The Relationship of Joint Hypermobility, Bone Mineral Density, and Osteoarthritis in the General Population: The Chingford Study

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ABSTRACT. ***Objective.*** The prevalence of hypermobility and its consequence in an aging female population is unknown. Case studies of patients with the benign joint hypermobility syndrome suggest both a tendency toward osteopenia and an association with premature osteoarthritis (OA). We assessed hypermobility and its relationship to bone mineral density (BMD) and OA in a postmenopausal female community population.

Methods. Joint hypermobility was assessed by the Beighton and the (more quantitative) Contompasis scores in 716 female subjects under followup in the Chingford Study (age range 53–72, mean 61 yrs, SD 5.8).

Results. We found 79 of 716 subjects (11%) had a hypermobility score > 1/9 on the Beighton scale (spine in 75/79); 82/716 had a Contompasis score > 22 (normal < 18). Only one had a 4/9 Beighton score indicative of generalized joint hypermobility. Subjects with Contompasis > 22 were more physically active and less likely to smoke. They had a reduced risk of knee OA (joint space narrowing) (OR 0.48, 95% CI 0.27–0.83, after adjusting for age, height, weight, and activity), but no change in risk of OA in spine or hands. Hip BMD was increased by 3% in this more hypermobile subgroup ($p < 0.05$). A similar effect was seen for knee OA, but not BMD in those with a Beighton score > 1.

Conclusion. Our data suggest that in this postmenopausal population the tendency to joint hypermobility may be a marker for fitness, manifested by reduced knee OA and increased hip BMD. The incidence of generalized hypermobility (Beighton > 4/9) was very low (0.14%) compared with the localized form (seen in 11%) and other studies. Those with mild degrees of hypermobility showed no evidence of premature OA or reduced BMD, as reported in some of the rarer heritable disorders of connective tissue. (J Rheumatol 2003;30:799–803)

Key Indexing Terms:
HYPERMOBILITY OSTEOPOROSIS OSTEOARTHRITIS

A hypermobile joint is one whose range of movement exceeds that which is normal for that individual, taking into consideration age, sex, and ethnic background[1]. A joint's range is determined by the tightness or laxity of its ligaments, and joint laxity can be considered to be a prerequisite for hypermobility.

In general, joint laxity is greatest at birth, declining rapidly through childhood, less rapidly during the teens, and more slowly during adult life[1]. Females are generally more lax jointed than males at all ages and there is a wide ethnic variation. Epidemiological studies using a variety of definitions have suggested hypermobility is seen in up to 10% of Western populations and may be up to 25% in other racial groups[2-4]. The extent to which joint hypermobility is symptomatic in the general population is unclear. Many studies of symptomatic joint hypermobility have been based on clinic populations, with likely attendant selection bias. In one such study, 15% of a rheumatology clinic population were hypermobile[5]. The prevalence of hypermobility and its consequences in an older postmenopausal community population has not previously been studied.

Hypermobility is seen as a common unifying feature in the hereditary diseases of connective tissue (HDCT) such as Ehlers Danlos syndrome (EDS)[6], Marfan's syndrome[7], and osteogenesis imperfecta[8]. It is also recognized as a feature of the benign joint hypermobility syndrome (BJHS)[9], said to exist when a hypermobile joint (or joints) becomes symptomatic. It is not known whether women in the community who manifest osteoarthritis (OA) and/or reduced bone density have other features to suggest an underlying HDCT.

We examined the occurrence of hypermobility in a general population to determine whether women with OA or osteoporosis might share phenotypic features of a genetic

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connective disorder, thereby representing a *forme fruste* or mild form of a HDCT.

There is some evidence that hypermobility is an important risk factor in the cause of OA[10]. This relationship could be a simple mechanical overuse phenomenon, or due to errors in collagen genes such as IX, XI, and V. Increased frequency of OA has been reported in EDS[6], where joints are less stable and prone to subluxation and dislocation, but can also occur in the Marfan syndrome[7] and BJHS[9]. Both chondromalacia patellae[11] and OA of the carpometacarpal joint[10] are recognized to be more common if the affected joint is lax. Osteoporosis and a tendency to fracture are major factors in osteogenesis imperfecta[8], but have also been reported to occur in EDS[12] and Marfan syndrome[13]. A recent study has suggested a trend toward osteopenia in patients attending a rheumatology clinic with the BJHS[9]. We assessed whether hypermobility is associated with a tendency to OA and osteoporosis at multiple sites in a normal aging female population.

MATERIALS AND METHODS

The Chingford Study population, established in 1988-89, is a well described cohort of 1003 women seen annually and described in detail[14,15]. The response rate at initial recruitment was 78%. The area from which the cohort was recruited is predominantly middle-class, with a range of all social groups. Ninety-eight percent of the women are white Caucasians. A socioeconomic profile was performed using the Acorn classification system, which is based on each subject's postal code (CACI International, London, UK). This system classifies subjects into 4 socioeconomic categories. The majority of the women studied (42%) belonged to group Cl (middle to lower class, white collar workers), 32% belonged to group A/B (professional workers), 17% to group C2 (manual/skilled workers), and 8% to group D/E (manual/nonskilled workers). The women in the study were similar to normal UK subjects in terms of smoking statistics, hysterectomy rates, height, and weight[14].

Bone mineral density (BMD) was measured at the lumbar spine (L1–L4) and at the femoral neck by dual-energy x-ray absorptiometry (DEXA) using a Hologic QDR 1000 machine. In our hands, this machine has a reproducibility of 0.6–1.6%. OA was classified radiologically using standard radiographs of the pelvis, thoracolumbar spine, hands, and weight-bearing knees. At baseline, all women had an anteroposterior (AP) radiograph of the hands and a weight-bearing AP radiograph of the knees taken with the legs in full extension. All radiographs were taken by the same technician using the same equipment. Views were standardized with the back of the knees in contact with the cassette, the patella centralized over the lower end of the femur, and the beam centered 2.5 cm below the apex of the patella, with a tube-to-film distance of 100 cm. Radiographs were read by a trained examiner for the presence of knee osteophytes and joint space narrowing (JSN) in each knee compartment, using a validated atlas[14]. Severity was graded on a 0–3 scale. Subjects with a grade of at least 1 (definite presence of an osteophyte or JSN) were classified as cases. Subjects were classified as having incident radiographic OA if they had a radiographic grade of 0 at baseline and subsequently developed at least a grade 1 osteophyte or JSN. Hand radiographs were also graded for OA, using the same radiographic criteria for the presence of distal interphalangeal joint osteophytes. Radiographs of the thoracic and lumbar spine were graded for OA on a 0–3 scale for the presence of osteophytes: 0 = none, 1 = minimal, 2 = definite, 3 = severe. Lumbar and thoracic spine OA (LSOA and TSOA) were defined as those graded I+ for each region[16]. The reproducibility of these grading techniques was good, with kappa scores for inter and intraobserver agreement ranging from 0.46 to 1.0.

Patients completed standardized questionnaires concerning joint pain, back pain, and risk factors for osteoporosis and a scale of physical activity originally derived from cardiac studies[17].

Hypermobility was assessed by the 9 point Beighton score[4] and a modification of the more quantitative Contompasis score (maximum 52)[7]. On the Contompasis system, 18 represents normal joint movement range, equivalent to Beighton score 0. A Contompasis score of 22 was chosen to represent a subgroup with some degree of increased hypermobility ("hypermobile group"). Relative risks and 95% confidence intervals (95% CI) were calculated and adjusted for potential confounders by logistic regression. For continuous variables, analysis of covariance was used to adjust for confounders.

RESULTS

Of 1003 women examined at baseline in 1989, 716 attended for the 1999 assessment (age range 53–72 yrs, mean 61, SD 5.8); 79 of 716 women (11%) examined had a hypermobility score > 1/9 on the Beighton scale. The spine was the site of joint hypermobility in the majority (75/79); 11% (82/716) had a Contompasis score > 22 (normal < 18). Only one had a 4/9 Beighton score indicative of generalized joint hypermobility[4].

Table 1 shows the crude characteristics of the hypermobile group (Contompasis > 22) versus the rest of the study population. They are taller and more physically active. Significantly more of the hypermobile group fell in the top tertile for physical activity. This group walked 5 miles/day and did more than 2 h vigorous sport. When comparing the hypermobile cases with the rest of the cohort, no difference was found in the prevalence of either back or knee pain, so there was no need to adjust.

Knee JSN in the cohort as a whole was inversely related to Contompasis score ($r = –0.1115$, $p = 0.034$). There was no relationship with knee osteophytes or OA in hands or spine. Tables 2 and 3 show the effect of hypermobility on BMD and risk of OA for different levels of Contompasis score, with confounders. By considering a less hypermobile group the contrast with the remaining cohort is less distinct. Only the subgroup with Contompasis > 22 was selected for further study, because at more extreme values the numbers became too small for analysis.

The hypermobile group had a reduced risk of knee OA (JSN) (OR 0.48, 95% CI 0.27–0.83, after adjusting for age, height, and weight), but no change in risk of OA in spine or hands. A similar effect was seen for knee OA when Beighton score was > 1.

Total hip BMD was increased by 3% in the more hypermobile subgroup (Contompasis > 22) (OR 0.79, 95% CI 0.13, $p < 0.05$, after adjusting for age, height, and weight), while there was no clear relationship with spine BMD. Those with Beighton > 1 showed no significant effect on BMD. When physical activity was added to the regression model, the association with knee JSN was stronger (although confidence intervals include 1), while the association with hip BMD weakened.

Table 1. Characteristics of 714 women comparing hypermobile women (Contompasis > 22) with healthy women. Data are mean/SD or number (%).

	Contompasis negative, n = 632	Contompasis positive (> 22), n = 82	p
Age, yrs	53.5 (5.9)	52.9 (5.6)	0.44
Height, m	161.6 (6.0)	162.9 (5.3)	0.05
Weight, kg	66.6 (11.1)	64.9 (9.8)	0.15
Spine BMD, g/cm^2	0.98 (0.16)	0.99 (0.15)	0.43
Hip BMD, g/cm^2	0.76 (0.11)	0.78 (0.13)	0.19
Knee osteophytes (%)	86 (14)	6 (7)	0.06
Knee joint space narrowing (%)	244 (39)	19 (23)	0.004
Knee pain (%)	136 (21)	17 (21)	0.45
Back pain (%)	402 (64)	51 (62)	0.45
Smoker (%)	146 (23)	15 (18)	0.39
Current HRT (%)	50 (8)	5 (6)	0.32
Top tertile of physical activity (%)	119 (19)	25 (30)	0.05

HRT: hormone replacement therapy.

Table 2. Mean BMD (p value) by category of Contompasis score and confounders.

		Contompasis ≥ 22, n = 82, controls = 634		Contompasis ≥ 20, n = 309, controls = 407	
Spine BMD					
Crude	0	0.97 (0.15)	p = 0.43	0.97 (0.16)	p = 0.43
	1	0.99 (0.15)		0.98 (0.16)	
Age	0	0.98 (0.15)	p = 0.58	0.98 (0.16)	p = 0.87
	1	0.99 (0.15)		0.98 (0.16)	
Age/height/weight	0	0.98 (0.15)	p = 0.42	0.98 (0.16)	p = 0.47
	1	0.99 (0.15)		1.98 (0.16)	
Physical activity	0	0.98 (0.15)	p = 0.55		
	1	0.99 (0.15)			
Back pain	0	0.98 (0.15)	p = 0.79		
	1	0.98 (0.15)			
Hip BMD					
Crude		0.76 (0.11)	p = 0.19	0.76 (0.12)	p = 0.27
		0.78 (0.13)		0.77 (0.11)	
Age		0.77 (0.11)	p = 0.21	0.77 (0.12)	p = 0.66
		0.78 (0.13)		0.77 (0.11)	
Age/height/weight		0.77 (0.11)	p = 0.05	0.77 (0.12)	p = 0.22
		0.79 (0.13)		0.78 (0.11)	
Physical activity		0.77 (0.11)	p = 0.16		
		0.79 (0.13)			
Back pain		0.77 (0.11)	p = 0.25		
		0.78 (0.13)			

DISCUSSION

We found the prevalence of generalized joint hypermobility identified by Beighton score in this postmenopausal population to be much lower than previous estimates, at 0.14%. However, this population was considerably older and Caucasian, where many previous studies were of African[4,18] or Asian groups, in children[2,19] or young adults[20,21]. The Chingford population has been shown to be comparable in a number of measurable variables to age-matched UK subjects[14] and to a postmenopausal population drawn from throughout the UK[22]. Eleven percent showed some evidence of hypermobility at a single site. For the majority this was in the compound movement of spinal and hip flexion in order to place hands on the floor. Although a Beighton score of 4/9 is often considered to imply a generalized syndrome[4], pauciarticular disease can itself be symptomatic[23], and the 1998 revised criteria for diagnosis of BJHS recognize that the diagnosis may rest on a Beighton score as low as 1, if other criteria are met[24]. We did not consider other features of the BJHS such as skin hyperextensibility, which might be considered a shortcoming.

We found radiological knee OA defined by JSN to be reduced in those displaying some hypermobility (Contompasis > 22), but no difference in osteophyte score.

Table 3. Risk of OA (OR 95% CI) for levels of Contompasis score with confounders.

	Contompasis ≥ 22, n = 82, controls = 634	Contompasis ≥ 20, n = 309, controls = 407
Knee osteophytes		
Crude	0.50 (0.21–1.19)	0.92 (0.58–1.43)
Age	0.53 (0.22–1.28)	0.99 (0.63–1.57)
Age/height/weight	0.48 (0.18–1.25)	1.06 (0.67–1.70)
Physical activity	0.39 (0.81–1.68)	
Back pain	0.43 (0.24–0.77)	
Knee joint space narrowing (JSN)		
Crude	0.47 (0.28–0.82)	0.69 (0.51–0.95)
Age	0.48 (0.28–0.82)	0.70 (0.51–0.96)
Age/height/weight	0.48 (0.27–0.83)	0.72 (0.53–1.00)
Physical activity	0.39 (0.13–1.14)	
Back pain	0.44 (0.24–0.78)	
Hand OA		
Crude	0.83 (0.46–1.50)	0.91 (0.63–1.32)
Age	0.90 (0.47–1.71)	1.04 (0.70–1.56)
Age/height/weight	0.90 (0.47–1.72)	1.06 (0.71–1.59)
Lumbar spine OA		
Crude	1.07 (0.51–2.24)	1.01 (0.66–1.56)
Age	1.23 (0.57–2.67)	1.14 (0.72–1.80)
Age/height/weight	1.30 (0.59–2.83)	1.22 (0.76–1.94)
Thoracic spine OA		
Crude	0.93 (0.45–1.93)	0.95 (0.62–1.46)
Age	0.98 (0.47–2.04)	0.99 (0.65–1.52)
Age/height/weight	1.04 (0.49–2.18)	1.05 (0.68–1.62)

Further, there was no evidence of radiological OA at other sites and no association with joint or spinal pain. This is not necessarily a contradiction of the finding of increased OA in hypermobile joints reported in previous studies, where OA is a sequela of more marked hypermobility in a given joint[25], e.g., in an unstable joint after anterior cruciate rupture. In this study very few subjects demonstrated hypermobility of the knees themselves.

It is interesting that those who demonstrated some hypermobility were in the top tertile for physical activity. Whether this represents inherited or acquired hypermobility (i.e., cause or effect) cannot be discerned here. It is recognized that hypermobility can be an advantage in performing many activities and is of increased incidence in dancers[25], athletes[21], and musicians[23,26,27], where it can facilitate ease of some movement or postures required. However, the more fragile tissues can also be at increased risk of injury[28]. When the effect of exercise in the hypermobile group was controlled for, the benefit on hip BMD was lost. The association may reflect the group's tendency to exercise rather than an inherent effect of hypermobility. The EVOS study of vertebral fracture[29] is one of a number of studies that have confirmed current and lifetime physical activity to be positively associated with hip BMD. Exercise programs have also been shown to increase hip BMD, proportionally more than spine, in postmenopausal women. Spine mobility, our most prevalent site of mobility, has been reported to be trainable and so might be considered "the odd man out" of the Beighton criteria.

The association with knee OA (JSN) declined when adjusted for exercise, suggesting exercise was not a major confounder in the relationship. Exercise is recognized to improve symptoms of knee OA[30], but is not known to benefit radiological change. Conversely, excessive weight-bearing exercise can be a risk factor for OA. The group of hypermobile subjects identified here seems to have less knee OA and modestly increased hip BMD, and be more physically active. Thus, hypermobility in a general aging population may be an advantage and a marker of "fitness" when it persists into later life.

There was no difference in the incidence of back and knee pain with the cohort as a whole. Thus, they cannot be considered to have the BJHS, since this is defined as joint hypermobility in the presence of pain symptoms[9,24,28]. The results of this study did not show any evidence of either premature OA or reduced BMD to suggest that in these subjects hypermobility is a marker for a *forme fruste* of a heritable disorder of connective tissue. A caveat is that these were not the severe rare cases. Our study is generalizable only to older female populations and cannot be considered to apply to rare diseases such as EDS and osteogenesis imperfecta. Nevertheless, our study suggests that hypermobility is not a common cause of joint problems in the postmenopausal population.

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