Eur Spine J (1997) 6:385–389

ORIGINAL ARTICLE

S. Roberts
I. W. McCall
J. Menage
M. J. Haddaway
S. M. Eisenstein

Does the thickness of the vertebral subchondral bone reflect the composition of the intervertebral disc?

Received: 7 January 1997
Revised: 17 April 1997
Accepted: 29 April 1997

S. Roberts (✉) · J. Menage
S. M. Eisenstein
Centre for Spinal Studies,
Robert Jones and Agnes Hunt Orthopaedic and District Hospital, Oswestry,
Shropshire, SY10 7AG, UK
Tel. +44-1691-404664;
Fax +44-1691-404054

I. W. McCall · M. J. Haddaway
Department of Diagnostic Imaging,
Robert Jones and Agnes Hunt Orthopaedic and District Hospital,
Oswestry, Shropshire, UK

Abstract Degeneration of the intervertebral disc, seen radiologically as loss of disc height, is often associated with apparent remodelling in the adjacent vertebral body. In contrast, maintenance or apparent increase in disc height is a common finding in osteoporosis, suggesting the properties of the intervertebral disc may be dependent on those of the vertebral body or vice versa. We have investigated this relationship by measuring the radiological thickness of the subchondral bone and comparing it to the chemical composition of the adjacent disc. Sagittal slabs were sampled from lumbar spines obtained at autopsy and X-rayed microfocally. The thickness of the subchondral bone was measured and correlated with the composition of the adjacent intervertebral disc. Eighty-three cadaveric endplates were studied from individuals aged 17–85 years. There was regional variation in thickness of the subchondral bone, being greater adjacent to the annulus than the nucleus, and the endplates cranial to the disc were thicker than those caudal. There was a positive correlation between the thickness of the subchondral bone and the proteoglycan content of the adjacent disc, particularly in the region of the nucleus. A weaker correlation was seen here between water content and thickness, whilst there was no significant correlation at the annulus or between the bone thickness and collagen content. The positive relationship between the radiographic thickness of vertebral subchondral bone and the proteoglycan content of the adjacent disc seen in human cadaveric material could be due to the bone responding to a greater hydrostatic pressure being exerted by discs with higher proteoglycan content than by those with less proteoglycan present. It is suggested that while this is true in "normal" specimens, the relationship becomes altered in disease states, possibly because of changes to the nutritional pathway of the disc, with resultant endplate-bone remodelling affecting the flow of solutes to and from the intervertebral disc.

Key words Intervertebral disc · Bony endplate · Proteoglycan content · Swelling pressure

Introduction

Degenerative changes in the intervertebral disc are often reported to occur concomitantly with alterations to the adjacent vertebral body, such as increasing sclerosis of the subchondral bone or osteophyte formation [1, 5]. An association between properties of the intervertebral disc and vertebral body is also indicated by the occurrence of the fish-vertebra deformity in some cases of osteoporosis. Here the intervertebral discs, with normal radiological ap-

Table 1 Age and location of specimens investigated

Specimen	Age (years)	Sex	No of discs	Level
1	17	M	5	L1-S1
2	25	M	5	L1-S1
3	30	M	2	L3-5
4	35	F	2	L1-S1
5	52	M	2	L3-5
6	66	F	2	L4-S1
7	73	F	2	L4-S1
8	74	F	2	L4-S1
9	75	M	5	L1-S1
10	76	M	4	L1-5
11	82	M	2	L4-S1
12	82	F	2	L4-S1
13	83	F	2	L4-S1
14	85	F	2	L4-S1

pearance, expand, compressing the osteoporotic bone of the vertebrae [7]; i.e. in this group healthy-appearing discs are associated with reduced bone mineral density.

Studies relating mechanical properties of vertebral bone and disc composition also indicate a relationship between the properties of these two tissues [9, 11, 12]. However, these studies provide evidence that "healthy" discs are associated with a maintenance of bone mineral density. For example, Keller et al. [12] found a positive correlation between compressive stiffness of subdiscal bone and fixed charge density (representing proteoglycan content) of the intervertebral disc, suggesting that a healthy disc with high proteoglycan content was coincident with high compressive stiffness of subchondral bone. The object of the present study was to investigate further the relationship between properties of subchondral vertebral bone and intervertebral disc. The radiological thickness of the subchondral bone was measured and correlated to properties of the adjacent intervertebral disc such as biochemical composition and state of degeneration, in addition to the age of the individual.

Fig. 1 The relationship between subchondral bone thickness and age based on values obtained from L4-5 of each lumbar spine (*SEM* standard error mean)

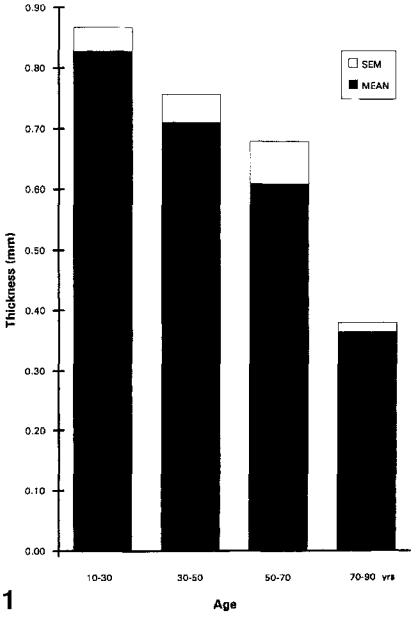
Fig. 2 The profile of subchondral bone thickness across the vertebrae (calculated as the mean of 72 endplates; bar represents 1 standard error)

Fig. 3 The relationship between subchondral bone thickness and proteoglycan content of the disc in the region of the nucleus of all specimens

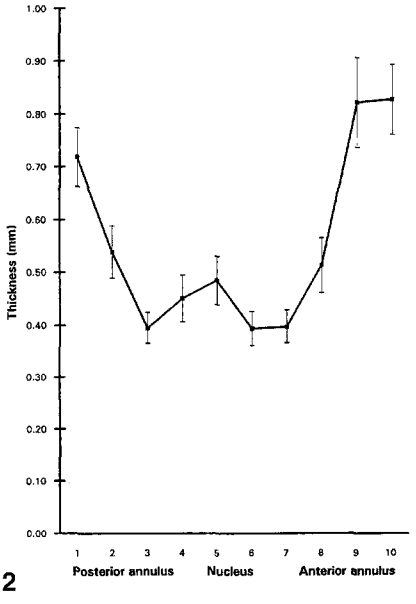
Materials and methods

Eighty-three endplates and adjacent intervertebral discs from the lumbar spines of 14 individuals, aged 17–85 years (mean 61 ± 24 years), were collected at autopsy (Table 1). There was no known skeletal pathology and the material was collected within 36 h of death. The lumbar spines were frozen, cut into motion segments through the vertebral body, and a mid-sagittal slab (approximately 1 cm thick) was removed. This was photographed, to provide a record of macroscopic degeneration, and microfocal plain radiographs were taken of the slab, using a fine-focus X-ray device and magnification technique with geometric enlargement. An E12 microfocal set was used with an exposure of 50 kV and 0.1 mAs and a focal spot size of 20 μ diameter.

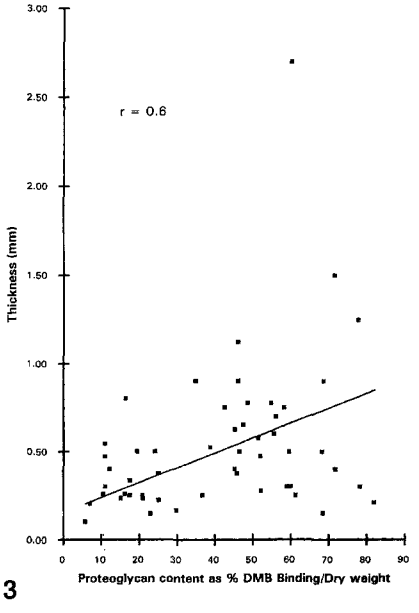
The specimens were graded for degeneration on a scale of 1–5, 1 representing minimum and 5 maximum degeneration, according to the macroscopic appearance of the slab [19]. This was then dissected into columns from the nucleus and annulus, which were in turn cut into horizontal slices 100–400 μm thick on a freezing microtome taking care to minimise dehydration. These slices were analysed for chemical composition. Water content was measured by drying to constant weight at 60° C [26]. The tissue was digested



1



2



3

Table 2 Mean values of the thickness, in millimetres, of the vertebral subchondral bone, cranial and caudal to the intervertebral disc ($P < 0.05$, t-test)

	Mean SD
Cranial ($n = 98$)	0.60 ± 0.55
Caudal ($n = 100$)	0.45 ± 0.34

Table 3 Correlation of endplate thickness with age and disc composition. The correlation between thickness of subchondral bone and e.g. proteoglycan was stronger in the nucleus region than elsewhere (Spearman's rank correlation)

	All		Nucleus	
	r	P	r	P
Proteoglycan	0.4	0.01	0.6	0.001
Water	–0.5	NS	0.4	0.01
Collagen	0.02	NS	–0.2	NS
Age	–0.6	0.001	–0.7	0.001

with papain (Sigma type IV, 12 iu/ml) in cysteine buffer at 60° C for 4 h or until digestion was complete. Aliquots of digests were used for estimating (1) proteoglycan content, as degree of dimethylmethylene blue binding (DMB, Uniscience) [4] and (2) hydroxyproline, as a measure of collagen content, using a modification of the automated method of Grant [6], after hydrolysis with HCl for 16 h at 110° C.

Subchondral bone thickness was measured from the radiograph (with a coefficient of variance of 4.8%) in the regions abutting the anterior and posterior annuli and the central nucleus, using an eyepiece (magnification × 8) and graticule. The thickness of bone was then correlated with the chemical composition of the adjacent cranial or caudal half of the intervertebral disc, as appropriate (obtained by taking mean values of the component slices). In addition, in 72 of the endplates a more detailed profile of the subchondral bone thickness was obtained by measuring the thickness at ten equal intervals from the anterior margin across to the posterior margin.

Statistical analyses were performed using a commercial package, Statgraphics (STSC, Rockville, Md.). Some variables did not have a normal distribution, so that non-parametric methods, such as Mann-Whitney U test and Spearman's rank correlation, were used where appropriate. Multiple regression was not carried out, as the variables being investigated are known to be strongly related, rendering this test inappropriate [10]. Student's t-test was used to test the difference between means where sample size was large and this was valid [10].

Results

The thickness of the subchondral bone decreased with increasing age, with a correlation coefficient of –0.6 ($n = 244$, Fig. 1). This remained at –0.67 even when the mean value of one endplate from a single vertebral level of each spine was used (i.e. $n = 14$). Other changes with age were an increase in degenerative grade ($r = 0.76$) and a decrease in proteoglycan content ($r = -0.6$).

The bony endplates cranial to the disc were significantly thicker ($P < 0.05$) than those caudal to the discs (Table 2), but the rate of change with age was the same at both sites. Similarly, the endplates were thicker in the region of the annulus, particularly at the anterior, compared to that found in the nuclear region (Fig. 2). There was no significant trend with any properties down the spine.

There was a positive and significant correlation between the thickness of the subchondral bone and the proteoglycan content of the intervertebral disc. The correlation was stronger in the region of the nucleus than elsewhere (Fig. 3, Table 3). Thus, specimens with a thick bony endplate had a high level of proteoglycan, typical of a healthy state, in their adjacent discs. No such relationship was seen between endplate thickness and collagen content, but there was a weak correlation with water content in the nucleus (Table 3).

Discussion

Decreased subchondral bone thickness with age found in the present study is likely to be a reflection of the general decrease in bone mineral density seen with increasing age [8]. Britton and Davie [2] reported that 25% of apparent bone density is lost in the lumbar spine between 25 and 75 years of age. The finding that the inferior vertebral endplate cranial to the disc was thicker than that caudal to it fits in with clinical observations of more vertebral fractures in the osteoporotic spine occurring in the superior aspect of the vertebral body than the inferior (unpublished data). Hence there appears to be local variations in the control of bone mineral density. Certainly loss of bone mineral content in osteoporosis does not occur simultaneously throughout the skeleton, but it commences and is more marked in the vertebrae than in any peripheral site [3].

A significant and positive correlation was found between the thickness of the vertebral endplate and the proteoglycan content of the adjacent intervertebral disc. Proteoglycans in tissue such as the intervertebral disc exert an osmotic pressure, leading to imbibition of water [23]. This in turn leads to the tissue being able to exert a swelling pressure. Hence, the relationship between disc proteoglycan and subchondral bone thickness found in the present study could be arrived at by the subchondral bone responding, according to Wolff's Law, to the greater load incident on intervertebral discs with a higher proteoglycan content than on those with a lower proteoglycan content. This correlation was greater at the nucleus than the annulus, possibly because the endplate structure and loading pattern at the periphery is more complex (with ligament insertion points, Sharpey's fibres etc.) than that found centrally. Bone mineral content and mechanical strength have been found to be greater at the anterior part of the vertebrae compared to the posterior [2], particularly in the outer region adjacent to the cortices. The stresses in the outer disc differ from those found in the central disc. Here compressive stresses are predominant, whereas in the outer annulus there is only a small compressive but large tensile component [14].

The results of the present study are in agreement with other studies on cadaveric spines. A similar relationship between proteoglycan content of discs and the mechanical properties, such as subdiscal bone stiffness, has been shown by Keller et al. [12]. Hansson and Roos [9] found macroscopic disc degeneration occurring in vertebrae of lower bone mineral content than was found in those with no degeneration. Similarly a decrease in compressive

strength and stiffness (which correlated strongly with bone density) has been reported to occur with increased degeneration of intervertebral disc [11]. All the above studies, as this one, were carried out on autopsy material. It appears, however, that there may be a different, or even opposite, relationship between the properties of subchondral bone and intervertebral disc in disease states. In degenerative disc disease or osteochondritis, for example, there is sclerosis of the vertebral body adjacent to degenerate discs, as seen radiologically [17]. The discs in such individuals could be expected to have a reduced proteoglycan content, since this is as much as 70% lower in degenerate discs than in age-matched control discs [18]. In an animal model of disc degeneration there is thickening of the vertebral endplates adjacent to degenerate discs [21]. A similar association between reduced disc space and reactive vertebral sclerosis is seen in many other spinal disorders, such as infection, trauma, neuroarthropathy, rheumatoid arthritis, calcium pyrophosphate dihydrate deposition and alkaptonuria [17].

Hence, it appears that in the normal spine, a high proteoglycan content in healthy disc could lead to an increased incident loading and more bone laid down subchondrally. If this is laid down by remodelling and increasing the thickness of trabeculae, as suggested by Resnick [16], a point might be reached at which channels in the subchondral bone are occluded. This is one of the pathways by which nutrients normally reach the disc [24]. The nutritive status of the disc is thought to be precarious, requiring only a small reduction of efficiency to compromise it [22]. Hence, restriction of vascular flow or available surface area for exchange, such as could occur by narrowed channels, might in turn lead to a decrease in available nutrients for normal disc cell metabolism and thence to disc degeneration [22]. This is known to alter the loading within the spine [13], which may then potentiate a pathological cycle leading to greater vertebral sclerosis and further degeneration of the disc.

Such a pathway as this would indicate a time scale of changes. There is indeed evidence for this, since whilst it is generally accepted that a decrease in disc height is typical of late-stage degenerative disc disease [1, 15, 17, 25], in the early stage of the disease there is often no loss of disc height [20]. Similarly, desert sand rats, which spontaneously develop degenerative disc disease, demonstrate changes in the subchondral bone, with increased volume and density of trabeculae, prior to degenerative histological changes in the intervertebral disc [28].

In osteoporosis, in contrast, the disc may be ballooned, protruding into the vertebral body. This could occur because there is overall loss of bone in the vertebral body, which would be less suited to resisting the discal hydrostatic pressure. A similar expansion of disc into the vertebral body has been reported in 20% of individuals with malignant involvement of vertebral body, compared to 2% of an age-matched control sample [27]. It would appear, therefore, that the relationship between properties of the intervertebral disc and adjoining vertebral bone is plastic and, typical of biological systems, capable of adapting to changing situations.

Conclusions

In this study on normal cadaveric spines we have shown there to be a positive correlation between the thickness of the bony endplate and the amount of proteoglycan in the adjacent disc. This could be arrived at due to bone remodelling in response to the hydrostatic pressure exerted by the proteoglycans of the disc. It is suggested that whilst this relationship holds true in "normal" cadaveric spines, it may not be so in disease states such as degenerative disc disease and osteoporosis. Here, altered bone density in the endplate could be expected to affect the nutritive state, and hence composition, of the intervertebral disc via its influence on the flow of solutes to and from the disc.

Acknowledgements We are grateful to the Arthritis and Rheumatism Council for financial assistance.

References

1. Bell GR, Modic MT (1992) Radiology of the lumbar spine. In: Rothman RH, Simeone FA (eds) The spine. Saunders, Philadelphia, pp 125–153
2. Britton JM, Davie MWJ (1990). Mechanical properties of bone from iliac crest and relationship to L5 vertebral bone. Bone 11:21–28
3. Chalmers J, Weaver JK (1963) Cancellous bone: its strength and changes with aging and an evaluation of some methods for measuring its mineral content. J Bone Joint Surg [Am] 48:299–308
4. Farndale RW, Buttle DJ, Barrett AJ (1986) Improved quantitation and discrimination of sulphated glycosaminoglycans by use of dimethylmethylene blue. Biochim Biophys Acta 883:173–177
5. Garfin F, Rydevik BL, Lipson SJ (1992) Spinal stenosis. In: Rothman RH, Simeone FA (eds) The spine. Saunders, Philadelphia, pp 791–826
6. Grant RA (1964) Estimation of hydroxyproline by the AutoAnalyser. Clin Pathol 17:685–686
7. Grieve GP (1988) In: Common vertebral joint problems, 2nd edn. Churchill Livingstone, Edinburgh, p 401
8. Haddaway MJ, Davie MWJ, McCall IW (1992) Bone mineral density in normal women and reproducibility of measurements in spine and hip using dual-energy X-ray absorptiometry. Br J Radiol 65:213–217
9. Hansson T, Roos B (1981) The relation between bone mineral content, experimental compression fractures, and disc degeneration in lumbar vertebrae. Spine 6:147–153

10. Hays WL (1988) Statistics. Holt, Rinehart and Winston, Fort Worth
11. Keller TS, Hansson TH, Abram AC, Spengler DM, Panjabi MM (1988) Regional variations in the compressive properties of lumbar vertebral trabeculae. Effects of degeneration. Spine 14:1012–1019
12. Keller TS, Ziv I, Moeljanto E, Spengler DM (1993) Interdependence of lumbar disc and subdiscal bone properties: a report of the normal and degenerative spine. J Spinal Disord 6:106–113
13. Kurowski P, Kubo A (1986) The relationship of degeneration of the intervertebral disc to mechanical loading conditions on lumbar vertebrae. Spine 11:726–731
14. McNally DS, Adams MA (1992) Internal intervertebral disc mechanics as revealed by stress profilometry. Spine 17:66–73
15. Modic MT, Masaryk TJ, Ross JS, Carter JR (1988) Imaging of degenerative disk disease. Radiology 168:177–186
16. Resnick D (1985) Degenerative diseases of the vertebral column. Radiology 156:3–14
17. Resnick D, Niwayama G. (1981) Degenerative disease of the spine. In: Resnick D, Niwayama G (eds) Diagnosis of bone and joint disorder. Saunders, Philadelphia, pp 1368–1415
18. Roberts S, Beard HK, O'Brien JP (1982) Biochemical changes of intervertebral discs in patients with spondylolisthesis or with tears of the posterior annulus fibrosus. Ann Rheum Dis 41: 78–85
19. Roberts S, Menage J, Urban JPG (1989) Biochemical and structural properties of the cartilage endplate and its relation to the intervertebral disc. Spine 14:166–174
20. Schiebler ML, Camerino VJ, Fallon MD, Zlatkin MB, Grenier N, Kressel HY (1991) In vivo and ex vivo magnetic resonance imaging evaluation of early disc degeneration with histopathologic correlation. Spine 16:635–640
21. Sether LA, Nguyen C, Yu S, et al (1990) Canine intervertebral disks: Correlation of anatomy and MR imaging. Radiology 175:207–211
22. Stairmand JW, Holm S, Urban JPG (1991) Factors influencing oxygen concentration gradients in the intervertebral disc: a theoretical analysis. Spine 16, 444–449
23. Urban JPG, McMullin JF (1988) Swelling pressure of the lumbar intervertebral discs: effect of age, spinal level, composition and degeneration. Spine 13:179–187
24. Urban JPG, Holm S, Maroudas A, Nachemson A (1977) Nutrition of the intervertebral disc. An in vivo study of solute transport. Clin Orthop 129:101–114
25. Vanharanta H, Sachs BL, Spivey M, et al (1988) A comparison of CT/discography, pain response and radiographic disc height. Spine 13:321–324
26. Venn MF (1979) Chemical composition of human femoral head cartilage: influence of topographical position and fibrillation. Ann Rheum Dis 38:57–62
27. White MJ, Jenkins JR (1991) Pathologic compression in spinal malignancy secondary to intervertebral disk expansion. Comp Med Imaging Graphics 15:373–377
28. Ziran BH, Pineda S, Pokharna H, Esteki A, Mansour JM, Moskowitz RW (1994) Biomechanical, radiologic, and histopathologic correlations in the pathogenesis of experimental intervertebral disc disease. Spine 19:2159–2163