

Hyperkyphotic Posture Predicts Mortality in Older Community-Dwelling Men and Women: A Prospective Study

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OBJECTIVES: To determine the association between hyperkyphotic posture and rate of mortality and cause-specific mortality in older persons.

DESIGN: Prospective cohort study.

SETTING: Rancho Bernardo, California.

PARTICIPANTS: Subjects were 1,353 participants from the Rancho Bernardo Study who had measurements of kyphotic posture made at an osteoporosis visit between 1988 and 1991.

MEASURES: Kyphotic posture was measured as the number of 1.7-cm blocks that needed to be placed under the participant's head to achieve a neutral head position when lying supine on a radiology table. Demographic and clinical characteristics and health behaviors were assessed at a clinic visit using standard questionnaires. Participants were followed for an average of 4.2 years, with mortality and cause of death confirmed using review of death certificates.

RESULTS: Hyperkyphotic posture, defined as requiring one or more blocks under the occiput to achieve a neutral head position while lying supine, was more common in men than women (44% in men, 22% of women, $P < .0001$). In age- and sex-adjusted analyses, persons with hyperkyphotic posture had a 1.44 greater rate of mortality (95% confidence interval (CI) = 1.12–1.86, $P = .005$). In multiply adjusted models, the increased rate of death associated with hyperkyphotic posture remained significant (relative hazard = 1.40, 95% CI = 1.08–1.81, $P = .012$). In cause-specific mortality analyses, hyperkyphotic posture was specifically associated with an increased rate of death due to atherosclerosis.

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CONCLUSION: Older men and women with hyperkyphotic posture have higher mortality rates. *J Am Geriatr Soc* 52:1662–1667, 2004.

Key words: kyphosis; hyperkyphosis; kyphotic posture; mortality; cohort study

Hyperkyphosis, commonly known as the dowager's hump, is frequently observed in older persons, yet little is known about its clinical significance. For example, its exact prevalence rates are unknown, and its causes other than vertebral fractures are not well defined. However, it is known that, in addition to being cosmetically undesirable, hyperkyphosis is associated with restrictive pulmonary disease¹ and poor physical function,^{2–4} suggesting that hyperkyphosis might be also associated with other adverse health outcomes.

Few studies have investigated the association between hyperkyphosis and mortality. One study reported that hyperkyphotic men, but not women, had an age-adjusted greater rate of mortality,⁵ but other possible confounding factors that might represent the true cause of increased mortality were not considered. It has previously been shown that older women with hyperkyphosis are at greater risk of pulmonary deaths, but there was limited power to adjust for possible confounders, and the risk of all-cause mortality was not investigated.⁶

Many methods have been used to measure the extent of kyphosis, but even a simple external physical measurement, suitable for clinical use, can be used to predict the risk of adverse health outcomes.^{3,7} It was hypothesized that hyperkyphosis, assessed using a simple clinical measurement of the occiput-to-table distance (when lying supine on an examination table), would be associated with increased mortality in older men and women.

METHODS

Subjects

The study population included participants from the Rancho Bernardo Heart and Chronic Disease Study, a

population-based cohort study first established in 1972 to study heart disease risk factors. Between 1988 and 1991, surviving residents were invited to participate in a study of osteoporosis. Eighty percent agreed to participate and gave informed written consent. The institutional review board of the University of California at San Diego approved the study protocol.

Kyphotic Posture Measurement

At the 1988–1991 clinic visit, kyphotic posture was measured with participants lying recumbent on the dual-energy x-ray absorptiometry (DXA) table as the distance from the occiput to table (units = 1.7-cm blocks placed under the participants' heads) (Figure 1). When lying supine on a flat surface, persons with normal posture are able to rest their heads in a neutral position without neck hyperextension, but individuals with hyperkyphosis cannot lie flat with their heads touching the same surface as the rest of their body unless they hyperextend their necks. In the current study, if study subjects were unable to lie with their head flat on the table in a neutral position without neck hyperextension, 1.7-cm blocks were placed underneath their head until a neutral position was achieved. Examiners judged the head to be in a neutral position when the participant's gaze was directed straight up toward the ceiling and the neck was neither hyperextended nor hyperflexed. The greater the number of blocks required for the subject to reach a neutral head position, the greater the amount of hyperkyphotic posture. This measure is similar to the distance between the occiput and the wall, another clinical indicator of hyperkyphosis.⁷

Questionnaire

Participants completed a self-administered, standardized questionnaire that included questions regarding health

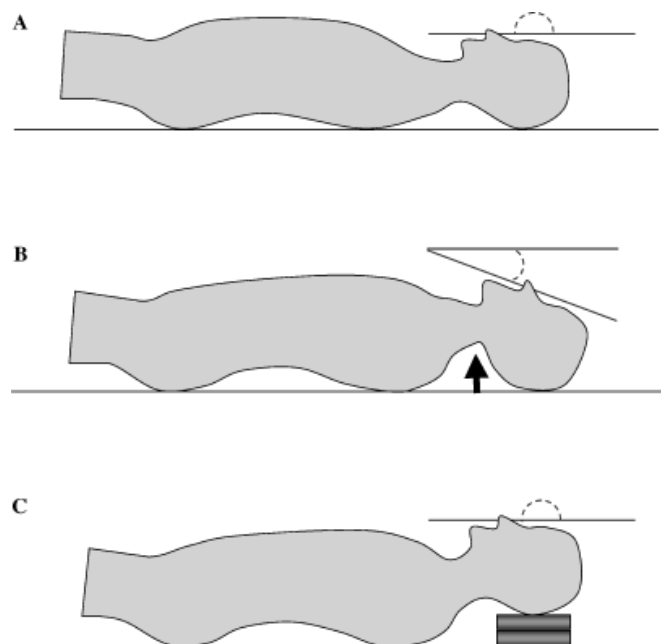


Figure 1. Measure of hyperkyphotic posture A: Neutral head and neck position. B: Hyperextended neck position. C: Head on blocks restores neutral head and neck position.

behaviors including history of smoking (current, past, or never), alcohol consumption (more than 12 drinks in the previous 12 months), regular exercise (self-reported regular physical activity three times or more per week), and self-reported health (ascertained separately as physical and emotional health, graded from not limited to severely limited). They also provided information regarding medical conditions including hypertension, diabetes mellitus, myocardial infarction, stroke, chronic obstructive pulmonary disease (COPD), cancer osteoarthritis, and clinical spine fractures, defined as self-reported spine fractures ascertained between 1972 and the baseline osteoporosis visit in 1988–1991. To assess their functional status, participants answered questions including whether they had any difficulty bending over to the floor, walking two to three blocks on level ground, or climbing a flight of stairs.

Examinations

At the 1988–1991 visit, bone mineral density was examined at the total hip, femoral neck, and lumbar spine (L1–L4) using DXA (QDR 1000, Hologic, Inc., Waltham, MA). Instruments were calibrated daily and had measurement precisions of 1% or less for the spine and 1.5% or less for the hip. Grip strength was measured using a hand-held dynamometer (Therapeutic Instruments Hand Dynamometer, Clifton, NJ). Height and weight were measured with the participant wearing light clothing without shoes. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Ascertainment of Death

Information on vital status was collected annually and was known for 80.5% of the participants through January 1997. The study center obtained death certificates for more than 96% of those who died. International Classification of Diseases, Ninth Revision, codes were used to classify causes of death as atherosclerosis (401–404, 410–414, 425, 428, 429.2, 430–438, 440–444, and 798), cancer (140–239), pulmonary (415–417, 480–487, 490–496, 500–508.8, and 510–519), or all other causes (nonatherosclerotic, noncancer, and nonpulmonary deaths).⁸

Statistical Analysis

After confirming that hazard rates were proportional throughout follow-up, Cox proportional hazards analyses were performed to determine the association between hyperkyphotic posture and subsequent mortality. Subjects were defined as hyperkyphotic if they required one or more blocks to achieve a neutral head position while lying flat. To assess for a possible dose-response relation between hyperkyphotic posture and mortality, subjects were also classified into four groups: those who required no blocks (referent group), one block, two blocks, and three or more blocks. Because men were more likely than women to be hyperkyphotic and also more likely to die, an interaction between sex, hyperkyphotic posture, and mortality was tested for.

To test for potential confounders of the association between hyperkyphotic posture and mortality, separate multivariable models that included hyperkyphotic posture, age, sex, and each candidate covariate were run to investigate

Table 1. Baseline Characteristics of Participants, Stratified by the Presence or Absence of Hyperkyphosis*

Baseline Characteristic	No Blocks (n = 827–930) [†]	≥ One Block (n = 381–423) [‡]	P-value
Age, mean ± SD	70.9 ± 9.3	78.3 ± 8.0	<.0001
Female, n (%)	606 (65.2)	172 (40.7)	<.0001
> 12 years education, n (%)	713 (86.2)	315 (82.7)	.11
Body mass index, kg/m ² , mean ± SD	25.0 ± 3.7	25.5 ± 3.9	.03
Spine bone density, gm/cm ² , mean ± SD	0.96 ± 0.20	0.98 ± 0.23	.18
Baseline spine fracture, n (%)	26 (2.8)	31 (7.3)	<.0001
Osteoarthritis, n (%)	329 (35.4)	123 (29.1)	.02
Stroke, n (%)	38 (4.1)	10 (2.4)	.11
Exercise, n (%) [‡]	668 (72.7)	264 (62.9)	.0003
Current smoking, n (%)	92 (10.0)	31 (7.3)	.11
Alcohol use, n (%)	741 (80.6)	303 (72.3)	.0007
Self-reported physical health	1.6 ± 0.8	2.0 ± 1.0	<.0001
Self-reported emotional health	1.3 ± 0.7	1.4 ± 0.7	.02
Self-reported difficulty climbing, n (%)	65 (7.0)	72 (17.0)	<.0001
Self-reported difficulty walking, n (%) ^b	57 (6.1)	61 (14.4)	<.0001

* Defined as having an occiput-to-table distance ≥ 1.7 cm. See Methods section for details.

[†] Sample size varies because of missing values.

[‡] Regular physical activity ≥ 3 times per week (yes/no).

SD = standard deviation.

how each potential confounder affected the association between hyperkyphosis and mortality. If the candidate covariate was significantly related to mortality ($P < .10$) or changed the beta-estimate of hyperkyphosis by more than 10%, it was included in the backward selection process. Covariates considered included age, sex, education, BMI, hypertension, diabetes mellitus, myocardial infarction, stroke, COPD, cancer osteoarthritis, clinical spine fractures, spinal bone density, exercise, current smoking (vs past or never), current or previous smoking (vs never), alcohol use, self-reported physical and emotional health, grip strength, and self-reported difficulty in bending, climbing or walking. Finally, all qualified candidate covariates were added to a multivariable model with all-cause mortality as the outcome variable. Backward selection with a P -value set at < 0.10 was used to select a parsimonious model.

In the analyses involving cause-specific mortality as an outcome, we ran a multivariable model for each cause of death that included hyperkyphotic posture, age, sex, and each individual candidate covariate to determine which covariates had the strongest effect on kyphotic posture. We retained the covariates that changed the beta-coefficient of kyphotic posture by 10% or more. SAS software was used for all analyses (SAS Institute, Cary, NC).

RESULTS

Baseline characteristics of the study cohort are listed in Table 1. Their mean age was 73 years (range from 45 to 98). The kyphosis measurement ranged from zero to 10 blocks (17 cm). At all levels, hyperkyphosis was more common in men than in women (Table 2). Using a cutoff point of ≥ one block versus no blocks to define hyperkyphosis, this condition was present in 172 (22%) of the women and 251 (44%) of the men. Using a hyperkyphosis cutoff of ≥ two blocks versus one or no blocks, 109 (14%) of the women and 177 (31%) of the men were considered hyperkyphotic.

Over an average follow-up of 4.2 years (range 0.068–8.77, median 3.9), 267 participants died. In age- and sex-adjusted analyses, persons with hyperkyphosis defined as needing ≥ one block to achieve a neutral head position had a 1.44 times greater rate of mortality than those without hyperkyphotic posture (95% confidence interval (CI) = 1.12–1.86, $P = .005$). With increasing kyphotic posture, there was a trend towards greater mortality that appeared to saturate above two blocks. The relative hazards were 1.25 for one block, 1.56 for two blocks, and 1.50 for ≥ three blocks compared with no blocks (Table 3). In age-adjusted analyses stratified by sex, regardless of kyphosis status, men had lower survival rates than women. Men with hyperkyphosis had the lowest overall survival rates, whereas survival rates of women with hyperkyphosis were better than men without hyperkyphosis but worse than women without hyperkyphosis (Figure 2). However, the relative degree of mortality risk conferred by hyper-

Table 2. Distribution of Kyphotic Posture by Sex

Number of Blocks*	Women (n = 778)	Men (n = 575)
	Frequency (%)	
0	606 (77.9)	324 (56.4)
1	63 (8.1)	74 (12.9)
2	57 (7.3)	67 (11.7)
3	22 (2.8)	54 (9.4)
4	10 (1.3)	23 (4.0)
5	8 (1.0)	14 (2.4)
6	9 (1.2)	10 (1.7)
≥ 7	3 (0.4)	9 (1.6)

* Occiput-to-table distance measured in number of 1.7-cm blocks. More blocks indicate greater kyphosis. See Methods section for details.

Table 3. Association Between Hyperkyphosis and Selected Other Variables and All-Cause Mortality in Older Men and Women

Hyperkyphosis Definition*	Age and Sex (n = 1,353)		Full† (n = 1,342)		Full+Spine Bone Mineral Density+Spine Fracture (n = 1,320)				
	Relative Hazard	(95% Confidence Interval)	P-value	Relative Hazard	(95% Confidence Interval)	P-value			
≥ 1 block	1.44	(1.12–1.86)	.005	1.40	(1.08–1.81)	.012	1.40	(1.07–1.82)	.014
1 block	1.25	(0.84–1.85)	.28	1.34	(0.90–2.00)	.15	1.35	(0.90–2.02)	.14
2 blocks	1.56	(1.09–2.25)	.016	1.54	(1.06–2.22)	.02	1.50	(1.03–2.19)	.03
≥ 3 blocks	1.50	(1.09–2.06)	.012	1.35	(0.98–1.87)	.07	1.36	(0.97–1.89)	.07

*Referent group is 0 blocks.

† Full model adjusted for age, sex, body mass index, osteoarthritis, current smoking, walking, climbing, and self-reported emotional health.

RH = relative hazard; CI = confidence interval.

kyphosis was the same in men and women (*P* for sex by kyphosis interaction = 0.53).

In the multivariable analyses, hyperkyphosis remained a significant predictor of increased all-cause mortality. Factors that did not meet screening criteria for inclusion in the backward selection process included education, hypertension, diabetes mellitus, myocardial infarction, stroke, COPD, cancer, spine fracture, spine bone density, grip strength, and alcohol use. Using backward selection, current or previous smoking, self-reported physical health, and physical activity were further excluded, leaving age, sex, BMI, osteoarthritis, current smoking, self-reported walking, self-reported difficulty climbing, and self-reported emotional health in the final model (relative hazard (RH) = 1.40, 95% CI = 1.08–1.81; *P* = .01). Further adjustment for spine bone density and clinical spine fracture did not make a substantial difference in the RH (Table 3).

In models adjusted for age and sex, hyperkyphosis was significantly associated only with deaths due to atherosclerosis. Of the various covariates screened, BMI changed the beta-coefficient for hyperkyphosis to the greatest degree (by at least 10%) in each of the cause-specific death models; therefore, it was the first covariate added to the model after age and sex. Further adjustment for BMI strengthened the associations between hyperkyphosis and each cause-specific death category, in particular deaths due to a pulmonary cause (RH = 2.44, 95% CI = 1.07–5.55; *P* = .03) (Table 4),

but in the full model, which included spine bone mineral density and self-reported physical health, hyperkyphosis was only weakly associated with pulmonary related deaths (*P* = .12). However, for deaths due to atherosclerosis, even in the full model, participants with hyperkyphotic posture had a significant 2.4 times greater rate of death (Table 4). Further adjusting individually for bone density, clinical spine fracture, or other variables known to affect cardiovascular mortality such as smoking, hypertension, diabetes mellitus, and physical exercise did not affect this association (data not shown).

DISCUSSION

Older community-dwelling persons with hyperkyphotic posture had greater mortality rates, with increasing severity of hyperkyphotic posture associated with greater rates. Hyperkyphotic posture was associated with an increased mortality rate due to atherosclerosis and possibly pulmonary causes in particular. Although hyperkyphosis is generally thought to be due to osteoporosis, adjustment for low bone density or clinical spinal fracture did not attenuate the greater rate of mortality seen in this study. In addition, after adjustment for multiple potential confounders, including demographic variables, comorbidities, health behaviors, and markers of frailty, the excess rate of mortality remained statistically significant.

These study findings place new importance on the clinical finding of hyperkyphotic posture. Prior studies suggest that hyperkyphosis is associated with poor physical function^{2,3} and restrictive pulmonary disease,¹ but none have fully investigated its relation to mortality risk. In addition, in this study population of older persons, hyperkyphosis was highly prevalent. Men were about twice as likely to be classified as hyperkyphotic, with upwards of 40% of the men and 20% of the women meeting the criterion of one or more block. Furthermore, even at this mild degree of hyperkyphotic posture, there was a definite greater rate of earlier mortality. Although it is currently thought that hyperkyphotic posture mainly affects women and that on its own is not clinically important, this study suggests otherwise.

The finding that men were more hyperkyphotic than women was intriguing and is possibly related to the measurement method used. In an earlier study that included both sexes, researchers measured thoracic curvature using an

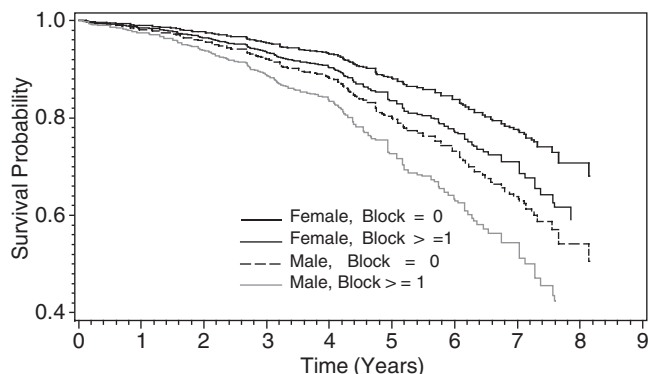


Figure 2. Age-adjusted survival curves of hyperkyphosis (having an occiput-to-table distance ≥ 1.7 cm), stratified by sex. See Methods section for details.

Table 4. Relative Hazards of Cause-Specific Death in Persons with Hyperkyphosis*

Cause of Death	Adjusted for Age and Sex		Adjusted for Age, Sex, and BMI				Full†		
	Relative Hazard	(95% Confidence Interval)	P-value	Relative Hazard	(95% Confidence Interval)	P-value	Relative Hazard	(95% Confidence Interval)	P-value
Atherosclerosis (n = 50)	1.86	(1.03–3.38)	.04	2.02	(1.10–3.70)	.02	2.38	(1.26–4.50)	.008
Cancer (n = 30)	1.74	(0.80–3.81)	.16	1.84	(0.84–4.05)	.13	1.76	(0.80–3.88)	.16
Pulmonary (n = 29)	2.03	(0.90–4.56)	.09	2.44	(1.07–5.55)	.03	1.96	(0.84–4.60)	.12
Other (n = 147)	1.31	(0.93–1.83)	.12	1.37	(0.98–1.94)	.07	1.23	(0.87–1.75)	.23

* Defined as having an occiput-to-table distance ≥ 1.7 cm. See Methods section for details.

† For atherosclerosis, model adjusted for age, sex, body mass index (BMI), stroke, osteoarthritis, and alcohol. For cancer, model adjusted for age, sex, body mass index, and physical health. For pulmonary, model adjusted for age, sex, BMI, spine bone mineral density, and physical health. For other causes, model adjusted for age, sex, BMI, exercise, climbing, and physical health.

architects' flexicurve and found that hyperkyphosis is more common in women than men.⁵ Because the flexicurve encompasses the area spanning C7 and S2 but does not include the more proximal cervical spine, forward curvature of the neck does not influence it. Both the cervical and thoracic spine anatomy influence the blocks method. A recent study examining cervical and thoracic curvature in ex vivo specimens in young and older men and women reported that older men had loss of the usual cervical lordosis; these sex differences in cervical anatomy could account for the greater prevalence in men of hyperkyphotic posture assessed using occiput-to-table distance, observed in the current study.⁹

Although hyperkyphotic posture is commonly believed to result from spinal osteoporosis, some studies suggest that it has other important determinants. For example, in an earlier study, the correlation between spinal deformity and thoracic angle of curvature (Cobb angle) was only 0.54; thus, spinal deformities only explained 29% of the variance of thoracic curvature.¹ Another study of osteoporotic women noted that those with hyperkyphosis in the absence of vertebral deformities had the same degrees of physical and emotional functional impairments as those with both hyperkyphosis and underlying vertebral deformities.⁷ Unlike these studies, the current study did not obtain spinal radiographs in all participants, but neither low bone density nor clinical spine fractures explained the increased mortality rate observed.

Why might hyperkyphosis be independently associated with increased mortality rates? It is possible that hyperkyphotic posture reflects an increased rate of physiological aging. Mouse gene knockout models that age prematurely show evidence of hyperkyphosis. In one such study, mice with a mutation in XPD, a gene that encodes a deoxyribonucleic acid (DNA) helicase responsible for DNA repair and transcription, demonstrated normal development but aged prematurely.¹⁰ In addition to having about a 50% shorter life expectancy, these knockout mice also develop severe kyphosis. Three other studies, involving mice with abnormal p53 function, mice defective in joining DNA double-strand breaks, and mice with a mutated *klotho* gene that is involved in the suppression of several aging phenotypes, all displayed more rapid aging and hyperkyphosis.^{11–13}

To gain further insight into possible mechanisms leading to earlier death, the association between hyperkyphosis

and cause-specific mortality was investigated. The results suggest that those with hyperkyphotic posture were approximately two times more likely to die from pulmonary causes, similar to previous work in the Study of Osteoporotic Fractures that reported that older women in the top decile of kyphotic posture had an age-adjusted 2.6 times greater risk of pulmonary death.⁶ However, in the current study, hyperkyphosis was no longer significantly associated with pulmonary deaths after further adjustment for spine bone density and self-rated physical health. There were only 29 pulmonary deaths in this study, and there may not have been the power to detect a hyperkyphosis effect on pulmonary mortality independent of spine bone density and self-rated health, but changes in thoracic anatomy caused by hyperkyphosis (regardless of its causes) may compromise lung function sufficiently to lead to an increased rate of pulmonary death. It was also found that those with hyperkyphotic posture had a 2.4 times greater mortality rate from atherosclerosis. The underlying explanation for this finding is less obvious, but mouse models of accelerated aging displayed both hyperkyphosis and premature death due to atherosclerotic causes, suggesting that there might be an underlying pathology that is common to atherosclerosis and hyperkyphosis.¹³

This study has some limitations. First, predominantly upper middle-class white community-dwelling persons were studied, and the study findings may not be applicable to other populations. Second, although clinical spine fractures could be controlled, it was impossible to determine whether clinically silent vertebral deformities could account for the findings. Third, although multiple factors that might confound the association between hyperkyphosis and mortality were accounted for, the possibility of residual confounding by subclinical disease, for instance, could not be excluded. Fourth, the small number of deaths in the cause-specific categories requires that the multivariable results be interpreted with caution. Lastly, cause of death was obtained from death certificates, which may have limited reliability in older persons.¹⁴ The study also has several strengths. First, it included older individuals from the community regardless of whether they had osteoporosis, so these results are more generalizable than previous studies on kyphosis that recruited individuals with pre-established osteoporosis. Secondly, both men and women were studied. Last, the measure of kyphosis used in this

study was easy and inexpensive to perform, making it an attractive potential clinical tool.

For years, the dowager's hump has been considered a disorder of older women presumed to result from vertebral osteoporosis. Known consequences of hyperkyphotic posture include height loss, reduced pulmonary function, and decreased physical function. This study demonstrates that hyperkyphotic posture disproportionately affects older men and that hyperkyphotic posture predicts increased mortality. More research is needed to further delineate the causes of hyperkyphotic posture, its associated adverse health outcomes, and possible treatments. Moreover, the realization that hyperkyphosis is not synonymous with vertebral fractures may lead to interventions specifically targeted at improving posture, possibly resulting in reduced mortality rates.

REFERENCES

1. Leech JA, Dulberg C, Kellie S et al. Relationship of lung function to severity of osteoporosis in women. *Am Rev Respir Dis* 1990;141:68–71.
2. Chow RK, Harrison JE. Relationship of kyphosis to physical fitness and bone mass on post-menopausal women. *Am J Phys Med* 1987;66:219–227.
3. Ryan SD, Fried LP. The impact of kyphosis on daily functioning. *J Am Geriatr Soc* 1997;45:1479–1486.
4. Kado DM, Huang MH, Barrett-Connor E et al. Hyperkyphotic posture and poor physical functional ability in older community dwelling men and women: The Rancho Bernardo Study. *J Gerontol A Biol Sci, Med Sci*, in press.
5. Milne JS, Williamson J. A longitudinal study of kyphosis in older people. *Age Ageing* 1983;12:225–233.
6. Kado DM, Browner WS, Palermo L et al. Vertebral fractures and mortality in older women. Study of Osteoporotic Fracture Research Group. *Arch Intern Med* 1999;159:1215–1220.
7. Leidig-Bruckner G, Minne HW, Schlaich C et al. Clinical grading of spinal osteoporosis: Quality of life components and spinal deformity in women with chronic low back pain and women with vertebral osteoporosis. *J Bone Miner Res* 1997;12:663–675.
8. International Classification of Diseases, 9th Revision, Clinical Modification. Washington, DC: U.S. Government Printing Office, 1994.
9. Boyle JJ, Milne N, Singer KP. Influence of age on cervicothoracic spinal curvature: An ex vivo radiographic survey. *Clin Biomech* 2002;17:361–367.
10. de Boer J, Andressoo JO, de Wit J et al. Premature aging in mice deficient in DNA repair and transcription. *Science* 2002;296:1276–1279.
11. Tyner SD, Venkatachalam S, Choi J et al. P53 mutant mice that display early ageing-associated phenotypes. *Nature* 2002;415:45–53.
12. Vogel H, Lim SD, Karsenty G et al. Deletion of Ku86 causes early onset of senescence in mice. *Proc Natl Acad Sci U S A* 1999;96:10770–10775.
13. Kuro-o M, Matsumura Y, Aizawa H et al. Mutation of the mouse *klotho* gene leads to a syndrome resembling aging. *Nature* 1997;390:45–51.
14. Lloyd-Jones DM, Martin DO, Larson MG et al. Accuracy of death certificates for coding coronary heart disease as the cause of death. *Ann Intern Med* 1998;129:1020–1026.