Musculoskeletal Disorders of the Hand and Shoulder in Patients with Diabetes Mellitus

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In addition to micro- and macroangiopathic complications, diabetes mellitus is also associated with several musculoskeletal disorders of the hand and shoulder that can be debilitating (1,2). Limited joint mobility, also termed diabetic hand syndrome or cheiropathy (3), is characterized by skin thickening over the dorsum of the hands and restricted mobility of multiple joints. While this syndrome is painless and usually not disabling (2,4), other musculoskeletal problems occur with increased frequency in diabetic patients, including Dupuytren's disease, carpal tunnel syndrome, palmar flexor tenosynovitis or trigger finger, and adhesive capsulitis of the shoulder (5–10). The association of adhesive capsulitis with pain, swelling, dystrophic skin, and vasomotor instability of the hand constitutes the "shoulder-hand syndrome," a rare but potentially disabling manifestation of diabetes (1,2).

Most previous studies of the association between diabetes and musculoskeletal syndrome have not included a control group (5,7,8,11–15) or differentiated between type 1 and type 2 diabetes (9,11,16), or included only a single musculoskeletal syndrome (4,7,9,13,14,16). We report the epidemiology of adhesive capsulitis, carpal tunnel syndrome, Dupuytren's disease, and flexor tenosynovitis in 100 patients with type 1 diabetes and 100 patients with type 2 diabetes, as well as in 100 control patients.

SUBJECTS AND METHODS

The sample consisted of type 1 and type 2 diabetic patients attending the Massachusetts General Hospital Diabetes Center, and nondiabetic control patients attending primary care practices. Three hundred consecutive patients (200 diabetic patients) participated in the study after giving informed consent. Less than 10% of eligible patients declined to participate. Patients were asked to complete a short written questionnaire about their medical, surgical, and orthopedic history, and were examined in a standard fashion by the same investigator (WA). The physical examination focused on hand and shoulder abnormalities. The presence of carpal tunnel syndrome was defined as pain and paresthesias of the first, second, and third fingers, plus a positive Tinel's or Phalen's sign. Dupuytren's disease was defined as palpable thickening of the palmar fascia, with flexor deformity of the second, third, fourth, or fifth fingers. Flexor tenosynovitis was diagnosed by palpating a nodule or thickened flexor tendon with locking phenomenon during extension or flexion of any fingers. Adhesive capsulitis of the shoulder was considered to be present when unilateral shoulder pain had been present for over 3 months and the range of external rotation and active and passive shoulder movements in all planes was less than 50% of normal. A history of prior surgery for any of these disorders was also considered as evidence of the disease.

Clinical characteristics of the patients, including type and duration of diabetes, and presence of retinopathy, nephropathy (defined as microalbuminuria, clinical proteinuria, or renal failure), neuropathy (peripheral, autonomic, or mononeuropathic manifestations), or coronary artery disease, were obtained from chart review. Hemoglobin A_{1C} (HbA_{1C}) levels, measured by liquid chromatography, were available through an electronic database for all diabetic patients. The first available results in the electronic database were in 1991, and all HbA_{1C} determinations (range, 1 to 30) for each patient were recorded. The mean HbA_{1C} level was calculated to provide an integrated index of glycemic control during follow-up between 1991 and 1998. Determination of HbA_{1C} levels before 1991 was not obtained. The nondiabetic range is 3.8% to 6.4%, with an interassay coefficient of variation of $<2.5\%$ for low and high values.

Statistical analysis was performed with one-way analysis of variance, Pearson chi-squared test, Student *t* test, or stepwise logistic regression, using STATA (Computing Resource Center, Santa Monica, California).

RESULTS

About 60% of the patients and controls were men (Table 1). Both retinopathy and neuropathy were common in diabetic patients. The prevalence of musculoskeletal disorders was greater in diabetic patients than in control patients (36% vs. 9%, $P < 0.01$). Adhesive capsulitis was present in 12% of the diabetic patients and none of the control patients ($P < 0.01$), Dupuytren's disease in 16% of diabetic and 3% of control patients ($P < 0.01$), and flexor tenosynovitis in 12% of diabetic and 2% of control patients ($P < 0.04$), while carpal tunnel syndrome occurred in 12% of diabetic patients and 8% of control patients ($P = 0.29$).

Musculoskeletal disorders were more common in patients with type 1 diabetes than in those with type 2 dia-

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Table 1. Characteristics of Nondiabetic Control Patients, and Patients with Type 1 or Type 2 Diabetes

Characteristic	Controls (n = 100)	Type 1 Diabetes (n = 100)	Type 2 Diabetes (n = 100)	*P* Value*
	Percentage or Mean ± SD			
Male sex	62	56	68	0.22
Age (years)	49 ± 16	40 ± 11	61 ± 11	<0.01
Duration of diabetes (years)		22 ± 11	11 ± 8	<0.01
Hemoglobin A_{1c}(%)		8.0 ± 1.6	8.2 ± 1.5	0.22
Retinopathy		68	42	<0.01
Nephropathy		38	13	<0.01
Neuropathy		56	60	0.65
Coronary artery disease		7	40	<0.01

* For comparison of all three groups (sex, age), or of patients, by type of diabetes.

betes (Figure). Forty-three patients with type 1 diabetes had either hand or shoulder disorders (37 with hand disorders, 6 with adhesive capsulitis of the shoulder, and 10 with both syndromes), compared with 28 patients with type 2 diabetes (24 with hand disorders, 4 with adhesive capsulitis of the shoulder, and 3 with both syndromes, $P = 0.03$).

The 71 diabetic patients with hand or shoulder syndromes were more likely to be female, have a longer duration of diabetes, and have retinopathy, nephropathy, or neuropathy, than were the remaining 129 diabetic patients (Table 2). Mean HbA_{1c} levels were somewhat higher in patients with hand or shoulder syndromes than in those without them (8.3% ± 1.6% vs. 8.0% ± 1.5%), but the difference was not statistically significant. In multivariate logistic regression models, only female sex and longer duration of diabetes were associated with the presence of hand or shoulder syndromes in patients with diabetes. Age, type of diabetes, HbA_{1c} level, retinopathy, nephropathy, neuropathy, and coronary artery disease were not found to be associated with hand and shoulder disease (Table 3).

DISCUSSION

Musculoskeletal disorders of the hand and shoulder occur more commonly in diabetic patients. In our study, these syndromes were about 4 times more frequent in diabetic than nondiabetic patients. While we did not assess the presence of diabetic cheiropathy, we observed increased rates of adhesive capsulitis of the shoulder, Dupuytren's disease, and flexor tenosynovitis in diabetic patients. Although these conditions were more common in patients with type 1 than type 2 diabetes, type of diabetes was not associated with hand and shoulder syndromes

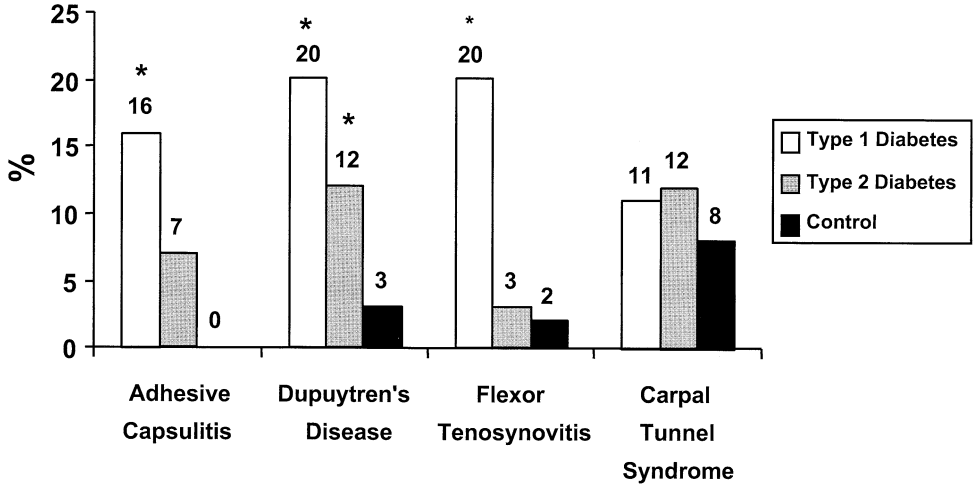

Figure. Prevalence of adhesive capsulitis, Dupuytren's disease, flexor tenosynovitis, and carpal tunnel syndrome in 100 patients with type 1 diabetes, 100 patients with type 2 diabetes, and 100 control patients. *P <0.05 versus control.

Table 2. Comparison of Diabetic Patients with or without Hand or Shoulder Syndromes

Characteristic	With Hand or Shoulder Syndromes (n = 71)	Without Hand or Shoulder Syndromes (n = 129)	*P* Value
	Number (%) or Mean ± SD		
Male sex	35 (50)	88 (68)	0.01
Age (years)	51 ± 13	50 ± 16	0.65
Duration of diabetes (years)	22 ± 10	14 ± 10	<0.01
Hemoglobin A_{1c} (%)	8.3 ± 1.6	8.0 ± 1.5	0.09
Retinopathy	55 (77)	55 (43)	<0.01
Nephropathy	26 (37)	25 (19)	<0.01
Neuropathy	53 (75)	63 (49)	<0.01
Coronary artery disease	15 (21)	32 (25)	0.56

after adjusting for duration of diabetes. Duration of diabetes is also strongly correlated with microangiopathic complications (17,18), and patients with hand and shoulder syndromes were more likely to have retinopathy, nephropathy, and neuropathy.

After adjusting for duration of diabetes, there was no association between HbA_{1C} level and hand and shoulder disorders, despite using the average HbA_{1C} level during a mean of 4 years. While a single HbA_{1C} level does not correlate with tissue levels of advanced glycosylation end products, average levels do correlate with skin glycation products (19,20), a well-accepted index of long-term glycemic control. A previous study failed to reveal an association between mean HbA_{1C} level during the prior 6 years and limited joint mobility (21). However, other investigators have observed positive associations between skin fluorescence (22) and pentosidine levels (23) with limited joint mobility, supporting a role of glycation in hand abnormalities in patients with type 1 diabetes. While our data suggest that glycemic control does not play a major role in the pathogenesis of hand and shoulder abnormalities in diabetic patients, it is possible that overall diabetic control, including during the years before those reflected in the available HbA_{1C} levels, is a determinant of the presence or absence of these musculoskeletal complications.

While the pathogenesis of adhesive capsulitis, Dupuytren's disease, and flexor tenosynovitis is not understood, glucose-induced collagen modifications might be an important component of these syndromes (1,2). Adhesive capsulitis of the shoulder is thought to be due to fibrosis and inflammation. Recent histological and immunohistochemical studies have shown fibroblast proliferation (24) and increased expression of cytokines (25) in patients with these syndromes. Diabetes can induce fibrosis by altering proliferative characteristics of several cell types (26,27), and also increase expression of cytokines (28).

Although not commonly recognized as complications of diabetes, we found that musculoskeletal diseases are present in almost 40% of diabetic patients. Examination of the hands and shoulders should be included in the evaluation of patients with diabetes.

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Table 3. Multivariate Associations between Selected Characteristics of Diabetic Patients and the Presence of Hand or Shoulder Syndromes

Characteristic (Unit)	Odds Ratio (95% Confidence Interval)	*P* Value
Female sex	2.2 (1.1–4.3)	0.02
Duration of diabetes (per 10 years)	1.8 (1.2–2.6)	0.01
Age (per 10 years)	1.00 (0.74–1.48)	0.77
Type 1 diabetes	1.3 (0.4–4.5)	0.67
Hemoglobin A_{1c} (1 SD)*	1.01 (0.86–1.18)	0.90
Retinopathy	2.0 (0.9–4.7)	0.10
Nephropathy	1.1 (0.5–2.5)	0.77
Neuropathy	1.4 (0.6–3.2)	0.45
Coronary artery disease	0.7 (0.3–1.7)	0.43

* 1 SD = 1.5%.

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Nonspecific Interstitial Pneumonitis As the Sole Histologic Expression of Hypersensitivity Pneumonitis

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The pathologic diagnosis of hypersensitivity pneumonitis requires the presence of a bronchiolocentric interstitial pneumonitis with poorly formed septal granulomas (1). In some cases, the granulomas are absent and only a diffuse interstitial pneumonitis is present. In contrast, nonspecific interstitial pneumonitis is a clinicopathologic entity that is characterized by a diffuse, mononuclear cellular infiltration of the alveolar septa often accentuated around bronchioles (2). Interstitial fibrosis may be present. It has been suggested that nonspecific interstitial pneumonitis may represent the sole histopathologic lesion of hypersensitivity pneumonitis, although the clinical characteristics of this entity are not well described. The failure to distinguish hypersensitivity pneumonitis from idiopathic nonspecific interstitial pneumonitis and to eradicate the provocative exposure can result in pro-