

CELIAC DISEASE

Protecting the bones should take precedence in medical nutrition therapy for patients.

By **Marsha McCulloch, MS, RD, LD**

To say that reduced bone density is common in patients with celiac disease is an understatement. In fact, sometimes bone loss is how celiac disease presents to doctors. “About 10% of the people seen in our Celiac Disease Center were diagnosed with celiac disease because of reduced bone density,” says Peter H.R. Green, MD, director of the Celiac Disease Center at NewYork-Presbyterian Hospital/Columbia University Medical Center and coauthor of *Celiac Disease: A Hidden Epidemic*.

More than 75% of adults with untreated celiac disease and overt malabsorption at the time of diagnosis have bone loss (osteopenia or osteoporosis).¹ Bone loss also affects about one-half of patients with subclinical celiac disease (who show minimal, transient celiac disease symptoms) and asymptomatic patients diagnosed with the condition as a result of testing that was prompted by a first-degree relative’s diagnosis.¹ However, only in rare cases is osteomalacia, a vitamin D deficiency disease that’s characterized by bone deformities and bone pain in addition to low bone mineral density, part of the initial presentation of celiac disease.²⁻⁴

Over time, loss of bone mass translates to increased risk of broken bones.⁵ A systematic research review published in January in *The Journal of Clinical Endocrinology & Metabolism* found that celiac disease was associated with a 30% increased risk of any fracture and a 69% increased risk of hip fracture.⁶ Providing effective, individualized medical nutrition therapy to prevent osteoporosis, and its precursor, osteopenia, to help reduce fracture risk in celiac disease patients requires understanding the ways in which the disease can impact bones.

Connection to Bone Disease

There are several reasons for the elevated risk of reduced bone density in celiac disease, Green says. He lists these factors as: malabsorption of nutrients, such as calcium and vitamin D; secondary hyperparathyroidism; autoimmune factors, including tissue transglutaminase (tTG) antibodies, which possibly impact bone remodeling; and inflammation, including increased circulating cytokines (chemical messengers) that interfere with bone formation.

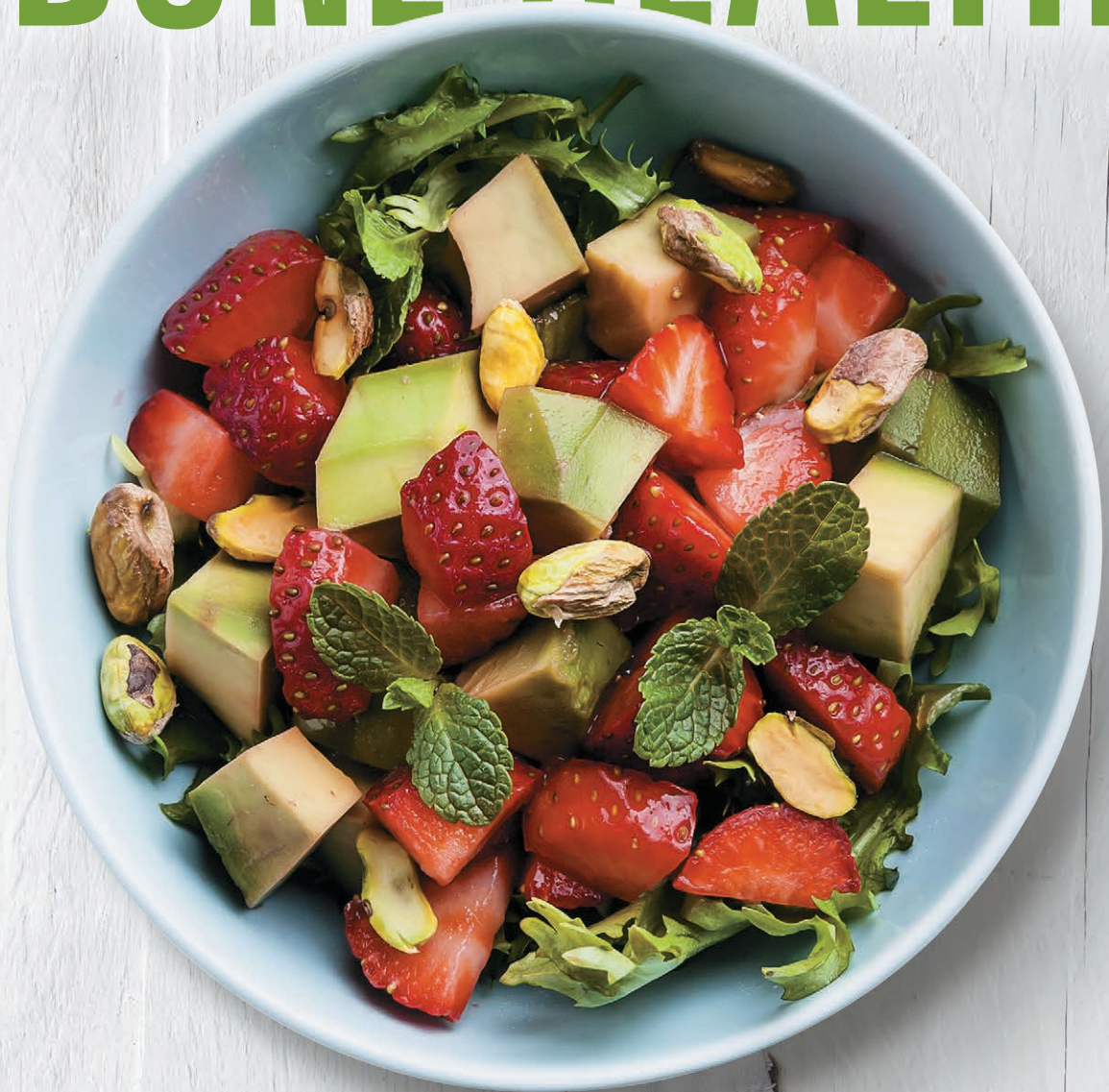
Nutrient Intake and Malabsorption

“In people with untreated celiac disease, gluten triggers destruction of the villi lining the small intestine, which means there’s less available surface area to absorb calcium, vitamin D, magnesium, and other nutrients important for bone health,” says Pam Cureton, RD, LDN, chair of Dietitians in Gluten Intolerance Diseases, a subunit within the Medical Nutrition Practice Group dietetic practice group of the Academy of Nutrition and Dietetics. “So their bones may not be getting enough of these nutrients, even if they’re taking in adequate amounts.

“Additionally, because lactase is produced in the tip of the villi, if patients have damaged villi they will also have less lactase and may be restricting their dairy intake due to lactose intolerance,” Cureton says. “So they’re often taking in less calcium and vitamin D, too.”⁷

Although one might think that people with dermatitis herpetiformis, the itchy, blistering skin manifestation of celiac disease, wouldn’t have the malabsorption and nutrient deficiencies of classic celiac disease that contribute to bone loss, this isn’t the case.⁸ “Those manifesting with

& BONE HEALTH





dermatitis herpetiformis frequently have less villous atrophy or lesion severity (up to 20% to 25% exhibit minimal pathology), but nutrient deficiencies are comparable to celiac disease,” says Nancy Patin Falini, MA, RDN, LDN, a dietitian in private practice specializing in gluten-related disorders in West Chester, Pennsylvania, and author of *Gluten-Free Friends: An Activity Book for Kids*.

Unfortunately, most of the research on dermatitis herpetiformis has focused on skin issues, so there’s much less data related to dermatitis herpetiformis and bone health compared with celiac disease, Falini says. A 2013 study comparing bone density in celiac disease patients, dermatitis herpetiformis patients, and healthy controls found that bone mineral content in dermatitis herpetiformis was significantly lower than in healthy controls but higher than in celiac disease. Specifically, decreased bone mineral density was found in 49% of dermatitis herpetiformis patients and 62% of celiac disease patients compared with only 29% of healthy people.⁸

Fortunately, nutrient absorption in celiac disease and dermatitis herpetiformis can be improved. “After following a strict gluten-free diet for a while, the villi do rebuild and the ability to absorb these nutrients returns,” Cureton says. “We’re starting to repeat the endoscopy after one year of being on a gluten-free diet to make sure that the villi have returned so absorption can take place.”

Much less is understood about nonceliac gluten sensitivity and bone health, Falini says. “Osteoporosis is an associated symptom in nonceliac gluten sensitivity, although the condition doesn’t appear to cause malabsorption,” she says. A preliminary 2014 study published in *BMC Medicine* found an increased frequency of bone mass loss in nonceliac gluten sensitivity (but not as high as in celiac disease), which was related to a

low BMI and was more common in patients who also had other food sensitivities, suggesting a possible role for malnutrition.⁹ Further research is needed.

Secondary Hyperparathyroidism

Some celiac disease patients have secondary hyperparathyroidism. In this condition, significant calcium malabsorption results in low blood levels of calcium, which triggers the parathyroid gland to secrete parathyroid hormone (PTH).¹⁰ PTH signals the bones to release calcium to bring calcium blood levels up to the desired range, contributing to bone loss. To counteract this, a patient has to consume enough calcium (in some cases, up to 2,000 mg per day) to turn off PTH, Green says. He adds that these high doses should be given only with careful monitoring of the patient, which may include assessing 24-hour urinary calcium levels.

Autoimmunity and Bones

Although it’s generally well known that antibodies against tTG are formed in the gut when individuals with celiac disease consume gluten (or more specifically, gliadin), what some people may not realize is that tTG is present in every tissue of the body—including bones, Green says. “Tissue transglutaminase is an enzyme with important functions, including joining proteins together, which is important for bone remodeling,” he says. “But, under the influence of gliadin, antibodies to tTG could block the actions of tTG in bone, indicating an autoimmune effect.”

However, this isn’t the only way autoimmunity may impact bones. In some cases, antibodies form against osteoprotegerin, which is a protein produced by osteoblasts (bone building cells) that’s important for inhibiting bone breakdown, Green explains. In a 2009 *New England Journal of Medicine* study, scientists reported finding antibodies against osteoprotegerin in a patient with celiac disease with high bone turnover and severe osteoporosis (whose bone density status didn’t improve with a gluten-free diet and nutrient supplementation), and in three other patients.¹¹ A larger study of patients with celiac disease published in 2012 in *World Journal of Gastroenterology* failed to find antibodies against osteoprotegerin.¹² So, antibodies to osteoprotegerin may not play a major role in celiac disease, although it’s uncertain at this point.

Inflammation and Other Immune System Bone Interactions

Beyond autoimmunity, there are other ways the immune system may interact with bones, which is a new scientific field of study referred to as osteoimmunology.¹³⁻¹⁵ “Immune cells called T-cells produce certain cytokines that promote the formation of osteoclasts, which break down bone,” says Matthew Greenblatt, MD, PhD, a resident in pathology at Brigham and Women’s Hospital in Boston, and a research fellow at Weill Cornell Medical College in New York City. “When someone with celiac disease consumes gluten, the production of these cytokines

is stimulated,” Greenblatt says. “This knowledge could potentially lead to treating such patients with agents that quiet the immune system in order to improve bone mass, though right now it’s unclear if this would offer any benefit to celiac patients.” At a minimum, it reinforces the importance of avoiding gluten for bone health in celiac disease.

Preliminary research by Laura McCabe, PhD, a physiology professor and director of the molecular metabolism disease program at Michigan State University in East Lansing, and colleagues also may hold some clues to improving bone health in patients with celiac disease by controlling inflammation. “In healthy male mice, we’re able to detect some general inflammation, and when we treat with a probiotic that has anti-inflammatory properties, we can enhance their bone density,” she says. “Our research used *Lactobacillus reuteri*, but there aren’t yet any studies that show one strain is better than another for bones.”

Until science reveals more about this connection, one thing everyone, including people with celiac disease, can do is build a healthy community of bacteria or microbiome.¹⁶ “The gut microbiome secretes factors that can impact our intestinal cells and maybe even enter our bloodstream and send signals, perhaps to improve calcium absorption,” McCabe says.

“Anything you put in your mouth can affect your microbiome. Consuming foods such as fruits and vegetables that contain prebiotic fibers supports beneficial microbes,” McCabe says. “On the other hand, eating a very high-fat diet can inflame the intestines in anyone (not just in disease states) and is thought to negatively affect the microbiome.”

Diet and Bone Health

The gluten-free diet clearly is the first step in protecting bone health in celiac disease. “We did a study showing that failure to heal the gut in celiac disease was associated with increased bone fracture risk,” Green says. “So, that’s an important reason for patients to be very strict with the gluten-free diet.”

Getting adequate nutrients needed to support bone health also is key, and patients need expert support to accomplish this in addition to following a gluten-free diet. “Many people incorrectly believe they have to consume several servings of dairy per day to maintain good bone health, which can be a scary belief for people with celiac disease who are dealing with bone health issues and are intolerant to dairy,” says Rachel Begun, MS, RDN, a consultant and natural chef in Boulder, Colorado.

“While milk products certainly offer calcium, vitamin D, and other nutrients important for bone health, so do a long list of other foods. This is where the expertise of the registered dietitian comes in—helping patients tailor a dietary plan that helps them meet their bone health needs with foods they can tolerate,” Begun says.

Nondairy sources of calcium include leafy greens, certain beans, almonds, figs, and fortified foods such as orange juice, Begun says. Vitamin D occurs naturally in few foods, but salmon and eggs are two good dietary sources. Good sources of magnesium include leafy greens, avocados, beans, brown rice, and millet, she adds.

“If someone with celiac disease and lactose intolerance has been off of gluten and dairy for a while and wants to challenge dairy products to see if they’ll work, I make sure they understand that tolerance of lactose is dose dependent,” says Carren Sellers, MMSc, RD, LD, CDE, CLT, who works with diabetes patients through Emory Healthcare and has a private practice in Atlanta. “So they shouldn’t challenge dairy by starting with a big glass of milk by itself. It would be better to try yogurt or a small glass of milk with a meal.”

Nutrient Supplementation

“If, after doing a good history, I find that celiac patients aren’t taking in good sources of calcium, vitamin D, magnesium, vitamin K, and other nutrients, such as the B vitamins, I recommend a good multivitamin/mineral supplement,” Cureton says, adding that they may need additional vitamin D and calcium beyond the multi, depending on their lab work.

“It’s essential to work closely with a patient’s doctor because no amount of supplementation for bone health will compensate for medical factors such as untreated hyperparathyroidism, excessive loss of calcium in the urine, or hormone imbalances that impact bone health,” says Susan Brown, PhD, author of *Better Bones, Better Body*, and director of the Center for Better Bones in East Syracuse, New York.

Calcium

Although calcium clearly is essential for bones, it’s important not to exceed recommended intake with supplements. “Too much calcium can saturate the system

Resources

- Academy of Nutrition and Dietetics Evidence Analysis Library — celiac disease: www.andeal.org
- *Celiac Disease: A Hidden Epidemic*, revised edition, by Peter H.R. Green, MD, and Rory Jones
- The Center for Better Bones: www.betterbones.com
- Dietitians in Gluten Intolerance Disease (DIGID): www.mnpgdpg.org/page/dietitians-in-gluten-intolerance-diseases
- *The Magnesium Miracle*, 3rd edition, by Carolyn Dean, MD, ND
- National Osteoporosis Foundation Bone Source: <https://my.nof.org/bone-source>

and precipitate out calcium, potentially contributing to kidney stones or atherosclerosis,” Brown says. “It’s also important to balance calcium and magnesium supplements. I recommend equal amounts of supplemental calcium and magnesium, assuming that some calcium is obtained from the diet.”

When supplementing with calcium, it’s important to remember that there’s a limit on how much calcium a person can absorb at one time, Sellers says. “I suggest no more than 500 mg of calcium at a time and advise patients against taking their calcium supplement at the same time as consuming calcium-rich foods, such as a sandwich with cheese, so they can absorb more calcium from each source.”

Magnesium

The majority of Americans consume magnesium below their estimated average requirement, and for someone with malabsorption, such as in celiac disease, risk of deficiency is even greater.¹⁷ Unfortunately, magnesium isn’t necessarily on the radar of patients concerned about bone health.

It may help dietitians to explain it to them this way: “If bones were just made of calcium, they would be brittle, like calcium carbonate, which is what chalk is made of. If you drop chalk on a hard surface, it will shatter, which is what is happening in people who have a lot of calcium in their bones but not enough of other nutrients, including magnesium, needed to make indestructible bones,” says Carolyn Dean, MD, ND, author of *The Magnesium Miracle*. “Magnesium gives bones much more resiliency, so they can sustain falls without breaking. Magnesium directs calcium to the bones properly and creates the right matrix. When you get enough magnesium, the matrix is much less brittle.”

Vitamin D

Research shows that people need to maintain a minimum vitamin D blood level of 32 ng/mL year-round to protect bone, and at least 50 ng/mL likely is better, Brown says. “In northern climates, the average person needs 4,000 to 5,000 IU of vitamin D to reach 50 ng/mL during the winter, and often at least 2,000 IU in the summer, but testing blood levels will help identify the best dose, and malabsorption can certainly impact the amount needed.”

Dean cautions against oversupplementing vitamin D, explaining that it might lead to a magnesium deficiency. “In order for supplemental or stored vitamin D to be converted to the active form, it requires magnesium,” she explains.

Vitamin K

Vitamin K also is important for bone health, especially vitamin K₂, which is produced by bacteria and is high in fermented foods, such as fermented soy (natto) and

fermented, aged cheese, Brown says.¹⁸ “Vitamin K₂ doesn’t increase bone density much, but it reduces bone fractures significantly. Research suggests 200 mcg per day of vitamin K₂, particularly the MK-7 form found in natto, is beneficial for bone health,” Brown says.

B Vitamins

The importance of the B vitamins in osteoporosis shouldn’t be overlooked.¹⁹ “There’s a genetic variation in the MTHFR, or methylenetetrahydrofolate reductase, allele (C677T) that’s common in people with celiac disease, and this variance can lead to high homocysteine due to impaired ability to metabolize methionine (an amino acid prevalent in protein-rich foods),” Brown says.

“Elevated homocysteine is not only very damaging to coronary vessels but also to other tissues, including collagen, which is important for strong bones. Not surprisingly, scientists have found a higher fracture risk in those with high homocysteine,” Brown says. Research suggests that supplementing with the methylated forms of folate (methylfolate) and B₁₂ (methylcobalamin) helps bypass this genetic glitch.²⁰

Do Bones Bounce Back?

“When celiac disease is diagnosed in adults, typically we’ll test the patient’s serum calcium and vitamin D levels, as well as parathyroid hormone, and get a bone density test (with DXA, or dual-energy X-ray absorptiometry), which we’d repeat after a year,” Green says.²¹ “We wouldn’t consider putting someone on osteoporosis medication unless we’ve repleted the calcium and vitamin D and have given them at least a year on that regimen. If bone density didn’t improve after a year or it deteriorated, then we’d consider using a medication, such as a bisphosphonate.” Bisphosphonates prevent osteoclasts from breaking down bone.²²

Depending on age and the duration of untreated celiac disease, some patients may not get complete bone healing, Cureton says.^{1,23} “We do build bone up until age 30, so children with celiac disease can return to a normal bone density faster because they’re at an age when the body is building bone,” she says.

Greenblatt adds: “The earlier in life a person with celiac disease switches to a gluten-free diet, the better the chance that they’ll recover bone mass. It’s also important not to overlook lifestyle interventions to increase bone mass, including exercise, avoiding excess alcohol, and avoiding smoking.”

— Marsha McCulloch, MS, RD, LD, is a nutrition writer and consultant in South Dakota.



For references, view this article on our website at www.TodaysDietitian.com.