Increased Prevalence of Celiac Disease and Need for Routine Screening Among Patients With Osteoporosis

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Background: There is an increased prevalence of osteoporosis among patients with celiac disease. However, the relative prevalence of celiac disease among osteoporotic and nonosteoporotic populations is not known, and the benefit of screening the osteoporotic population for celiac disease remains controversial.

Methods: We evaluated 840 individuals, 266 with and 574 without osteoporosis, from the Washington University Bone Clinic by serologic screening for celiac disease. Individuals with positive serologic test results for antitissue transglutaminase or antiendomysial antibody were offered endoscopic intestinal biopsy to confirm the diagnosis of celiac disease. Individuals with biopsy-proven celiac disease were treated with a gluten-free diet and followed up for improvement in bone mineral density.

Results: Twelve (4.5%) of 266 patients with osteoporosis and 6 (1.0%) of 574 patients without osteoporosis tested positive by serologic screening for celiac disease. All but 2 serologically positive individuals underwent intestinal biopsy. Nine osteoporotic patients and 1 nonosteoporotic patient had positive biopsy results. The prevalence of biopsy-proven celiac disease was 3.4% among the osteoporotic population and 0.2% among the nonosteoporotic population. All biopsy-positive individuals tested positive by antitissue transglutaminase and antiendomysial antibody. The antitissue transglutaminase levels correlated with the severity of osteoporosis as measured by T score, demonstrating that the more severe the celiac disease the more severe the resulting osteoporosis. Treatment of the patients with celiac disease with a gluten-free diet resulted in marked improvement in T scores.

Conclusions: The prevalence of celiac disease among osteoporotic individuals (3.4%) is much higher than that among nonosteoporotic individuals (0.2%). The prevalence of celiac disease in osteoporosis is high enough to justify a recommendation for serologic screening of all patients with osteoporosis for celiac disease.

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CELIAC DISEASE IS AN ANTIgen-driven enteropathy of the small intestine, resulting from an inappropriate immune response to dietary gliadin, a component of wheat proteins.[1] Celiac disease can have a varied clinical presentation, with most symptoms being attributed to malabsorption.[2,3] The discovery of tissue transglutaminase as the predominant autoantigen of celiac disease allowed for the development of standardized and quantitative serologic screening tests.[4] These tests have facilitated the widespread screening of asymptomatic individuals and have altered our perception of the incidence of celiac disease. However, despite the observation that celiac disease is much more common than previously appreciated, and despite the availability of serologic tests for screening, we still do not know which groups of individuals will most benefit from screening for celiac disease.

Adults with newly diagnosed celiac disease have a low bone mineral density (BMD), and treatment of these individuals with a gluten-free diet increases their BMD.[5-8] However, studies[9-12] screening asymptomatic osteoporotic individuals for the presence of celiac disease have yielded conflicting results. Given these results, current practice for the workup of postmenopausal women presenting with osteoporosis does not include serologic screening for the presence of celiac disease. In an attempt to resolve these issues, we performed a large prospective screening trial for the presence of celiac disease in osteoporotic and nonosteoporotic individuals.

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METHODS

PROTOCOL

The study protocol was approved by the institutional review board at Washington Univer-

Table 1. Enrolled Study Population

Variable	Osteoporotic Group (n = 266)	Nonosteoporotic Group (n = 574)
Female, %	90.6	90.2
Age, mean ± SD, y	57.0 ± 12.8	63.2 ± 13.2*
No. of patients with celiac disease	9	1*
Prevalence of celiac disease, %	3.4	0.2

*$P<.001$ compared with the osteoporotic group.

sity School of Medicine. All individuals presenting to the Washington University Bone Clinic from July 1, 2000, to July 1, 2002, were offered the opportunity to participate. Individuals taking corticosteroids, individuals with known celiac disease or prior workup for celiac disease, and individuals with known malignant neoplasms were excluded from the study.

At the time of enrollment, patients signed an informed consent, had a physical examination, and completed a questionnaire. The questionnaire included questions about drug therapy, weight loss, diarrhea, fractures, and history of celiac disease and cancer. All enrolled patients had undergone BMD measurement of the hip, femoral neck, and spine using dual-energy x-ray absorptiometry. The World Health Organization definitions were used to define osteoporosis; individuals were defined as being osteoporotic if they had a T score of –2.5 or less in the spine, hip, or femoral neck and nonosteoporotic if their lowest T score was greater than –2.5.[13] If the T score was –2.5 or less at more than 1 site, the lowest T score was used to classify the patient, and the BMD at that site was used to monitor therapy. Routine laboratory tests, including a complete blood cell count, serum 25-hydroxyvitamin D, parathyroid hormone (PTH), and bone-specific alkaline phosphatase, were performed at the time of enrollment.

Individuals also received serologic testing for IgG antigliadin, IgA antigliadin, IgA antitissue transglutaminase (anti-TTG), and IgA antiendomysial antibody (anti-EMA). Reagents for the antigliadin and anti-TTG tests were from INOVA Diagnostics, Inc (San Diego, Calif); reagents for anti-EMA were from Binding Site (Birmingham, England). Patients who tested positive for anti-TTG (≥20 U) or anti-EMA (positive test results with serum samples diluted 1:10) were offered a small-bowel biopsy to confirm the diagnosis of celiac disease. Serum IgG and IgA antigliadin antibodies were detected by a semiquantitative enzyme-linked immunosorbent assay. The samples were classified as negative (<20 U), weakly positive (20-30 U), or moderately to strongly positive (>30 U). IgA anti-EMA was detected by an indirect immunofluorescence technique using monkey esophagus as a substrate. Serum samples were screened at a 1:10 dilution, and samples testing positive at this dilution were then retested for quantitative positivity. IgA anti-TTG antibodies were tested by a semiquantitative enzyme-linked immunosorbent assay using native human TTG as a substrate. The samples were classified as negative (<20 U), weakly positive (20-30 U), or strongly positive (>30 U).

Individuals testing positive for anti-TTG or anti-EMA were offered an esophagogastroduodenoscopy with 8 random biopsies of the distal duodenum or proximal jejunum. Gastrointestinal pathologists at Barnes-Jewish Hospital, St Louis, who were unaware of the patients' serologic test results interpreted the biopsy results. Biopsy specimens were classified by Marsh staging.

Patients with positive biopsy results were given instruction by a registered dietician to follow a gluten-free diet. Patients with positive biopsy results also filled out a Rome II questionnaire, which is a survey of gastrointestinal symptoms.[14] At 6 and 12 months, individuals with celiac disease were interviewed by a physician (W.F.S.) to monitor compliance with the gluten-free diet, and their routine blood chemistries were measured. After 12 months on a gluten-free diet, BMD measurements were repeated. For each of the patients with osteoporosis and celiac disease, 4 age- and sex-matched individuals among those with osteoporosis but without celiac disease were identified. These control patients were further studied with blood biochemistry tests and were asked to complete a Rome II questionnaire.

BMD MEASUREMENT

The BMD of the lumbar spine and the left hip and femoral neck were measured by dual-energy x-ray absorptiometry, using a QDR-4500W densitometer (Hologic Inc, Waltham, Mass). At the Washington University Bone Clinic, the precision of this technique is 1.12% at the lumbar spine (anterior posterior) and 1.27% at the hip and femoral neck. The BMD was expressed as grams per square centimeter and converted to T scores using the manufacturer's calculations, which are based on data from the third National Health and Nutrition Examination Survey.

STATISTICAL ANALYSIS

Fisher exact test or Mann-Whitney test was used to determine differences in categorical variables (**Tables 1**, **2**, and **3**). A standard *t* test was used to determine differences in continuous variables between celiac disease patients and controls (**Table 4**). Data were analyzed using Prism 4.0 (GraphPad Software, San Diego).

RESULTS

ENROLLMENT

Patients followed up in the Washington University Bone Clinic were invited to enroll. The enrolled population comprised 266 individuals with osteoporosis and 574 individuals without osteoporosis. The enrolled population was largely female, white, and postmenopausal; these characteristics reflect the patient population of the Washington University Bone Clinic. There was no significant difference in the sex or ages of the 2 groups, but the nonosteoporotic group was older (Table 1).

PREVALENCE OF CELIAC DISEASE

In the osteoporotic and nonosteoporotic groups, more than three quarters of the patients had negative results for all of the serologic tests (Table 2). Approximately 20% of individuals from each group tested positive for IgA or IgG antigliadin antibodies. One patient in the osteoporotic group and 2 patients in the nonosteoporotic group had positive results for IgA anti-TTG but negative results for anti-EMA. One patient in each group had negative results for anti-TTG and positive results for anti-EMA. These findings did not reach statistical significance when comparing the 2 groups. There were 9 patients in the osteoporotic group and 1 patient in the nonosteoporotic group who had positive results for all of the serologic tests; this difference was statistically significant.

All individuals with positive results for serum IgA anti-TTG or positive results for IgA anti-EMA were offered an upper gastrointestinal endoscopy with small-

Table 2. Serologic Testing for Celiac Disease in the Osteoporotic and Nonosteoporotic Groups

Serologic Test*			Osteoporotic Group (n = 266)			Nonosteoporotic Group (n = 574)		
Antigliadin	TTG	EMA	No. (%)	No. With Biopsy Performed	No. With Positive Biopsy	No. (%)	No. With Biopsy Performed	No. With Positive Biopsy
–	–	–	201 (75.6)	0	0	444 (77.4)	0	0
+	–	–	53 (19.9)	0	0	124 (21.6)	0	0
+	+	–	1 (0.4)	1	0	2 (0.3)	2	0
–	+	–	1 (0.4)	1	0	2 (0.3)	0	0
–	–	+	1 (0.4)	1	0	0	0	0
+	–	+	0	0	0	1 (0.2)	1	0
+	+	+	9 (3.4)†	9	9	1 (0.2)	1	1

Abbreviations: EMA, antiendomysial antibody; TTG, antitissue transglutaminase.
*Minus sign indicates negative test result; plus sign, positive test result. Antigliadin is IgG or IgA.
†$P<.001$ compared with the nonosteoporotic group.

Table 3. Characteristics of the Osteoporotic Patients With Celiac Disease

Patient No./ Sex/Age at Diagnosis of Celiac Disease, y	Weight Loss, kg	T Score	*z* Score	Hemoglobin, g/dL*	25-Hydroxyvitamin D, ng/mL†	Parathyroid Hormone, pg/mL‡	Alkaline Phosphatase, U/L§	TTG, U‖	EMA¶	Rome II#	Drug Therapy**
1/F/40	3.6	–4.5	–4.6	9.5	15	87	64	171	1:40	b, e, f	h
2/F/71	11.3	–3.9	–1.7	12.9	12	94	272	120	1:320	a, b, e	h
3/F/74	9.1	–2.7	–0.7	11.1	15	120	73	120	1:160	d	h, i
4/M/39	0	–4.0	–3.9	13.6	14	52	234	148	1:320	d	h
5/F/75	0	–2.5	–0.6	10.4	28	86	112	61	1:40	c, e	h
6/F/55	0	–2.8	–1.7	12.6	27	65	105	76	1:20	d, e	h, i
7/M/41	0	–3.2	–3.1	14.7	2	47	47	208	1:160	None	h
8/F/62	5.4	–3.7	–1.7	12.3	17	71	85	108	1:40	a, b, e	h, i
9/F/54	9.1	–2.6	–2.0	14.0	12	74	71	30	1:40	Not applicable	g, h

Abbreviations: EMA, antiendomysial antibody; TTG, antitissue transglutaminase.
*Hemoglobin normal values, 12.0 to 16.0 g/dL for women and 13.5 to 17.5 g/dL for men.
†25-Hydroxyvitamin D normal values, 0 to 55 ng/mL.
‡Parathyroid hormone normal values, 12 to 72 pg/mL.
§Alkaline phosphatase normal values, 81 to 213 U/L.
‖Antitissue transglutaminase normal values, less than 19.9 U.
¶Antiendomysial antibody normal values, negative values.
#Rome II diagnoses: a, heartburn; b, irritable bowel syndrome (diarrhea predominant); c, bloating; d, unspecified bowel disease; e, fecal incontinence; and f, proctalgia fugax.
**Drug therapy: g, hormone therapy; h, alendronate sodium; and i, raloxifene hydrochloride.

intestine mucosal biopsies to establish the diagnosis of celiac disease. Sixteen of the 18 eligible individuals consented. Ten of the 16 biopsied individuals had histologic diagnosis of celiac disease. Biopsies were classified by Marsh staging. The 10 positive biopsy specimens were Marsh stage 3. The 6 negative biopsy specimens were histologically normal. None of the biopsies were Marsh stage 1 or 2. Nine of the biopsy-positive individuals were osteoporotic, and all of these individuals had positive results of serologic testing for IgA anti-TTG and IgA anti-EMA. The prevalence of biopsy-proven celiac disease among the osteoporotic group was 3.4%, whereas that among the nonosteoporotic group was 0.2% (Table 1).

CHARACTERISTICS OF PATIENTS WITH CELIAC DISEASE AND OSTEOPOROSIS

Questionnaires and routine blood chemistry studies were used to address the question of whether the 9 individuals with celiac disease and osteoporosis had other symptoms or laboratory values suggestive of the presence of celiac disease. Five had significant weight loss and 3 were anemic (Table 3). Although weight loss and anemia are associated with celiac disease, the prevalence of this finding was not significantly different from that reported by osteoporotic individuals without celiac disease at the time of enrollment. To better evaluate differences between the presentation and clinical course of individuals with celiac disease and osteoporosis and those with osteoporosis alone, we attempted to identify 4 age- and sex-matched osteoporotic individuals for each individual with osteoporosis and celiac disease. There were too few age-matched men in the pool of potential osteoporotic control patients, so we substituted age-matched women. A comparison of results of laboratory tests obtained at the time of presentation revealed that the celiac disease patients had significantly higher PTH levels and significantly lower 25-hydroxyvitamin D levels than the con-

Table 4. Characteristics of the Osteoporotic Patients With Celiac Disease and of the Osteoporotic Control Subjects*

Characteristic	Celiac Disease (n = 9)	Control Subjects (n = 36)
Age, y	56.6 ± 14.5	61.5 ± 13.7
Female, %	77.7	88.8
Height, m	1.64 ± 0.08	1.59 ± 0.07
Weight, kg	60.5 ± 17.4	61.6 ± 13.8
Hematocrit, %	37.0 ± 5.0	39.6 ± 4.5
Calcium, mg/dL	9.1 ± 0.5	9.3 ± 0.4
25-Hydroxyvitamin D, ng/mL	16.9 ± 6.2†	26.6 ± 13.0
Parathyroid hormone, pg/mL	44.3 ± 22.4‡	53.2 ± 39.2
Alkaline phosphatase, U/L	118.1 ± 79.6	105.3 ± 94.9

SI conversion factor: To convert calcium to millimoles per liter, multiply by 0.25.

*Data are given as mean ± SD unless otherwise indicated.

†P = .003 compared with the control subjects.

‡P = .02 compared with the control subjects.

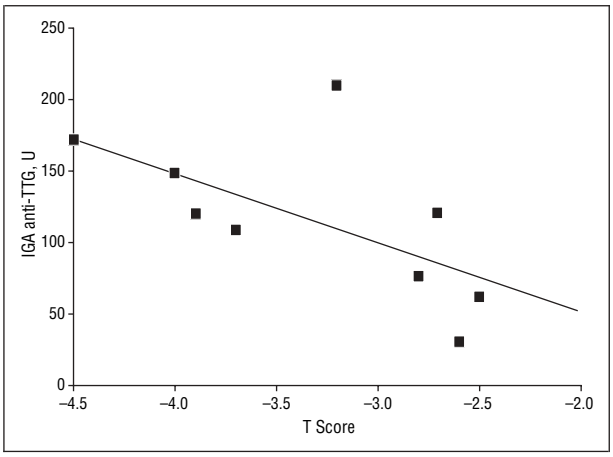

Figure 1. Correlation of T scores with IgA antitissue transglutaminase (anti-TTG) levels in the 9 patients with celiac disease and osteoporosis (R^2=0.37).

Table 5. Results of the Rome II Questionnaire Among the Osteoporotic Patients With Celiac Disease and Among the Osteoporotic Control Subjects*

Gastrointestinal Symptom	Celiac Disease (n = 9)	Control Subjects (n = 36)
Rumination syndrome	0	0
Functional chest pain	0	1
Functional heartburn	2	6
Functional dysphagia	0	0
Functional dyspepsia	0	2
Aerophagia	0	2
Functional vomiting	0	0
Irritable bowel syndrome	3	3
Bloating	1	4
Functional constipation	0	7
Functional diarrhea	0	0
Unspecified bowel disorder	3	10
Functional abdominal pain	0	0
Unspecified abdominal pain	0	0
Gallbladder dysfunction	0	1
Sphincter of Oddi dysfunction	0	0
Functional incontinence	5	3
Proctalgia fugax	1	2
Pelvic floor dysfunction	0	0
None	1	5

*Data are given as numbers of patients.

trols, although all of their 25-hydroxyvitamin D levels were in the normal range (Table 4).

Individuals with osteoporosis and celiac disease and their age- and sex-matched controls were given a Rome II questionnaire, a validated instrument for the evaluation of gastrointestinal complaints (**Table 5**). Thirty-one control patients and 8 celiac disease patients completed the questionnaire. Seven of the individuals with celiac disease and osteoporosis met the criteria for 1 or more gastrointestinal diagnoses. Six met the criteria for irritable bowel syndrome (diarrhea predominant) or unspecified bowel disease, both of which are marked by diarrhea. Five of the 8, including 5 of the 6 women, had fecal incontinence. Of the 19 gastrointestinal symptom complexes that could potentially be identified by the Rome II questionnaire, only fecal incontinence occurred at a statistically higher rate in the celiac disease patients. One of 8 celiac disease patients and 5 of the 31 controls did not meet the criteria for any of the gastrointestinal syndromes.

All 9 of the osteoporotic patients with celiac disease had been receiving medical therapy for osteoporosis before the diagnosis of celiac disease. All were taking alendronate sodium, 3 were taking raloxifene hydrochloride, and 1 was taking hormone therapy. Therefore, despite aggressive medical therapy, they all had T scores in the osteoporotic range.

CORRELATION OF IgA ANTI-TTG WITH T SCORES IN PATIENTS WITH CELIAC DISEASE AND OSTEOPOROSIS

All of the patients with celiac disease and osteoporosis had elevated levels of anti-TTG antibody. Tissue transglutaminase has been identified as the autoantigen of celiac disease and the predominant antigen to which anti-EMA is directed. We sought to determine if the IgA anti-TTG levels correlated with the severity of osteoporosis as measured by the T score. The anti-TTG values were plotted against the patients' lowest T scores (spine, hip, or femoral neck) (**Figure 1**). There was a correlation with an R^2 value of 0.37, indicating that the more severe the celiac disease the more severe the resultant osteoporosis. There was no correlation of T scores with anti-EMA values.

RESPONSE OF BMD TO A GLUTEN-FREE DIET

Eight of the 9 celiac disease patients with osteoporosis maintained a gluten-free diet for a year. Comparison of pretreatment T scores with those after a year on a gluten-free diet demonstrated improvement in 6 of the 8 patients (**Figure 2**). All of the celiac disease patients who had elevated levels of alkaline phosphatase or PTH before therapy normalized those values after a year on a gluten-free diet. Moreover, all the celiac disease patients who

had lost weight regained the weight on the gluten-free diet, and those who had diarrhea reverted to normal bowel habits. The improvement in BMD for celiac disease patients on the gluten-free diet was greater than that expected for osteoporotic patients receiving standard therapy.

COMMENT

Although there has been widespread agreement that osteoporosis is a common manifestation of celiac disease and that adults with newly diagnosed celiac disease increase their BMD when treated with a gluten-free diet, there has been considerable controversy as to whether the prevalence of celiac disease is higher among patients with osteoporosis and whether there is usefulness in screening patients with osteoporosis for celiac disease. Four previous studies[9-12] have addressed the prevalence of celiac disease in osteoporosis and the usefulness of screening for celiac disease in patients with osteoporosis, but they have come to conflicting conclusions.

Two of the 4 previous studies do not advocate screening for celiac disease in the osteoporotic patient population. Mather et al[10] studied 100 patients with low BMD who were screened for the presence of IgA anti-EMA. Seven patients tested positive for IgA anti-EMA at low titers (<1:20). All patients underwent upper endoscopy and biopsy; none were given the diagnosis of celiac disease. Gonzalez et al[12] screened 127 Argentinian postmenopausal osteoporotic women and 747 control women for the presence of IgA and IgG antigliadin antibodies and IgA anti-EMA; individuals with positive serologic test results underwent endoscopy with small-bowel biopsy. One osteoporotic patient and 6 control patients were given the diagnosis of celiac disease. No difference in prevalence was seen between the 2 groups.

Two of the 4 previous studies support screening for celiac disease in the osteoporotic patient population. Lindh et al[11] screened 100 Swedish patients with osteoporosis for IgA antigliadin and found that 11 (11.0%) had positive results, compared with reports of 1% positive in the general population; however, no intestinal biopsies were performed to confirm the diagnosis of celiac disease. Nuti et al[9] screened 255 osteoporotic Italian women for IgG antibody to gliadin and found that 53 (20.8%) tested positive. These individuals were then tested for IgA anti-TTG antibodies; 24 tested positive, yielding a rate of serologic positivity of 9.4%. Intestinal biopsies were obtained in 10 of the IgA anti-TTG–positive women; 6 were diagnostic of celiac disease. If the rate of biopsy-proven celiac disease was the same for all 24 IgA anti-TTG antibody–positive women, 14 individuals would have been diagnosed as having celiac disease, for a prevalence of 5.5%. The individuals diagnosed as having celiac disease had elevated PTH levels, prompting the authors to conclude that screening for IgA anti-TTG is indicated in osteoporotic patients with increased PTH.

Our study is the largest screening study of osteoporotic individuals for the presence of celiac disease, to our knowledge. This study was performed in a tertiary referral center, and it is possible that similar screening in a primary care setting would yield different results. The 3.4% prevalence of celiac disease found in our study is most similar to that found by Nuti et al,[9] in the largest of the 4 previous studies. We also found that most celiac disease patients with osteoporosis had biochemically evident secondary hyperparathyroidism with 25-hydroxyvitamin D deficiency, consistent with the notion that vitamin D malabsorption or poor intake is common in this population.[9,15] Although bone biopsies were not performed in our study, the biochemical picture is compatible with osteomalacia, a presumption strengthened by the modestly elevated alkaline phosphatase in these patients, which is typical of the increased osteoblast activity in hypomineralized bone. If osteomalacia is present in these osteoporotic patients, their already high risk of fractures may increase further, adding to the rationale of identifying and properly treating such high-risk subjects.

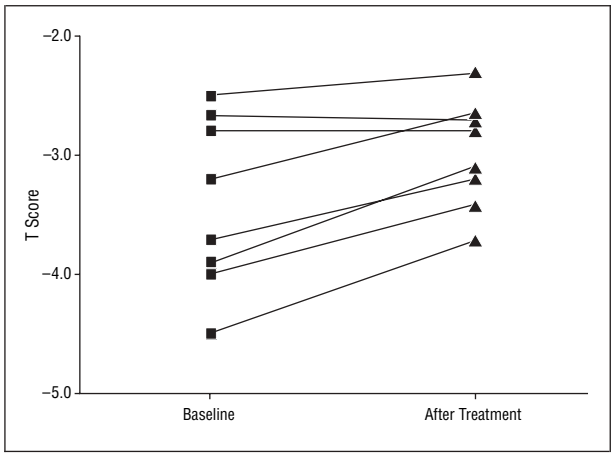

Figure 2. T scores at baseline and after 1 year of a gluten-free diet in the 8 patients with celiac disease and osteoporosis who completed a year of therapy. Posttreatment T scores are significantly higher than pretreatment T scores by paired samples *t* test (*P*=.02).

In contrast to the 4 previous studies[9-12] that only examined women, we also enrolled men. The prevalence (7 [2.9%] of 239 women) of celiac disease among the osteoporotic population did not substantially change when the small number (n=27) of men was removed from the analysis. Although the number of osteoporotic men in our study was small, they had a high prevalence (7.4%) of celiac disease, suggesting that screening men with idiopathic osteoporosis is particularly warranted.

We noted a high rate of antigliadin antibodies in the osteoporotic (19.9%) and nonosteoporotic (21.6%) populations. Nuti et al[9] described a similar level of antigliadin antibodies in osteoporosis. The high levels of positivity combined with a low level of specificity (as demonstrated by the small percentage of antigliadin-positive individuals who had positive results for anti-TTG or anti-EMA) suggest that these antibodies have no role in celiac disease screening in osteoporosis. We also used IgA anti-EMA and IgA anti-TTG as screening tests instead of one or the other, as used in the other studies,[9-12] although the same celiac disease patients would have been identified if we had used either test alone. All of those who were biopsy positive for celiac disease had positive serologic test results for anti-TTG and anti-

EMA. Anti-TTG titers are correlated with histologic severity.[16] The severity of celiac disease as assessed by anti-TTG titer correlated with the severity of osteoporosis as assessed by T score. Although the increased prevalence of osteoporosis in celiac disease is well established, this is the first correlation of osteoporosis severity with serology titers, to our knowledge.

We noted 8 individuals who had positive results for IgA anti-TTG or IgA anti-EMA but negative results for the other; of these 8 individuals, the 6 who underwent biopsy had normal histologic findings on intestinal biopsies. It is unclear if these are unaffected individuals with false-positive serologic test results or individuals in an early stage of celiac disease. These individuals will have repeat serologic studies and biopsies in 2 years to evaluate progression to celiac disease.

We offered endoscopic evaluation and small-intestine biopsies to individuals testing positive for IgA anti-EMA or IgA anti-TTG; with this strategy, IgA-deficient individuals with celiac disease would have been missed. Selective IgA deficiency affects 1 in 500 individuals.[17] In IgA-deficient blood donors, 9.8% of IgA-deficient individuals tested positive for IgG anti-TTG antibodies.[17]

The prevalence of osteoporosis among postmenopausal white women is 20%.[18] Among postmenopausal white women in our study, there was a prevalence of celiac disease of 2.9% among patients with osteoporosis and 0.2% among those without osteoporosis. From this, we can calculate a prevalence of celiac disease among postmenopausal white women of 0.64%. This is similar to the prevalence of 0.75% reported in a serologic study[19] among the general population in the United States and slightly less than the 1.2% reported among 7532 adults aged 45 to 76 years in England.[20]

All but 1 of the 9 osteoporotic individuals we identified as having celiac disease had other symptoms or laboratory values that might have suggested the presence of celiac disease. Anemia, weight loss, and gastrointestinal symptoms were frequently seen in this group. However, the mean hematocrit level was not different from that seen in osteoporotic patients without celiac disease. Moreover, gastrointestinal complaints were common in the patients with and without celiac disease. One could argue that screening all patients with osteoporosis for celiac disease is not necessary because almost all patients with osteoporosis and celiac disease have other problems that should have flagged them for testing for celiac disease. One difficulty with this argument is that these other problems, especially anemia and gastrointestinal complaints, are common in the osteoporotic patient population; their lack of specificity for celiac disease diminishes their usefulness as prompts for celiac disease screening. Moreover, although 8 of the 9 osteoporotic individuals we identified as having celiac disease had other problems that could have prompted screening for celiac disease, none of them were screened before presentation to our tertiary referral center.

As noted, our study corroborates the notion that secondary hyperparathyroidism is common in patients with osteoporosis and celiac disease, most likely as a consequence of vitamin D deficiency and malabsorption.[9,15] Although an increased serum PTH by itself might not be a useful criterion to initiate screening for celiac disease in osteoporotic individuals, it is reasonable to propose that patients with osteoporosis and evidence of 25-hydroxyvitamin D deficiency be tested for celiac disease, especially if clinical signs of the disorder are present.

Treatment with a gluten-free diet for a year resulted in improved BMD in individuals with celiac disease and osteoporosis. This is consistent with previous studies[7,8] noting similar improvements in BMD in treated adult celiac disease patients. In addition to the improvement in BMD, treatment with a gluten-free diet resolved hyperparathyroidism, diarrhea, and weight loss. These observations indicate that the diagnosis of celiac disease was correct and that individuals were compliant with their diet.

In conclusion, we found that the prevalence of celiac disease among osteoporotic patients was much higher than among the nonosteoporotic population and high enough to justify a recommendation that all individuals with osteoporosis undergo serologic screening for celiac disease. IgA anti-TTG or anti-EMA is suitable for screening; individuals with positive results on serologic screening should be evaluated with endoscopy and small-intestine mucosal biopsy to establish the diagnosis of celiac disease. Treatment of these individuals with a gluten-free diet will improve BMD. In our institution, the cost of anti-TTG testing is $45. If the prevalence of celiac disease among the osteoporotic population is 3.4%, it would cost about $1500 to identify a celiac disease patient by serologic screening.

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Correction

Duplicate Publication: The letter to the editor by Alexander C. Chester, MD, titled "A Single-Payer National Health Insurance: We Gave Twice at the Office" was inadvertently published twice in the August 9/23 (2004; 164:1702) and November 8 (2004;164:2281) issues of the ARCHIVES.