Diabetes Mellitus as a Risk Factor for the Development of Lumbar Spinal Stenosis

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ABSTRACT:

Background: Diabetes mellitus is a multi-organ disorder affecting many types of connective tissues, including bone and cartilage. Certain skeletal changes are more prevalent in diabetic patients than in non-diabetic individuals. A possible association of diabetes mellitus and lumbar spinal stenosis has been raised.

Objectives: To compare the prevalence of diabetes mellitus in patients with spinal stenosis, degenerative disk disease or osteoporotic vertebral fractures.

Methods: A cross-sectional analysis was performed of 395 consecutive patients diagnosed with spinal stenosis, degenerative disk disease or osteoporotic vertebral fractures. All the patients were examined by one senior author in the outpatient orthopedic clinic of a large general hospital between June 2004 and January 2006 and diagnosed as having lumbar spinal stenosis (n=225), degenerative disk disease (n=124), or osteoporotic vertebral fractures (n=46).

Results: The prevalence of diabetes mellitus in the three groups (spinal stenosis, osteoporotic fracture, degenerative disk disease) was 28%, 6.5% and 12.1%, respectively, revealing a significantly higher prevalence in the spinal stenosis group compared with the others ($P = 0.001$). The higher prevalence of diabetes in the stenotic patients was unrelated to the presence of degenerative spondylolisthesis.

Conclusions: There is an association between diabetes and lumbar spinal stenosis. Diabetes mellitus may be a predisposing factor for the development of lumbar spinal stenosis.

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KEY WORDS: diabetes mellitus, lumbar spinal stenosis, degenerative spondylolisthesis

Diabetes mellitus is a multiorgan disorder affecting many types of connective tissues, including bone and cartilage [1,2]. As such, certain skeletal changes are more prevalent in diabetic patients than in non-diabetic individuals [1]. Sakellaridis [3] found that DM was more common in patients

DM = diabetes mellitus

operated on for lumbar disk disease compared with similar patients undergoing surgery for other conditions. Some studies reported a high prevalence of degenerative spondylolisthesis in diabetic patients [4]. A possible association of DM and lumbar spinal stenosis was raised in a previous study that examined the correlation between systemic disease and spinal stenosis [5]. The current study is a cross-sectional analysis comparing the prevalence of DM in 395 consecutive patients diagnosed with spinal stenosis, degenerative disk disease or osteoporotic vertebral fractures. We hypothesized that DM would be more common in the patients with spinal stenosis than in those with degenerative disk disease or osteoporotic fractures.

PATIENTS AND METHODS

The study was approved by the medical center's Institutional Review Board, which concluded that the nature of the study was such that written patient consent was not required.

The study group comprised all patients examined by one of the senior authors (Y.M.) in the Orthopedic Outpatient Clinic in a large general hospital between June 2004 and January 2006 and diagnosed with lumbar spinal stenosis (n=225), degenerative disk disease (n=124), or osteoporotic vertebral fractures (n=46). All eligible patients seen at the clinic during the study took part in the research. Overall, approximately 1800 patients had been examined in the clinic during that period. Each patient considered eligible for inclusion in the study underwent an evaluation that included general medical history, physical examination, lumbar spine radiographs (anteroposterior and lateral views), and computed tomography scans. Some of the patients also had magnetic resonance imaging of the lumbar spine and a technetium bone scan as indicated. For inclusion in the spinal stenosis group, patients had to have clinical symptoms of neurogenic claudication for more than 3 months, with patent tibialis posterior and dorsalis pedis arteries on physical examination, and evidence from CT scan and/or MRI of central stenosis < 9 mm diameter [6]. For inclusion in the degenerative disk disease group, patients had to have back pain without radiculopathy for more than 3 months, with evidence on CT scan and/or MRI of degenerative disk disease

without evidence of spinal stenosis. Osteoporotic vertebral fractures were diagnosed by a combination of a history of acute back pain, local tenderness at the fracture site, and the typical appearance of such a fracture on plain radiograph bone scan, CT and/or MRI scans with a DEXA score of less than -2.5.

The patients were queried about the use of insulin injections or oral hypoglycemic agents, and those on either medication were classified as being diabetic, as were the patients who were managed solely by low sugar/carbohydrate diet. The subjects diagnosed as having spinal stenosis, degenerative disk disease or osteoporotic fractures were classified into two groups according to their DM status (i.e., diabetic versus non-diabetic). The prevalence of DM was compared among the spinal stenosis, osteoporotic fracture and degenerative disk disease groups. We suspected that the prevalence of DM could be affected by the different mean ages in these groups and therefore examined the prevalence of DM in three different age groups: < 50 years, 50–60 years, > 60 years.

The parameters of age and gender were assessed for the diabetic and for the non-diabetic patients in the three groups. The presence of degenerative spondylolisthesis was assessed for the diabetic and for the non-diabetic patients in the lumbar spinal stenosis group to investigate whether the prevalence of spinal stenosis in the diabetic patients is connected to the presence of degenerative spondylolisthesis. Degenerative spondylolisthesis was assessed by measuring the forward translation of the L3 vertebral body relative to L4, the L4 relative to L5, or the L5 relative to S1 on lateral lumbar radiographs.

Statistical analysis was performed using the SPSS software (version 12.1; SPSS Inc., Chicago, IL, USA) with a 5% significance level. The chi-square test and Fisher's exact test were used for non-parametric values, and Student's *t*-test for parametric values. The age differences between the three groups were compared using a one-way analysis of variance with Tukey's method for multiple comparisons. A multivariate analysis with logistic regression was used for evaluating independent risk factors for DM. Since all patients were examined by one person (Y.M.), we calculated the inter-observer reliability. We assessed the prospect of two observers assigning the same diagnosis to the same CT scan and/or MRI. Overall, we assessed 10 CT scans and/or MRI scans from each group. Evaluating the inter-observer reliability yielded a percent agreement of 80% to 100%. The kappa value was 0.857 (*P* < 0.01), which represents an excellent level of agreement.

RESULTS

The prevalence of DM in the spinal stenosis group, the osteoporotic fracture group and the degenerative disk disease group was 28%, 6.5% and 12.1% respectively, revealing a significantly higher prevalence in the spinal stenosis group compared with the osteoporotic fracture and degenerative disk disease groups

Table 1. Prevalence of diabetes mellitus in patients with spinal stenosis, degenerative disk disease and osteoporotic fracture

Diagnosis	Non-diabetic patients No. (%)	Diabetic patients No. (%)	P value
Spinal stenosis	162 (72%)	63 (28%)	‹ 0.001
Degenerative disk disease	109 (87.9%)	15 (12.1%)	0.974
Osteoporotic fractures	43 (93.5%)	3 (6.5%)	0.253

P values were obtained using chi-square test and were compared to the aged matched general population in Israel

(*P* = 0.001, Pearson chi-square). Comparing the prevalence of DM in the three groups to the prevalence of DM in the general population demonstrated a statistically significant difference in the spinal stenosis group only [Table 1]. There was no statistically significant age difference between patients in the spinal stenosis group (mean age 65 ± 11.49 years, range 30–91) and those in the osteoporotic fracture group (mean age of 69 ± 12.2 years, range 49–92), but the patients in the spinal stenosis group were significantly older than those in the degenerative disk disease group (54 ±3.37 years, range 27–81; *P* < 0.001, ANOVA with Tukey's method for multiple comparisons). A subgroup analysis of the three different age groups (< 50 years, 50–60 years, > 60 years) showed a higher prevalence of DM in the stenotic patients in all three age groups. Interestingly, the difference in the prevalence of DM between the spinal stenosis group and the degenerative disk disease group was more pronounced in the younger age groups [Table 2].

When we used a multivariate analysis with logistic regression to identify independent risk factors for DM, only age

Table 2. Prevalence of diabetes mellitus in patients with spinal stenosis, degenerative disk disease and osteoporotic fracture according to the three studied age groups (total = 395 patients)

Age group	Diagnosis	Non-diabetic patients No. (%)	Diabetic patients No. (%)	Total no.
‹ 50 yrs	Spinal stenosis	27 (81.8%)	6 (18.2%)	33
	Degenerative disk disease	49 (100%)	0 (0%)	49
	Osteoporotic fractures	5 (100%)	0 (0%)	5
50–60 yrs	Spinal stenosis	35 (83.3%)	7 (16.7%)	42
	Degenerative disk disease	28 (96.6%)	1 (3.4%)	29
	Osteoporotic fractures	4 (100%)	0 (0%)	4
› 60 yrs	Spinal stenosis	100 (66.6%)	50 (33.3%)	150
	Degenerative disk disease	32 (69.6%)	14 (30.4%)	46
	Osteoporotic fractures	34 (91.9%)	3 8.1%	37

Table 3. Multivariate analysis with logistic regression for spinal stenosis and age as independent risk factors for diabetes mellitus

Risk factor	Odds ratio	95% confidence interval for odds	*P* value
Age	1.042	1.018–1.066	‹ 0.001
SS vs. osteoporotic fractures	6.809	2.007–23.093	= 0.002
DDD vs. osteoporotic fractures	3.52	0.925–13.391	= 0.065

SS = spinal stenosis, DDD = degenerative disk disease

Table 4. Occurrence of degenerative spondylolisthesis in the diabetic and non-diabetic patients with spinal stenosis

Diabetes status	Degenerative spondylolisthesis L4-5	Degenerative spondylolisthesis L3-4	Degenerative spondylolisthesis L3-4 & L4-5
Non-diabetic	43	2	2
Diabetic	7	–	–

and spinal stenosis were found as statistically significant independent risk factors for DM [Table 3].

Among the 225 patients with spinal stenosis, 111 were males (49%) and 114 were females (51%). In the degenerative disk disease group 51 (41%) were males and 73 (59%) were females and in the osteoporotic vertebral fractures group 12 (26%) were males and 34 (74%) were females. There was no significant difference in female/male ratios in the diabetic and non-diabetic stenotic patients (*P* = 0.556, Fisher's exact test). The mean age of the 63 diabetic patients was 64.7 years, compared to 66.8 years for the 162 non-diabetic patients (*P* = 0.214, *t*-test). The mean duration of DM in this group was 8.26 years. Twenty diabetic patients were treated with insulin, 24 with oral hypoglycemic agents, 16 were managed by low sugar/carbohydrate diet, and 3 patients did not keep a dietary regimen.

In the spinal stenosis patients, degenerative spondylolisthesis limited to one level was observed in 52 patients: 50 of them had slipping at the L4-5 interspace and the other 2 patients at the L3-L4 interspace. Two patients had a double slip at both levels. More patients in the non-diabetic group had L4-5 degenerative spondylolisthesis (26.5% compared to 11.1%, *P* = 0.012, Fisher's exact test) [Table 4].

DISCUSSION

DM is a common condition that causes metabolic disturbances in many organs [1,3]. It affects 8% of the population in Israel [7], a prevalence similar to that in other western countries, e.g., 8.2% in Greece [8] and 10.2% in men and 7.4% in women aged 45–64 years in Finland [9]. The current cross-sectional study showed that DM is more common among patients with lumbar spinal stenosis than among patients who have degenerative disk disease without lumbar

stenosis and patients with osteoporotic vertebral fractures.

The Copenhagen Osteoarthritis Study, a cross-sectional epidemiological survey of 4151 persons, reported a prevalence of degenerative spondylolisthesis of 8.4% of the women and 2.7% of the men [10]. The prevalence of degenerative spondylolisthesis in our stenosis group was 24.7%. The results of previous studies on the association of degenerative spondylolisthesis and DM were conflicting. Frymoyer [4] reported that degenerative spondylolisthesis is more prevalent in diabetic patients, while a community-based study by Vogt et al. [11] did not find any correlation between a history of DM and the prevalence of L4-5 degenerative spondylolisthesis. The latter authors attributed these conflicting results to a selection bias, stating that diabetic patients may seek medical or orthopedic care more frequently than non-diabetic patients, thereby accounting for the apparently high prevalence of spondylolisthesis in the diabetic population. In the current study, L4-5 degenerative spondylolisthesis was significantly more common in the non-diabetic patients with spinal stenosis compared to the diabetic ones. We can therefore conclude that the high prevalence of spinal stenosis in the diabetic patients is not connected to the presence of degenerative spondylolisthesis.

Diabetic neuropathy is one of the conditions commonly considered in the differential diagnosis of lumbar spinal stenosis. Although there is a real risk of mistaken diagnosis [12], it is unlikely that the high prevalence of DM in our spinal stenosis group can be ascribed to misdiagnosis. All patients in the lumbar spinal stenosis group had clinical symptoms of neurogenic claudication with CT and/or MRI findings that supported the diagnosis of lumbar spinal stenosis. However, a mild neuropathy might predispose the stenotic diabetic patient to experience neurogenic claudication.

It is possible that some of the younger patients with spinal stenosis had congenital as opposed to degenerative stenosis. Our literature search failed to elicit any reliable or validated quantitative radiographic assessment of symptomatic congenital lumbar spinal stenosis. Congenitally stenotic patients classically present at an earlier age, typically in their late forties and early fifties, with multiple level involvement in contrast to their degenerative stenosis counterparts [13]. In our study, only 33 of the 226 patients with spinal stenosis were younger than 50 years old [Table 1]. The prevalence of DM in this subgroup of patients was 18.2% and there was no significant difference between them and the other patients in terms of the involved disk level. Therefore, the high prevalence of DM in the spinal stenosis patients could not be explained by a trend towards congenital spinal stenosis among them.

The mechanism by which DM may predispose a patient to spinal stenosis is unclear. Lumbar spinal stenosis is usually caused by a reduction in the space available for the neural elements due to new bone formation and remodeling, or to

occlusion of the spinal canal by hypertrophic tissues, such as ligamentum flavum. This process usually begins with disk dehydration, followed by loss of disk height and bulging of the annulus fibrosus and infolding of the ligamentum flavum into the spinal canal [14]. Consequently, the intervertebral disk plays a key role in the pathophysiology of spinal stenosis. The changes found in the cartilaginous matrix in diabetic patients may differ from the normal aging process in two important ways: an increased non-enzymatic cross-link of proteins by sugar glycosylation at lysine residues and a decreased rate of proteoglycan synthesis [15]. Lumbar disks from diabetic animals have lower hydration and an inferior ability to resist osmotic changes [16]. Similarly, proteoglycans with lower buoyant density and substantially under-sulfated glycosaminoglycan were found in disk specimens excised from diabetic patients [17]. These changes may lead to accelerated disk degeneration [17]. Nevertheless, we did not find a statistically significant higher prevalence of DM in the degenerative disk disease group compared to the lumbar spinal stenosis and osteoporotic vertebral fracture groups. In support of our observation, Videman and co-researchers [18] compared MRI evidence of spinal degeneration in nine pairs of monozygotic twins discordant for insulin-dependent DM and found no evidence that insulin-dependent DM has any major effect on disk degeneration.

Other factors may contribute to the association between spinal stenosis and DM. For example, it is well known that spinal stenosis may develop as a complication of several metabolic bone diseases, including Paget's disease of the bone and diffuse idiopathic skeletal hyperostosis [19]. The resultant spinal canal narrowing may manifest clinically as classic neurogenic claudication. DISH is a disorder in which both spinal and extraspinal bony proliferation and overgrowth occur, leading in some cases to lumbar spinal stenosis [20]. Ossification occurs both at the ligamentum flavum and facet joint similarly to degenerative lumbar spinal stenosis. Interestingly, DISH is associated with obesity and with DM [21,22]. Kawaguchi et al. [23] studied 20 patients with lumbar spinal stenosis due to ossification of the posterior longitudinal ligament or the ligamentum flavum and found that 35% of them were obese and 30% were diabetic. In addition, the microangiopathy associated with DM may interfere with nutrient diffusion through the vertebral endplates, leading to disk degeneration. It is not surprising, therefore, that DM may also be a risk factor for the development of lumbar spinal stenosis. Indeed, Moskowitz and colleagues [24] proposed the hyperglycemic sand rat as a model for disk degeneration and hyperostosis. Moreover, DM was also linked to ossification of the posterior longitudinal ligament, a condition that may affect the lumbar spine as well [25].

DISH = diffuse idiopathic skeletal hyperostosis

Our study has some obvious limitations, mainly its cross-sectional nature, which does not allow for DM to be investigated as a risk factor for lumbar spinal stenosis but as an associated factor. Another limitation is the fact that spinal stenosis, vertebral osteoporotic fractures, and degenerative disk disease may simultaneously exist in the same patient.

In conclusion, our study demonstrates an association between DM and lumbar spinal stenosis. It implicates DM as a possible predisposing factor for the development of lumbar spinal stenosis.

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