissue changes—and, in particular, DC, LJIM and CTS—were all prevalent in T2DM patients. DC was the most common type of hand change in such patients, and was more frequently horizontal, radially shifted and more severe than in the controls. Also, these hand changes correlated with age, duration of diabetes and microangiopathic complications.

Conflicts of interest statement

Nothing to declare.

References