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AJNR Am J Neuroradiol 2001, 22 (8) 1620-1627
http://www.ajnr.org/content/22/8/1620

AJNR Am J Neuroradiol 22:1620–1627, September 2001

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BACKGROUND AND PURPOSE: **Increased fat content in vertebrae may indicate bone weakness. Vertebral proton MR spectroscopy (^{1}H MRS) quantitatively measures vertebral fat relative to water. Thus, ^{1}H MRS measurements of percent fat fraction (%FF) and spectral line width (LW) of vertebral bone marrow may differ between subjects with and those without MR imaging evidence of weakened bone.**

METHODS: **We measured %FF and LW in 22 subjects with (15 men and 7 women, aged 26 to 80 years) and 72 control subjects without (33 male and 39 female subjects, aged 15 to 87 years) MR findings of weakened bone, including prominent Schmorl's nodes, endplate depression, vertebral wedging, and vertebral compression fractures. In those with bone weakness, ^{1}H MRS data were sampled from an intact vertebra, usually L2. Data were analyzed for differences by age and sex. We compared the mean %FF and LW in subjects with and in those without bone weakness by use of Student's *t* test.**

RESULTS: **The %FF increased linearly with age in the control subjects, ranging from 20.5% in the second and third decades of life to 49.4% in eighth or ninth decades of life. Across all age groups, male control subjects had a higher aggregate %FF than did female control subjects. Male control subjects tended to have a greater LW than did female control subjects, but differences between the sexes within or across age groups were not significant. Contrary to expectations, LW was greatest in the oldest control subjects and lowest among younger control subjects, but there were insufficient data points to make definitive conclusions. Overall, %FF was a relative 45% higher in subjects with weakened bone compared with control subjects (48.8 vs 33.6 [$P < .001$]). The subjects with evidence of vertebral bone weakness also had a higher overall mean LW (37 vs 29 Hz [$P < .002$]), but this finding is of uncertain importance.**

CONCLUSION: **The %FF was significantly higher within the L2 vertebral body in 22 subjects with weakened bone compared with the control group, suggesting that it could serve as a measure of bone quality. The LW measurements did not yield meaningful conclusions.**

The literature suggests that bone strength is multifactorial and may depend not only on bone density but also on bone-marrow quality (1, 2). Osteoporosis, for example, has been shown to be associated with increased fat content in the bone marrow (3–6). Marrow fat may reflect bone weakness (7).

Proton MR spectroscopy (^{1}H MRS) can provide quantitative information about certain bone constituents, most prominently, fat (8–12). Other MR techniques also allow quantitative bone analysis, but these are based on magnetic susceptibility considerations and on T2 relaxation measurements (9, 13–16), which may be too complex for routine clinical applications. Thus, although these alternate techniques hold promise, ^{1}H MRS may be easier to apply and interpret.

We published normative ^{1}H MRS data that included lipid-water ratios (LWR) and spectral line widths (LW) for a group of healthy subjects (17). In this study, we expanded our control group by adding ^{1}H MRS data from individuals with normal lumbar MR imaging findings. In addition, we included ^{1}H MRS data from a group of patients with MR findings of vertebral weakness for comparison with those from the control subjects. We investigated whether ^{1}H MRS can provide diagnostic clues to help appraise vertebral biomechanical competence. If so, it could add important information to diagnostic lumbar MR imaging, in that localized ^{1}H MRS can be easily applied and attached to routine MR imaging without substantial time penalty.

Received November 7, 2000; accepted after revision March 20, 2001.

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TABLE 1: Summary of results by decades of age*

Age Decades*	n	Lipid-Water Ratio	% Fat Fraction	n	Line Width (Hz)
Decades 2 and 3					
Normal	20	0.27	20.5	15	25.9
Abnormal	3	0.57	32	3	35.5
Difference (%)			56		37
Schmorl's nodes	3	0.57	36	3	35.5
Decades 4 and 5					
Normal	26	0.53	32.5	15	31.2
Abnormal	9	0.88	41	8	38.6
Difference (%)					24
Schmorl's nodes	4	0.89	40	4	44.3
Wedging	4	0.92	41	4	39.0
Endplate depression	1	0.67	40	1	26.6
Decades 6 and 7					
Normal	18	0.87	42.6	12	30.2
Abnormal	5	1.06	49.6	3	30.8
Difference (%)			16		2
Schmorl's nodes	5	1.06	51	5	30.83
Decades 8 and 9					
Normal	8	1.12	49.4	3	40
Abnormal	5	1.79	63.2	1	38
Difference (%)			21		−6
Schmorl's nodes	2	1.48	60	2	47.5
Compression fractures	3	2.00	67	3	37.9
All decades					
Normal	72	0.60	33.6	42	29
Abnormal	22	1.08	48.8	16	37.1
Difference (%)			45		28

* Types of weakened bone (breakdown of the abnormal cases) are shown within each decade group.

Methods

We studied 72 control subjects (33 male and 39 female subjects, aged 15 to 87 years) without and 22 subjects (15 men and 7 women, aged 26 to 80 years) with MR imaging evidence of vertebral bone weakness. The group of control subjects included 57 people from our previous study (17). The 72 control subjects also included 11 volunteers and 61 subjects who underwent MR imaging to evaluate back pain but who exhibited no imaging signs of bone weakness. The 22 subjects with evidence of bone weakness were clinical patients who underwent lumbar MR imaging for low back pain and who had findings that supported a diagnosis of weakened bone. We excluded patients with known, diffuse marrow disease and a known history of radiation or steroid therapy. All subjects in this study had had ^{1}H MRS added to their routine MR study in accordance with an approved clinical protocol. The ^{1}H MRS sequence added 3 to 5 minutes to the routine MR imaging procedure.

The MR imaging findings of bone weakness included prominent Schmorl's nodes (n = 14), endplate depression (n = 1), wedging of vertebrae (n = 4), and vertebral body compression fractures (n = 3) (Table 1). Schmorl's nodes represent a form of intraosseous disk herniation, which often is associated with bone weakness. Endplate depression is the late result of fractures localized to one of the vertebral endplates. Vertebral wedging reflects an old compression fracture with no obvious fracture lines or fracture fragment(s) but with anterior height loss. Vertebral compression fractures are vertebrae with inhomogeneous tissue changes, sometimes associated with obvious fracture lines, fracture fragments, or bone displacement.

To be included in this study, a subject was required to undergo ^{1}H MRS, usually of the L2 vertebral body, and a sagittal T1-weighted MR imaging of the lumbar spine to allow for visual assessment of lumbar vertebrae. Most subjects had single-voxel spectra. Eleven control subjects from our earlier study also had multivoxel ^{1}H MRS (2D chemical-shift imaging). One of our authors (D.S.) reviewed the clinical MR images of patients who had undergone ^{1}H MRS and determined that MR imaging showed bone weakness. The L2 vertebra was targeted for ^{1}H MRS data sampling, because it usually is less affected by spondylosis or degenerative disk disease. In the patients with bone weakness, ^{1}H MRS measurements were made in vertebrae that were not compressed or otherwise abnormal, usually L2. If L2 was compressed or otherwise altered in structure, a neighboring vertebra was used.

The ^{1}H MRS techniques and voxel placement have been described in detail (17). All measurements were performed on a Siemens Vision 1.5-T unit (Erlangen, Germany). The stimulated echo-acquisition mode sequence was used; its advantages over point-resolved spectroscopy have been discussed (17). The software applied is part of the ^{1}H MRS package for the Siemens Vision system (Siemens, Erlangen, Germany) and has United States Food and Drug Administration approval.

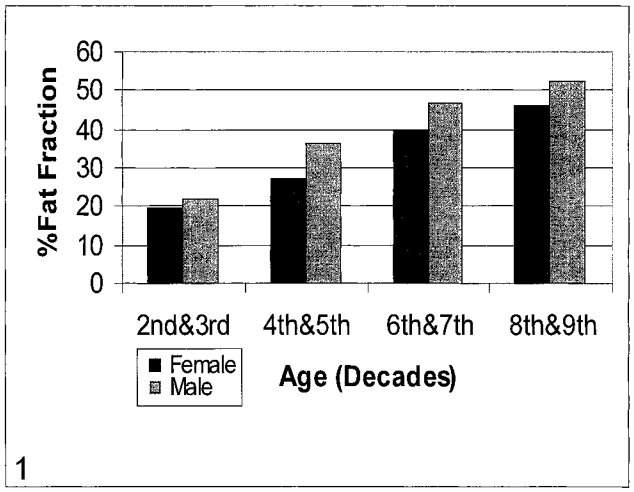
The ^{1}H MRS divides the global MR signal from bone into two major segments: water and lipid. The water signal comes mostly from red marrow, and most lipid signals stem from yellow marrow. The spectra of ^{1}H MRS have a water peak and a lipid peak (10, 18–22). Although the lipid signal is composed of at least eight fractions (23), it is the methylene group at 1.6 ppm that contributes the largest signal. The two major signals (water and lipid) are separated by 3.1 ppm. Signal peaks can vary from subject to subject and are influenced not only by the water/lipid proton quantity but also by the surface coil in use, the distance between the voxel and surface coil, and by the tissue environment. Therefore, instead of measuring the absolute signal peak for signal quantification, we derived a lipid-water ratio (LWR) for each voxel. Relative vertebral fat content can be expressed in LWR, fat fraction (FF), or percent fat fraction (%FF). For the purpose of clarity and consistency, we will use %FF as the preferred standard measurement in the remainder of this study. All values are derived from this equation: FF = LWR / (LWR +1). A spectrum with a lipid peak of 50 mm and a water peak of 25 mm has a LWR of 2 (50/25). The FF and %FF are derived directly from LWR: an LWR of 2.0 results in a FF of 0.66 (2/(2+1) and in an %FF of 66% (FF × 100).

In 42 control subjects and 16 patients with weakened bone, the ^{1}H MRS spectra also were evaluated for LW. The smaller number of samples for this evaluation reflects its late addition to the ^{1}H MRS studies. In a few subjects, the LW was erroneously omitted. The LW is determined by measuring the signal's full width at half height (FWHH). The LW stems largely from susceptibility produced by the inhomogeneity of the magnetic field caused by trabeculae. The potential of LW to serve as a measure of bone density was first suggested by Schick et al (9). The LW, commonly measured in Hz, depends on the distribution of the static magnetic field, which influences water and lipid peaks in the same way. We used the water peak for LW measurements, because it always consists of a single peak and thus is more suitable for FWHH (9). The LW measurements for control subjects are presented in our previous article (17). For this analysis, we obtained additional LW measurements for control subjects. All 22 subjects with MR findings of bone weakness had LW measurements, in addition to LWR and %FF.

The ^{1}H MRS data (LWR, %FF, LW) for control and abnormal vertebrae are listed by decade of age and summarized in Table 1. The data for %FF and LW were separately arranged in a manner that allowed analysis of age and sex and compar-

TABLE 2: Summary of results, control and abnormal subjects

Variable by Age Decade	Male Controls		Female Controls			All Control Subjects		Abnormal Bone		
	n	Mean (SD)	n	Mean (SD)	*P*	n	Mean (SD)	n	Mean (SD)	*P*
% Fat fraction										
Decades 2 and 3	9	21.8 (5.6)	11	19.5 (5.9)	<.25	20	20.5 (6)	3	32 (24.2)	<.2
Decades 4 and 5	13	36.4 (12.2)	13	27.4 (9.8)	<.025	26	32.5 (11.9)	9	46 (5.8)	<.001
Decades 6 and 7	7	46.9 (15.7)	11	39.7 (8.7)	<.2	18	42.6 (12)	5	49.6 (10.9)	<.1
Decades 8 and 9	4	52.3 (7.7)	4	46.1 (17.6)	<.4	8	49.4 (13)	5	63.2 (7.3)	<.02
All decades	33	36.6 (11.3)	39	30.6 (9.5)	<.01	72	33.6 (10.5)	22	48.8 (10)	<.001
Line width (Hz)										
Decades 2 and 3	6	22.7 (4)	9	28 (6.1)	<.07	15	25.9 (5.4)	3	35.5 (12.9)	<.2
Decades 4 and 5	8	33.8 (6.4)	7	28.2 (5.7)	<.10	15	31.2 (6.1)	8	38.6 (7.9)	<.05
Decades 6 and 7	4	30.4 (3.3)	8	30.1 (5.3)	<.99	12	30.2 (4.8)	3	30.8 (8.2)	<.99
Decades 8 and 9	1	43.7 (NA)	2	38.4 (12.9)	NA	3	40 (9.7)	1	38 (NA)	NA
All decades	18	29.3 (5.2)	24	28.8 (5.7)	<.99	42	29 (5.5)	16	37.1 (8.8)	<.002



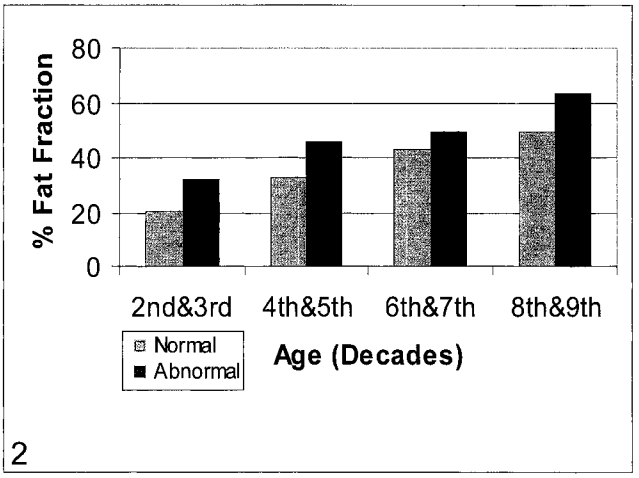


FIG 1. Relationship of age, sex, and percent fat fraction (%FF). Patients are grouped by decades of age; within each decade group, male and female subjects are separately represented. There is a linear increase of %FF with age and a difference in this variable between male and female subjects.

FIG 2. %FF for both normal and abnormal bone, by decades of age. Abnormal bone has a higher %FF in all age groups.

ison of control and abnormal bone (Table 2). Statistical evaluation was conducted with Student's *t* test. Commercially available software (Excel; Microsoft, Redmond, Washington) was used.

Results

Percent Fat Fraction in Control Subjects: Age- and Sex-Related Differences

There was a linear rise in %FF with age, ranging from 20.5% for the second and third decades of life to 49.4% for the eighth and ninth decades. In the aggregate, male subjects had higher %FFs than did female subjects in all age categories (Table 2, Fig 1). This sex difference was most pronounced in the fourth through fifth and sixth through seventh decades, but was significant only for the fourth and fifth decades ($P < .025$) and for the total group of 72 control subjects ($P < .01$).

Percent Fat Fraction in Subjects with Weakened Bone

In the first age grouping (second and third decades), the %FF in the abnormal group was 56% higher than that in the control subject group (32 vs 20.5 [Tables 1 and 2, Fig 2]). It was consistently higher in all other age groups. The difference in %FF between subjects with and those without weakened bone was significant for the fourth and fifth ($P < .001$) and eighth and ninth decades ($P < .02$). For the group as a whole, the %FF was a relative 45% higher in the subjects with weakened bone, which also was significant ($P < .001$).

There were 14 subjects with Schmorl's nodes (Fig 3). This constituted our largest disease category. The %FF of subjects with Schmorl's nodes was consistently higher in all age categories compared with age-matched control subjects (Table 1). The %FF in these patients was a relative 76% high-

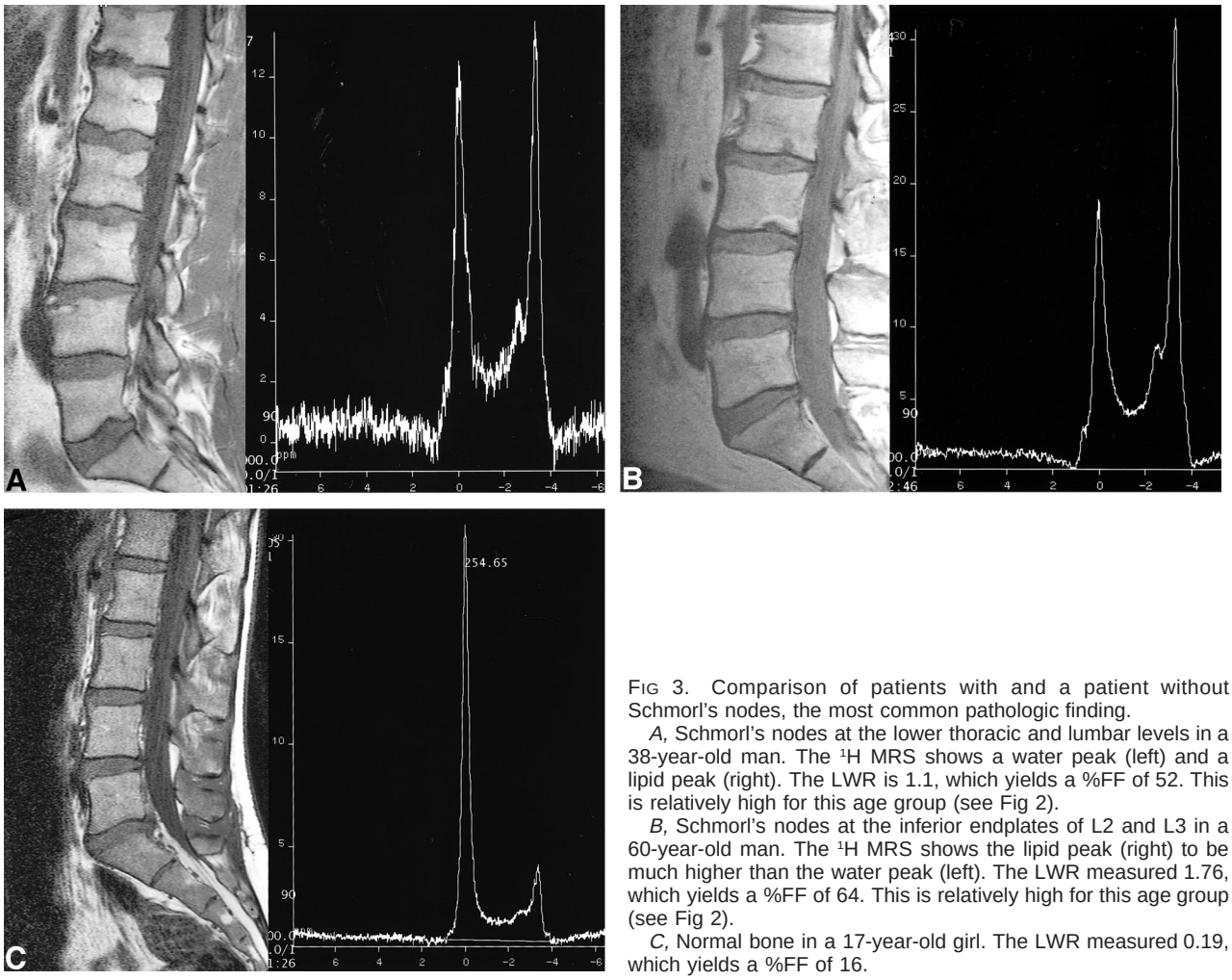


FIG 3. Comparison of patients with and a patient without Schmorl's nodes, the most common pathologic finding.

A, Schmorl's nodes at the lower thoracic and lumbar levels in a 38-year-old man. The ^{1}H MRS shows a water peak (left) and a lipid peak (right). The LWR is 1.1, which yields a %FF of 52. This is relatively high for this age group (see Fig 2).

B, Schmorl's nodes at the inferior endplates of L2 and L3 in a 60-year-old man. The ^{1}H MRS shows the lipid peak (right) to be much higher than the water peak (left). The LWR measured 1.76, which yields a %FF of 64. This is relatively high for this age group (see Fig 2).

C, Normal bone in a 17-year-old girl. The LWR measured 0.19, which yields a %FF of 16.

er in the second and third, 23% higher in the fourth and fifth, 20% higher in the sixth and seventh, and 22% higher in the eighth and ninth decades of life. Compression fractures (Fig 4) were observed only in the eighth and ninth decades. These three individuals had a %FF that was 36% higher than that of age-matched control subjects (Table 1). Wedging of vertebrae was found in four individuals, all in their fourth or fifth decade of life (Table 1). Their %FF was 26% higher than that of age-matched control subjects.

Line Width in Control Subjects: Age- and Sex-Related Differences

The LW was almost identical in fourth and fifth versus sixth and seventh decades (31.2 vs 30.2 Hz [Tables 1 and 2]). The LW was highest in the eighth- and ninth-decade group (40 Hz) and was lowest in the second- and third-decade group (25.9 Hz). There were some differences by sex, but these were not statistically significant (Table 2).

Line Width in Subjects with Weakened Bone

The LW of subjects with weakened bone was larger than that of control subjects in two age categories (second- and third-decade and fourth- and fifth-decade groups): 37% and 24%, respectively (Tables 1 and 2). The LW was almost even in the sixth- and seventh-decade group (+2%) and slightly lower in the eighth- and ninth-decade group (-6%). In the entire group, the subjects with weakened bone had an average LW 28% greater than that of control subjects.

Discussion

Change of Vertebral Fat Content with Age

Vertebral marrow fat has been reported to increase with age (24–26). Quantitative histologic studies on age-related changes in bone have shown that the change from hematopoietic to fatty marrow is gradual, steady, and progressive (24).

In this study, additional normative measurements were generated for certain ^{1}H MRS data, foremost of which was %FF. We had observed that the fat content of vertebrae increases linearly with age (17). This observation has been confirmed (27) and is further supported by the current data from 72 subjects. The %FF of subjects in the age category of 11 to 30 years (second- and third-decade group)

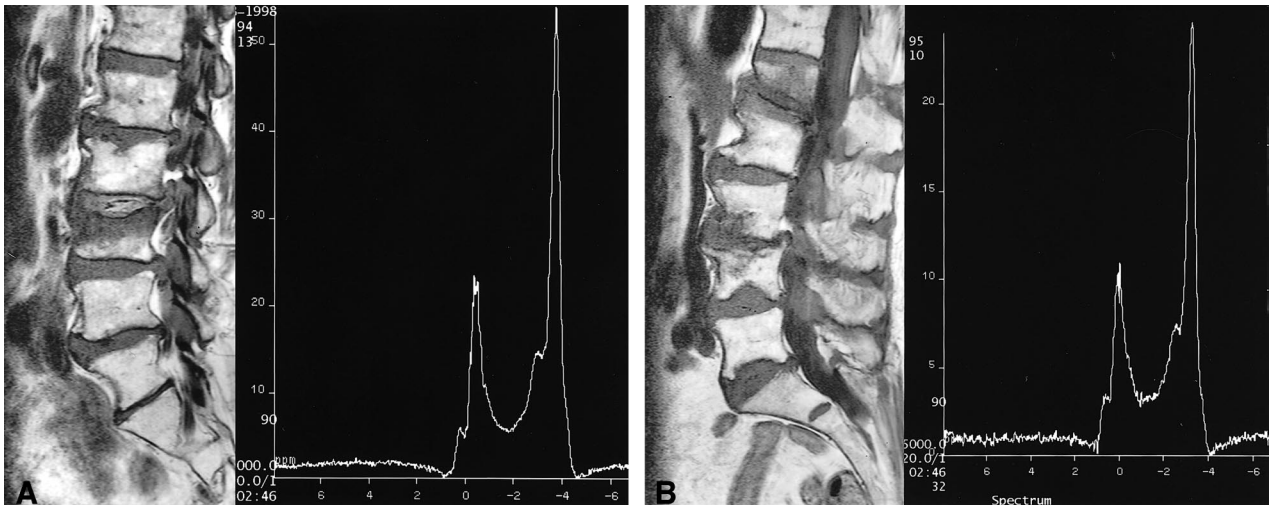


FIG 4. Examples of compression fractures.

A, An 87-year-old man with recent compression fracture of L3 and Schmorl's node at the superior endplate of L2. The ^{1}H MRS at L2 revealed a LWR of 2.3, for a %FF of 70, which is relatively high for this age group.

B, An 80-year-old woman with recent compression fracture of L1, probable fracture at the inferior L3 vertebral body, and inferior endplate depression at L4 and L5. The ^{1}H MRS at L2 shows a very prominent lipid peak. The LWR measured 2.4, for a %FF of 71, which is relatively high for this age group.

was 20.5% versus 49.4% in the age category of 71 to 90 years (eighth- and ninth-decade group [Table 1, Fig 2]). Kugel et al (27), in a recent analysis of age differences in the proton spectrum of vertebral bone marrow, also observed an increase in %FF with increasing age, from 24% in the age group of 11 to 20 years to 54% in the group aged 61 years or older.

Differences in Vertebral Fat Content by Sex

The current, larger data pool supports the trend shown in our previous report. In the entire population, male control subjects had a higher %FF than did female control subjects in all age categories. This difference was most pronounced in the age groups of 31 to 50 years and 51 to 70 years but was statistically significant only among control subjects aged 31 to 50 years ($P < .025$), in which the %FF was a relative 32.8% higher in men, and among the total group of 72 control subjects ($P < .01$).

This sex-related difference is supported by reports that suggest that bone marrow in men has a higher lipid content or that red marrow in women contains less fat and is more cellular than that in men (28–31). A number of reports disagree with these hypotheses, however (32–34). Kugel et al (27) also studied sex-specific differences in the proton spectra of vertebrae. They observed that the proportion of fat in the vertebral bone marrow in female subjects was less than that in male subjects. This difference was largest in the age group of 31 to 50 years (male vs female subjects, 12%).

Increased fat content among male subjects could be interpreted to denote weakened bone. This is unrealistic and contrary to clinical experience. We believe that increased marrow fat found in men is a constitutional phenomenon and reflects their normal tissue texture. Only when fat content increases beyond the norm can it be interpreted as abnormal. As is true for dual-energy x-ray absorptiometry (DXA), the availability of nomograms is crucial. Similar to bone-mineral density, measurements are both age- and sex-dependent.

Relationship of Line Width to Age and Sex

The density and spatial orientation of the trabeculae influence the microscopic homogeneity of the magnetic field inside the marrow (9, 20, 32). This led Schick et al (9) to use LW as a variable in MR bone densitometry. Increased bone density is expected to cause greater magnetic field inhomogeneity and wider spectral peaks. Conversely, decreased bone density narrows the signal peaks.

We previously explored LW measurements among control subjects of various ages and also searched for sex-related differences. The earlier findings did not support the expected LW narrowing with age. In this report, for which additional LW measurements were obtained, the cumulative data show that LW was slightly higher among the older age groups, a finding that runs contrary to expectation (Table 2, Fig 2). The collected data lead us to conclude that LW cannot be used to appraise bone density. Men are known to have a higher bone density than women (35, 36), as are younger compared with older subjects. Although we expected a widened LW in men and in the younger age groups, it was not significantly larger in men or among the young. The LW probably is influenced by factors other than bone trabecula. These data lead us to conclude that LW is not suitable for osteodensitometry. At this time, we are uncertain

about the diagnostic value of LW. More data from a larger subject pool probably are needed.

Relationship of Vertebral Fat Content to Bone Weakening

Our data show that patients with MR imaging findings of bone weakness have a consistently higher %FF compared with control subjects within the same age group (Tables 1 and 2, Fig 2). The difference ranged from a relative 16% (sixth- and seventh-decade group) to 56% (second- and third-decade group).

It is known that increased marrow fat content can lead to bone weakness (3, 4, 7, 37). Conversion of red to yellow marrow with aging is a well-known phenomenon (38). In osteoporosis, an increase in bone marrow fat cannot be ignored (5). Histologic and histomorphologic measurements of osteoporotic vertebrae have shown reductions in cancellous bone accompanied by a decrease in hematopoetic marrow and a corresponding increase in fat cells. Dunnill et al (24) observed that with aging, the increase in marrow fat is even more marked than the decrease in cellular marrow, presumably because fatty marrow is replacing bone as well as hematopoetic tissue. This process also may occur under certain pathologic conditions. Additional fat cells are necessary to replace age-related trabecular bone loss and to fill bone resorption cavities (5, 24–26, 32, 39, 40).

Hypothetically, increased marrow fat content could affect bone strength in various ways. First, there could be a passive increase in marrow fat. Trabecular rarefication with thinning is commonly reported as the main cause of bone weakness in osteoporosis. Trabecular thinning results in open spaces among the trabecular mesh. Some have suggested that there is compensatory filling of these spaces with fatty marrow (5, 24–26, 32, 39–41). Therefore, increased vertebral fat content could mirror bone loss.

Second, vertebral bone marrow could act as a biomechanical support medium. Some believe that vertebral marrow quality is another important determinant of vertebral strength (2). The intertrabecular spaces that contain bone marrow have been reported to act as energy dampers. Marrow composition may affect elasticity of the bone superstructure; red marrow is said to contribute to hydrostatic strengthening, whereas fatty marrow is associated with greater compressibility of vertebrae. The combination of hematopoetic marrow with the collagen and hydroxyapatite forms a comparatively tough material. Fatty marrow would cause hydrostatic weakening of a vertebra.

Third, bone marrow relates to the regulation of bone turnover. Marrow fat is observed to influence the quality of trabecula (7). Nuttal et al (42) have reported that bone-marrow stromal cells can undergo adipogenesis or osteoblastogenesis. There is a reciprocal relationship between adipocytes and osteoblast phenotypes; excessive expression of one versus the other may have significance in the context of osteoporosis. Thus, a decrease in osteoplastogenesis in bone marrow may result in increased adipogenesis (43). Predominance of fatty marrow therefore could be a result of increased adipogenesis and have a negative effect on osteogenesis.

On the basis of these considerations, it appears that bone mineral and bone density are not the only factors to consider when estimating biomechanical competence. Instead, a combination of factors come into play, including above-listed ones (1, 2, 6).

To our knowledge, no reports in the radiology literature have examined the association of increased vertebral marrow fat content and bone weakness. Many reports have focused on MR imaging and compression fractures, with the main interest directed toward distinguishing benign from malignant vertebral fractures (44–48), but they have concentrated only on the compressed vertebra, not on the bone environment. In this study, we performed ^{1}H MRS of uncompressed vertebrae, usually L2, in subjects who had some MR imaging evidence of weakened bone.

Increased vertebral fat content can be suspected on routine MR images when vertebral bone marrow has bright T1 signals. However, ^{1}H MRS allows quantitative assessment of vertebral fat. Our initial findings must be verified in other, similar analyses. If confirmed, ^{1}H MRS should be strongly considered as an add-on to lumbar MR imaging, particularly in patients with clinical suspicion of bone weakness.

Relationship of Line Width to Bone Weakening

Bone tissue may be a silent partner in the shaping of vertebral spectra, by widening the LW in an environment of dense bone (9, 20, 32) and by causing the LW to narrow in an environment of increased marrow fat. Our data suggest no convincing relationship between LW and bone density. In the ''all decades'' group, the LW in subjects with weakened bone was an average 28% higher compared with age-averaged control subjects (Tables 1 and 2). This statistically significant difference in LW (29 Hz vs 37.1 Hz) runs counter to our expectation and is of uncertain importance. Therefore we believe that LW cannot be used as a measure of bone weakening.

We propose that future ^{1}H MRS studies evaluate all five lumbar vertebrae and use larger voxels for data collection. This will provide a larger tissue sample, similar to that used for lumbar-spine DXA. Improved scanning techniques allow whole lumbar-spine measurements within 5 minutes. Future ^{1}H MRS research also must concentrate on comparisons with a noninvasive, reference-standard assay for bone density, such as DXA. We are presently engaged in a DXA-^{1}H MRS correlation study (49).

Future investigations should also compare sex-related differences in %FF in cohorts with bone weakness. Since our LW measurements did not allow definitive conclusions, further LW data should be compiled to help formulate a more definitive opinion about its diagnostic merits.

Conclusion

The %FF reflects bone fat content relative to water. This analysis suggests that %FF can serve as a measure of bone quality, in that increased %FF values were associated with bone weakness in 22 subjects.

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