Factors Associated with Lumbar Intervertebral Disc Degeneration in the Elderly

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Abstract

BACKGROUND CONTEXT: Lumbar intervertebral disc degeneration (DD) precedes degenerative diseases of the lumbar spine. Various factors in addition to normal aging are reported to be associated with DD, and recently atherosclerosis and risk factors for cardiovascular diseases (cardiovascular risk factors) have received much attention; however, the links between these risk factors and DD are unclear.

PURPOSE: By correlating magnetic resonance images with suspected degenerative disc risk factors such as obesity, cardiovascular risk factors and atherosclerosis we hope to clarify the factors associated with DD.

STUDY DESIGN/SETTING: An observational study.

PATIENT SAMPLE: Two hundred seventy adults (51 - 86 years old) who participated in a health promotion program.

OUTCOME MEASURES: DD evaluated based on the signal intensity of MR T2-weighted mid-sagittal images of the lumbar spine.

METHODS: Age, gender, body mass index (BMI), low-density lipoprotein cholesterol (LDLc), triglyceride, glycosylated hemoglobin, brachial-ankle pulse wave velocity as an index of atherosclerosis, osteo-sono-assessment index calculated from quantitative ultrasound assessment of the calcaneus as an index of bone mineral density, history of low back pain, smoking and drinking habits, and physical loading related to occupations and sports were assessed. The univariate relationships between DD and the variables were evaluated, and finally, odds ratios (OR) and 95% confidence intervals for the associations of each factor with DD were calculated using logistic regression at each disc level.

RESULTS: Aging correlated significantly with DD of L1/2 (OR, 2.14), L2/3 (OR, 3.56), L3/4 (OR, 2.84) and L4/5 (OR, 3.05); high BMI, with L2/3 (OR, 2.98), L3/4 (OR, 3.58), L4/5 (OR, 2.32) and L5/S1 (OR, 3.34); high LDLc, with L4/5 (OR, 2.65); occupational lifting, with L1/2 (OR, 4.25); and sports activities, with L5/S1 (OR, 3.36).

CONCLUSIONS: Aging, high BMI, high LDLc, occupational lifting and sports activities are associated with DD. The results of this study raise our index of suspicion that cardiovascular risk factors and particular physical loading may contribute to DD; however additional studies are required to further investigate associations between DD and these factors.

Introduction

Lumbar intervertebral discs degenerate with normal aging [1-4]. One study using magnetic resonance imaging (MRI) on healthy women reported about 30% of the subjects in their twenties had lumbar intervertebral disc degeneration (DD), while about 90% of the subjects in their seventies had DD [4]. Nevertheless, DD also precedes lumbar degenerative diseases, such as lumbar disc herniation and lumbar spinal canal stenosis; therefore, various studies aiming to identify risk factors for DD have been completed. The importance of heredity has become increasingly clear following the twin studies of Battie et al.[1,5] and Sambrook et al.[6]. It is reported that individuals with specific gene polymorphisms might develop DD earlier than individuals without these genetic variants [7-9]. In addition, acquired factors, including obesity [3,10,11], diabetes mellitus [12,13], smoking [12,14,15], physical loading related to occupations and sports [5,16-19], and bone mineral density (BMD) [3,20,21], have been associated with DD.

In industrialized nations, the human life span has been extended because of medical advances and improvements in eating habits; therefore, we are concerned that the number of patients who have lumbar degenerative diseases will increase, and thereby medical expenses also. Accordingly, we need to clarify which acquired factors promote DD so as to establish preventive measures against DD.

Recently, suspicions have arisen that atherosclerosis and occlusion of the abdominal aorta and the lumbosacral arteries result in insufficient blood flow and nutrition for the lumbar intervertebral discs and, consequently, might contribute to DD [2,22-24]. Kauppila et al. examined and confirmed this association between DD and atherosclerosis using autopsies, radiographs and MR aortographs [2,22,23]. It is well known atherosclerosis is accelerated by some factors which are known as cardiovascular risk factors. Interestingly, obesity, diabetes mellitus and smoking are not only suspected risk factors for DD, but are also cardiovascular risk factors. Furthermore, obesity and smoking is highly correlated with lifestyle, and type 2 diabetes can be triggered by overeating or lack of exercise in people predisposed to type 2 diabetes by specific hereditary factors. Jhawar et al. noted this, and prospectively and longitudinally have examined the associations between lumbar disc herniation and cardiovascular risk factors in nurses [12]. They found that lumbar disc herniation was associated with diabetes, high cholesterol, hypertension, smoking and a myocardial infarction before age 60. If an association between atherosclerosis, cardiovascular risk factors and DD is conclusively shown, this suggests that behaviors that help prevent atherosclerosis and cardiovascular diseases, which have only a weak association with orthopedic diseases, by early improvements in lifestyle, would reduce the frequency not only of cardiovascular diseases but also of DD and lumbar degenerative diseases as well. This could lead to the establishment of preventive measures against DD and lumbar degenerative diseases.

Consequently, we constructed this observational study to clarify the associations between DD, evaluated by MRI, and suspected risk factors for DD including atherosclerosis and cardiovascular risk factors.

Materials and Methods

Participants

In 2002 and 2003, we publicly recruited adults over 50 years old to participate in a health promotion program by advertising in local newspapers in three municipalities (Tsukuba City with 190,000 inhabitants, Ogano Town with 12,500 and Taiyo Village with 11,000). The program included light weight- and endurance-training for about one year and physical examinations before and after the exercise program. The main purposes of this project were the development of an index of older people's health and a total exercise program to maintain and improve their living function and the establishment of a health promotion system. When we recruited participants, we did not ask whether they had suffered any low back disorders.

Figure 1 shows the study profile. Three hundred forty-eight individuals received written and oral information about the study. Forty-five participants who did not provide written informed-consent or had any serious illness or abnormality according to screening by physicians involved in this project were excluded. Three hundred three individuals were examined with MRI. The imaging was performed on 255 participants before the exercise program and after 12-18 months on 48 participants who could not be examined before the program for various reasons. We excluded 33 participants: 16 because of poor images and 17 because of uncertainty about their disc levels. The study's subjects consisted of 270 adults (96 males and 174 females) with a mean age of 68.4 years (range: 51-86 years). This study was approved by the Human Subjects Institutional Review Board of the Institute of Health and Sport Sciences, University of ＊＊＊＊＊＊＊ (Notification Number 29).

Assessment of disc degeneration

We examined MR T2 density-weighted fast spin-echo saggital images (TR 4000 ms/TE 125 ms) of the subjects' lumbar spine using a 0.2-Tesla imager (AIRIS Mate, Hitachi Medical AG, Tokyo, Japan) with a surface coil. Slice thickness was 6.0 mm with no interslice gap, matrix 256 × 256 and field of view 300 × 300 mm. The imager was a low field system. However, Merl et al. reported no statistically relevant difference in diagnostic accuracy between high-field and low-field (0.2-Tesla) MRI as measured by clinical or surgical gold standard in the spine, and a high degree of concordance between high- and low-field MRI has also been confirmed [25]. In our study, a total of 1,347 intervertebral discs from L1/2 to L5/S1 in the mid-saggital images were assessed. The degree of degeneration was classified into five grades by a modified Pfirrmann's classification (Table 1, Figure 2), with Grades IV and V considered degenerated. Pfirrmann et al. used both signal intensity and disc height categories for classification [26]. However, it was difficult to assess the images of adults over 50 years old by Pfirrmann's classification because the grades from signal intensity and disc height disagreed. It has been reported that signal intensity loss is significantly correlated with the morphological level of DD and also with both the water and proteoglycan content of a disc [27]. Therefore, we used a grading based on signal intensity only. The images were assessed independently by two orthopedic surgeons who were unaware of the subject's status. Finally, a consensus decision was reached in conference and was used for the statistical analysis.

We assessed interrater and intrarater agreement by calculating kappa statistics (dichotomous variables). The kappa coefficient for interrater reliability was 0.81. Repeated measurements were done at 2-month intervals for 40 images (200 discs), chosen at random, to estimate intrarater reliability. The intrarater agreement coefficient was 0.89.

MRI for evaluating DD was performed on 222 participants (Group A) before the exercise program, and after 12-18 months on 48 participants (Group B) who could not be examined before the program. In addition, Group A involved 88 participants (Group A') of whom a pair of MR images were taken – one before the program and the other 18 months later. To verify that there was no significant progression of DD due to aging of the participants over 18 months and thereby to confirm that the 48 images for group B were appropriate for analysis, we chose 40 pairs of images at random from Group A' and compared images within each pair. The agreement coefficient from kappa statistics for the pair of images was 0.90, which was higher than the interrater and intrarater agreement coefficients. Therefore, no progression due to aging over 18 months could be detected by our grading method.

Physical findings

Each subject's height and weight were recorded and their body mass index (BMI) was calculated.

Laboratory measurements

Blood samples were collected and serum low-density lipoprotein cholesterol (LDLc), triglyceride (TG) and glycosylated hemoglobin (HbA_{1c}) were measured. All blood samples were obtained in the morning following an overnight fast.

An index of atherosclerosis

Pulse wave velocity (PWV) is known to be an indicator of arterial stiffness, and has been regarded as a marker reflecting vascular damage [28,29]. PWV is the speed at which a pulse travels between two points and is related to the square root of the elastic modulus according to the Moens-Korteweg equation [30]. Therefore, the stiffer the artery, the faster the PWV. To assess atherosclerosis we used a simple and noninvasive method of measuring brachial-ankle PWV (baPWV) that has recently been made available. The subjects were examined in a supine resting position, using an automated device with an oscillometric method (form PWV/ABI, Colin AG, Ltd, Aichi, Japan) [28,29].The average of the left and right baPWVs in each participant was used for the analysis.

A total index of bone mineral density

Quantitative ultrasound assessment of the calcaneus was performed using an Acoustic Osteo-Screener (AOS-100, Aloka AG, Tokyo, Japan) [31]. The speed of sound (SOS) and the transmission index (TI) were measured, and from them the osteo sono-assessment index (OSI), which is given by $OSI = TI \times SOS^2$, was calculated as a total index of BMD.

Questionnaire and telephone interview

A questionnaire containing demographic data, physical and mental health status and lifestyle factors was given to the participants to complete. The following three questions concerning experience of low back pain (LBP), current smoking habits and current drinking habits were used for the analysis: Have you experienced LBP during your lifetime? Do you smoke cigarettes? Do you drink alcoholic beverages?

We conducted a telephone interview about occupational and sports histories to clarify the associations between DD and physical loading. We asked the following two questions about the occupation that the participants had been engaged in for the longest time: Have you ever engaged in an occupation that involved lifting weights of more than 10 kg for more than one third of your working hours? Have you worked as an occupational driver? The question concerning sports history was as follows: Have you ever participated in a sport more than 3 times per week for more than 5 years, and, if so, what kind of sport?

Statistical analysis

The values measured as continuous data were divided into binary categorical variables to make the prediction rule clear. The cutoff points between low and high values were set at 70 years for age and 25 kg/m^2 for BMI according to the criteria of the Japan Society for the Study of Obesity [32]. The cutoff points were set at 140 mg/dl (3.6 mmol/L) for LDLc and 150 mg/dl (1.7 mmol/L) for TG according to those of the Japan Atherosclerosis Society [33], 5.8% for HbA_{1c} from the standard range (4.3-5.8) of the Japan Diabetes Society [34]; and 1400 cm/sec for baPWV according to a report suggesting baPWV as a new marker for cardiovascular risk [35]. There are no generally accepted criteria of OSI, so the cutoff point was chosen to be 2.4 arbitrarily to provide equal-size groups for statistical analysis. We categorized experience of LBP during lifetime, current smoking and drinking habits as “with” or “without”. We used only two categories for the smoking and drinking habits because we did not ask our subjects details of their histories of smoking and drinking in our questionnaire. The participants who answered “yes” to the respective questions about occupational and sports histories were categorized into the occupational lifting group, the occupational driving group and the sports group. Table 2 shows the characteristics of the participants. The univariate relationships between DD and the variables were evaluated using chi-square tests at each disc level, and the odds ratios (ORs) were calculated. The variables that showed substantial correlation ($P < 0.10$) with DD at one or more disc levels and the gender, for adjusting gender differences, were entered into logistic regression analysis at each disc level. The ORs and their 95% confidence intervals (CI) were calculated for DD, and P values less than 0.05 were considered significant. Co linearity among the independent variables was considered for inclusion in the regression model. The Pearson’s correlation coefficient between age and baPWV was 0.48, and the correlation coefficients among other variables were less than 0.21.

We analyzed each disc level separately because it has been suggested that the effects of mechanical factors such as occupational and sports histories could vary with disc level.

Statistical analyses were performed using the computer software JMP version 5.1 (SAS Institute Inc., Cary, NC) [36].

Results

Disc degeneration (Grades IV, V) was observed in 140 discs (52%) at L1/2, 159 discs (59%) at L2/3, 159 discs (59%) at L3/4, 181 discs (67%) at L4/5 and 156 discs (58%) at L5/S1. The proportions of DD were 57.3% (274 discs) in males and 60.0% (521 discs) in females but these were not significant.

Univariate Results

Results of the univariate analysis are shown in Table 3. Aging was substantially correlated ($P < 0.10$) with DD from L1/2 to L4/5; high BMI, with L2/3, L3/4 and L5/S1; high LDLc, with L4/5 and L5/S1; high baPWV, with L1/2 and L2/3; low OSI, with L5/S1; occupational lifting, with L1/2 and L4/5; and sports, with L5/S1. Gender, TG, $HbA_{1c,}$ history of LBP, current smoking and drinking habits and occupational driving had no correlation with DD.

Multivariate Results

Considering clinical and statistical significance, our logistic regression model was constructed using eight variables as shown in Table 4. Aging was significantly correlated with L1/2 (OR 2.14; CI, 1.15-3.99), L2/3 (OR, 3.56; CI, 1.86-7.03), L3/4 (OR, 2.84; CI, 1.50-5.50) and L4/5 (OR, 3.05; CI, 1.55-6.16); high BMI, with L2/3 (OR, 2.98; CI, 1.52-6.05), L3/4 (OR, 3.58; CI, 1.85-7.21), L4/5 (OR, 2.32; CI, 1.18-4.72) and L5/S1 (OR, 3.34; CI, 1.70-6.81); high LDLc, with L4/5 (OR, 2.65; CI, 1.33-5.52); occupational lifting, L1/2 (OR, 4.25; CI, 1.60-13.48); and sports, with L5/S1 (OR, 3.36; CI, 1.31-9.90). Gender, baPWV and OSI were not correlated with DD at any level.

Discussion

We have clarified the factors associated with MRI evaluated DD. Aging, obesity, high LDLc, occupational lifting and sports activities are associated with DD at one or more disc levels. Atherosclerosis had previously been associated with DD [2,22,23]. Cardiovascular risk factors that accelerate atherosclerosis have also been suspected of being associated with DD [3,10-15]. We had the opportunity to examine baPWV by a simple and noninvasive method, and so we used baPWV as an index of atherosclerosis and investigated the association between DD and baPWV. However, we did not find a significant association. It is reported that baPWV may provide qualitatively similar information to aortic PWV; however, it also reflects muscular arterial stiffness of the leg [37]. In addition, PWV is thought to be a marker of the early stages of atherosclerosis [38]. We surmise that the blood flow to the lumbar spine was maintained even in our high baPWV group participants and that baPWV may not be a good enough indicator of the blood flow to discs.

Among the cardiovascular risk factors that we investigated, high BMI was significantly associated with DD at four disc levels. The association between DD and obesity has been previously reported [3,11] and Liuke et al. found that past obesity is also associated with DD more than present obesity [10]. Therefore, it seems that obesity has some influence on the process of DD. Further research to elucidate the exact mechanism is needed because both direct mechanical stress on the intervertebral discs and indirect effects of atherosclerosis as a cardiovascular risk factor are suspected to be mechanisms through which obesity affects DD.

Our study showed that high LDLc was also significantly associated with DD at L4/5 with a high OR of 2.65. In a cross-sectional study on patients with long-term nonspecific LBP, Kauppila et al. studied the association between LDLc and DD but no correlation was found [22]. On the other hand, Jhawar et al. reported a significant association between self-reported lumbar disc herniation and high cholesterol in the prospective Nurses' Health Study, and indicated that high cholesterol might affect DD [12]. However, this study had the limitation that identification of lumbar disc herniation was judged only from questionnaires which asked whether participants had a physician-diagnosis of herniated lumbar disc and confirmation by computed tomography or MRI—the researchers did not perform their own examinations. Although our results do not show the cause because our study is an observational study, we directly evaluated DD by MRI, and found that DD was significantly associated with high LDLc. However, in our study DD was not associated with baPWV measured as an index of atherosclerosis, and even though LDLc is a systemic factor, only one disc level was significant. Accordingly, our results also indicate the possibility that high LDLc influences DD in other ways than through atherosclerosis, and that additional factors that we did not investigate affect DD. A future prospective study should clarify the associations between DD, atherosclerosis and LDLc.

It has been reported that diabetic sand rats had more dehydrated discs than those of a control group [13], and diabetes increased the risk of lumbar disc herniation in the Nurses' Health Study [12]. However, high HbA_{1c} was not significantly correlated with DD in our results. Our high HbA_{1c} group involved a subgroup that had abnormal levels of HbA_{1c}, but were not diagnosed with diabetes. If DD has only a weak association with hyperglycemia as previously reported [39], it would not be possible for a study such as ours to clarify the association.

Similarly to diabetes, smoking has a reportedly weak association with DD [14], and there were a small proportion of current smokers among our subjects. Therefore, our inability to demonstrate an association between smoking and DD may be more indicative of an inadequate sample size than the lack of an actual relationship.

By investigating whether physical loading is associated with DD, level by level, we found that occupational lifting was significantly associated with L1/2 and sports activities were significantly associated with L5/S1. It has been reported that heavier lifetime occupational physical loading was associated with DD in the upper lumbar region [5], and weightlifting led to slightly more degeneration in the lower thoracic spine [18]. Although we did not assess the thoracic spine, we suspect that physical loading during lifting of heavy objects, regardless of occupation or sport, is concentrated throughout the thoraco-lumbar junction and causes DD. Several investigators previously reported that gymnasts [17] and soccer players [19] had a higher incidence of DD and that DD in elite athletes with LBP at the Sydney Olympic Games was most common at L5/S1 [16]. Our result supports these studies. The degree and the disc level of DD might vary with the type of sports; however, we were unable to identify the type of sports activities and the disc level that were most likely to result in DD because our sports group was too small and it was necessary to group together all sports.

Our major study limitation is that our study is an observational study. Accordingly, the correlations between DD and several factors in our study do not indicate their causes. In addition, because of the number of independent variables compared and the methods available, it is possible that some of the significant associations identified may be artifactual. However, this work lays the foundation necessary to further elucidate the causes and mechanisms of DD and we hope that more detailed and prospective studies based on our results would be able to clarify them. And, the accumulated influence of cardiovascular risk factors and physical loading on DD also has to be estimated for the establishment of preventive measures against DD and lumbar degenerative diseases. Furthermore, our results should be interpreted in view of a potential selection bias that our subjects were Japanese in a health promotion program. Our participants might therefore have been more interested in health-care and lifestyle than the average person, and people who had severe LBP and osteoporosis might have excluded themselves from our study.

Conclusions

In our observational study, aging, high BMI, high LDLc, occupational lifting and sports activities were independently associated with DD at one or more disc levels. The results of this study raise our index of suspicion that cardiovascular risk factors and particular physical loading may promote DD, but additional studies are required to investigate this further. We hope that our findings will be useful in establishing preventive measures against DD and lumbar degenerative diseases.

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