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Low 25-Hydroxyvitamin D and Myofascial Pain: Association of Cancer, Colon Polyps, and Tendon Rupture

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ABSTRACT

Background: Myofascial pain that has been associated with cancer and increased risk of morbidity and mortality in cancer patients is intrinsically associated with low magnesium and low 25-hydroxyvitamin D (25(OH)D). Therefore, this physical finding was used as a clinical diagnostic proxy.

Objective: The objective of this study was to assess the association and prevalence of disease in individuals with myofascial pain and low 25(OH)D in a county with low magnesium in the drinking water.

Design: This is a retrospective cross-sectional study of a chart review of 269 subjects to assess subjects presenting with myofascial pain (assessed by tender trigger points) and 25(OH)D concentrations below 30 ng/mL or a history of 25(OH)D deficiency compared to those without these exposures.

Results: The association between the exposure of low 25(OH)D levels and myofascial pain was compared to all cancers, colon polyps, and tendon ruptures. The odds of having cancer with the combined exposures was 10.14 times the odds of not having either exposure (95% confidence interval [CI], 5.08, 20.25, $p < 0.001$). For adenomatous colon polyps, the odds ratio (OR) was 7.24 (95% CI, 3.83, 13.69, $p < 0.001$), and for tendon rupture, the OR was 8.65 (95% CI, 3.76, 19.94, $p < 0.001$). Of 80 subjects who had both myofascial pain and 25(OH)D less than 30 ng/mL, 74 were tested for red blood cell (RBC) magnesium. Half of those subjects had RBC magnesium concentrations < 4.6 mg/dL, and 23% had levels below the reference range (4.0–6.4 mg/dL).

Conclusion: Myofascial pain as assessed by tender trigger points and 25(OH)D deficiency showed a significant association with cancer, adenomatous colon polyps, and tendon rupture. Further studies to verify these results are needed, especially in areas where there is low magnesium in the drinking water.

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Introduction

Multiple studies have shown that both vitamin D deficiency, as measured by total serum 25-hydroxyvitamin D (25(OH)D), and magnesium deficiency are common among patients with myofascial pain and fibromyalgia. In clinical research, magnesium supplementation has been shown to be a beneficial treatment for the associated myofascial pain, and vitamin D3 (cholecalciferol) supplementation has been inconsistent in its effectiveness for this condition [1–8]. Furthermore, myofascial pain has been associated with cancer and increased risk of morbidity and mortality in cancer patients [9–13].

Numerous papers have linked 25(OH)D deficiency and magnesium deficiency to a variety of conditions, such as cancer (including breast, colon, prostate, and melanoma), coronary artery disease, and stroke [14–26]. Polymorphisms of the vitamin D receptor (VDR) have also been associated with cancer such as breast, ovarian, uterine, melanoma, and colon. In humans, the effects of 1-alpha, 25-dihydroxyvitamin D, the active form of vitamin D, are mainly mediated by the vitamin D receptor [27–36].

Magnesium is vital to the production of the hormone vitamin D. The vitamin D binding protein and the 3 enzymes (1-alpha hydroxylase, 24-hydroxylase, and 25-hydroxylase) that determine the 25(OH)D and 1-alpha, 25-hydroxyvitamin D concentrations are dependent on magnesium as a cofactor. Therefore, the intake of magnesium can affect vitamin D metabolite concentrations [14,15,37]. Magnesium is also important for the body's function of over 600 enzymes, regulation of activity of several ion channels, and stabilization of negatively charged molecules such as adenosine triphosphate, adenosine diphosphate, RNA, and DNA [38].

The reference range for total serum 25(OH)D is still being debated, partly due to its dependence on various health outcomes. It has been suggested that the serum 25(OH)D concentration should be greater than 30 ng/mL. The recommended daily allowance (RDA) is also being debated, and depending on the agency, falls between 400 and 1000 IU/day. The upper limit of intake for vitamin D supplements to avoid toxicity is highly variable depending on the agency evaluating. It does not appear that magnesium intake was taken into consideration when the RDA and upper limit of normal were formulated [14,15,37,39–41]. In

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addition, age, gender, skin color, sun exposure, living in latitudes above 37° N, and genetic variations in the vitamin D production pathways can affect 25(OH)D concentrations in the body [39].

Multiple etiologies of magnesium deficiency have been discovered, to include low dietary intake, genetic or acquired aberrations of gastrointestinal absorption, renal or gastrointestinal excretion, and medications that alter any of the above [38,42]. Approximately 99% of the total body magnesium is in bone and intracellular soft tissue. However, it is difficult to reliably assess the body's magnesium reserves, even using current clinical tests such as serum magnesium and red blood cell (RBC) magnesium. Both tests can produce results within the current reference range in individuals who have total body deficiency, because the body works hard to maintain a narrow range of magnesium blood levels [39,43].

Soft water has been recognized as an influencing factor for multiple health outcomes. Studies of populations living in soft water municipal districts have concluded that low magnesium in drinking water increases the prevalence of cancer and cardiovascular disease [26,43–47]. Although drinking water is an important source for magnesium intake, it can vary as much as 100-fold depending on geographic location, the use of water filters or softeners, and desalination. Magnesium and calcium are the major contributors to "water hardness," which is often reported as milligrams of calcium carbonate equivalent per liter [48–50]. The U.S. Geological Survey defines 4 levels of hardness: soft, 0–60 mg/L of calcium carbonate; moderately hard 61–120 mg/L; hard 121–180 mg/L; and very hard >180 mg/L [49].

San Francisco, California, is a soft water municipal district where the average hardness of tap water is 46 mg/L, the average magnesium concentration is 3.9 mg/L, and the average calcium concentration is 11 mg/L [51]. In comparison, the average water hardness of tap water in Bodega Bay, California, a coastal community located 65 miles northwest of San Francisco, is 413 mg/L, with an average magnesium concentration of 40 mg/L and average calcium concentration of 100 mg/L [52]. It is assumed that the average individual drinks about 2 L of water daily. The magnesium RDA for a woman is about 320 mg [39]. Therefore, if she is drinking tap water from San Francisco, she will meet only 2.4% of her magnesium RDA from water (7.8 mg/2 L). In comparison, a woman drinking water from the Bodega Bay Municipal Water District could meet 25% of her magnesium RDA.

Other sources of water such as softened water, reverse osmosis filtered, distilled, and desalinated water, along with many packaged/bottled waters, do not contain significant or even measurable amounts of magnesium. In comparison, high-mineral-content bottled waters can contain over 100 mg/L of magnesium and over 300 mg/L of calcium [48,49].

Therefore, due to San Francisco's geographic location of 37° N and a low-magnesium water source, these factors together may pose a health concern for some individuals, because it may increase the risk of vitamin D as well as magnesium deficiency.

In this study, we used myofascial pain/tender trigger points as a clinical proxy for low magnesium levels and hypothesize that this, along with low 25(OH)D levels, are exposures that have multiple sequelae as outcomes from these deficiencies.

Materials and methods

In this retrospective cross-sectional study, all medical charts for patients visiting a San Francisco internal medicine practice between January and June 2015 were reviewed. A total of 269 patient consecutive records were reviewed. There were no exclusions. The records were scored for age, gender, height, weight, amount of time living in the Bay Area, skin tone, food and beverage preferences/use, food nutritional content, drug use, sunscreen use, smoking history, total serum 25(OH)D concentrations (vitamin D2 and D3), RBC magnesium concentrations, history of vitamin D deficiency or documented level of total serum 25(OH)D below 30 ng/mL, blood calcium concentrations, and myofascial pain determined by sensitivity of tender trigger points. All medical and surgical conditions recorded in the chart were tallied and include any cancers, hypertension, cholesterol levels, documented atherosclerosis, incidence of myocardial infarctions, transient ischemic attacks or stroke, aneurysms, cardiac arrhythmia, hypothyroid, history of colon polyps, and types of surgical procedures.

The 2 exposures of interest in this study were myofascial pain as assessed by tender trigger points and vitamin D. Tender trigger points were assessed during clinical exams by the same clinician. The tender points commonly examined were the fascial and/or tendon insertions of the following: proximal brachio-radialis muscle, triceps brachii, biceps brachii, infraspinatus, trapezius (periscapular region), scalenes, semispinalis capitis, levator scapulae, pes anserinus, flexor digitorum longus, ileotibial tract and insertions, and gluteal fascia region. A positive result was reported when light pressure produced significant pain, which could be easily located and reproduced by the patients themselves. Subjects were determined to have vitamin D deficiency if they had total serum 25(OH)D concentrations below 30 ng/mL or a history of low vitamin D levels.

Data analyses were carried out using the statistical software package Stata (Release 14, StataCorp, College Station, TX).

Body mass index (BMI) was made into a categorical variable for comparison between groups and used as a continuous variable in all other analyses. The quintiles 1 to 5 have the following ranges: 17.02 to 20.28, 20.31 to 22.32, 22.47 to 24.61, 24.69 to 28.46, and 28.5 to 51.4. There were approximately 54 patients in each category. To show the age distribution of the population, age was categorized into 5 levels and used as a continuous variable in all other analyses.

The association between low 25(OH)D levels and sensitivity of tender trigger points was compared to all cancers, adenomatous colon polyps, and tendon ruptures/tears. These 3 conditions were chosen for analysis because they were well documented in the medical record with not only physical exam but also with surgical and or consultation letters and pathology reports. Each one of these measures is binary, so logistic regressions were performed using age, gender, and BMI as possible confounders.

Results

Table 1 summarizes the characteristics of the subjects in this study. Charts of 269 patients who had an office visit between January 2015 and June 2015 were reviewed. Participants were

Table 1. Proportion of age, gender, and BMI who have cancer, colon polyps, or tendon rupture[a].

	N (Proportion of Positive)		
	All Cancer	Colon Polyps	Tendon Rupture
Age			
18–44	25 (4%)	6 (17%)	25 (0%)
45–54	40 (13%)	20 (15%)	40 (5%)
55–64	61 (20%)	59 (32%)	61 (11%)
65–74	77 (32%)	76 (49%)	77 (13%)
75–95	66 (47%)	66 (52%)	66 (23%)
p Value	<0.001	0.008	0.018
Gender			
Male	68 (38%)	59 (46%)	68 (16%)
Female	201 (24%)	168 (40%)	201 (11%)
p Value	0.022	0.43	0.31
BMI			
Q1	54 (30%)	48 (44%)	54 (4%)
Q2	54 (28%)	45 (42%)	54 (20%)
Q3	54 (15%)	41 (29%)	54 (11%)
Q4	55 (33%)	46 (35%)	55 (15%)
Q5	52 (33%)	47 (55%)	52 (13%)
p Value	0.204	0.126	0.128

BMI = body mass index.
[a]Significance levels were determined with a Pearson's χ^2.

68 men (25%) with a mean age of 66 (range 28 to 89) and 201 women (75%) with a mean age of 63.6 (range 18 to 95).

The study subjects were all ambulatory and productive individuals of middle to higher income. They all had access to health care and were conscious of the importance of healthy food choices, oftentimes buying organic foods and avoiding processed foods.

All 269 study subjects had lived in the soft water municipalities of San Francisco and its surrounding Bay Area communities for at least 10 years. Use of sunscreen among the subjects varied. Most subjects wore sunscreen only when outdoors for extended periods of time. Many of the subjects applied sunscreen on their faces and sometimes on their arms for outdoor excursions. Some subjects reported rarely wearing sunscreen. Nearly all of the subjects were of medium to light complexion, regardless of genetic makeup. There were no diagnoses of malabsorption or fibromyalgia among the study subjects.

All patients who were determined to be positive had more than 8 tender trigger points found on exam. In patients who were deemed negative, no tender trigger points could be found. No patient had only 1–7 trigger points recorded in the record.

As a standard of this preventive and diagnostic medicine practice, a generalized dietary history was taken routinely during physical exams and recorded in patients' medical records. The practitioner-led survey recorded each patient's consumption of fruits, vegetables, protein sources, gluten products, nuts, seeds, and fermented foods. Beverage choices, including water type, were also surveyed. An overview of the recorded dietary histories of study subjects revealed that they did not consume magnesium-rich foods such as nuts and seeds, small fish, and green leafy vegetables on a daily basis. Though most patients were aware of the importance of consuming calcium-rich foods, they were unaware of the importance of consuming magnesium-rich foods.

Consumption of alcoholic beverages and caffeine was common among the study subjects. Many also drank packaged/bottled spring, sparkling, purified, or reverse osmosis water that had very low to no mineral content. No subject reported drinking mineral water with significant magnesium or calcium content.

Of the 269 subjects, 195 had either a history of vitamin D deficiency or a documented total serum 25(OH)D concentration < 30 ng/mL, 118 had trigger point tenderness documented on exam, and 80 had both a low 25(OH)D and trigger point tenderness. For 129 subjects, only one exposure was known; the other was unmeasured and assumed to be absent. For 22 subjects, neither 25(OH)D deficiency nor myofascial pain was present. The status of both exposures was unknown for 6 subjects.

There were 3 medical outcomes of interest: cancers, colon polyps, and tendon rupture/tear. Logistic regressions examined the association between each of these outcomes using total serum 25(OH)D deficiency and tendon trigger point tenderness as exposure variables. Age, gender, and BMI were considered as confounders to these associations. Age and gender were found to confound the relationships and were included in the final analysis, whereas BMI did not and was excluded from further analysis.

Of 269 subjects, 97 had one or more incidence of 19 different types of cancer. Nineteen subjects had squamous cell skin cancer, 16 breast, 15 basal cell, 11 prostate, 6 melanoma, 6 uterine, 4 colon, and 4 cervical. More than one type of cancer was found in 18 subjects, and some subjects had more than one incidence of a specific type of cancer, such as squamous cell skin cancer.

The logistic regression shown in Table 2 shows the odds ratios for all cancers, adenomatous colon polyps, and tendon ruptures for the exposures of 25(OH)D deficiency and tendon sensitivity, as well as the odds ratios from combining the exposures into a single variable. The odds ratios (ORs) for having the medical outcomes were between 4 and 10 for those with

Table 2. Odds ratios for all cancers, adenomatous colon polyps, and tendon rupture for the exposures of total serum 25(OH)D deficiency and tendon sensitivity and Odds ratios from combining the exposures into a single variable[a].

	All Cancers (*N* = 269)		Adenomatous Colon Polyps (*N* = 269)		Tendon Rupture (*N* = 269)	
	OR (95% CI)	*p* Values	OR (95% CI)	*p* Values	OR (95% CI)	*p* Values
25(OH)D deficiency	9.50 (3.59, 25.16)	<0.001	5.72 (2.55, 12.84)	<0.001	4.84 (1.52, 15.44)	0.008
Tendon Sensitivity	6.79 (3.41, 13.50)	<0.001	6.07 (3.23, 11.39)	<0.001	6.01 (2.51, 14.38)	<0.001
Combined exposures	10.14 (5.08, 20.25)	<0.001	7.24 (3.83, 13.69)	<0.001	8.65 (3.76, 19.94)	<0.001

25(OH)D = 25-hydroxyvitamin D, OR = odds ratio.
[a]Age and gender were controlled for in all logistic regressions. All missing values were considered to be controls (outcome free).

tendon sensitivity or 25(OH)D deficiency compared to those without those exposures. In addition, in this study population, being female significantly decreased the odds of having cancer when compared to men. The combined exposure variable for those who had both 25(OH)D deficiency and tendon sensitivity ($n = 80$) showed an OR for cancer, adenomatous colon polyps, and tendon rupture higher than either one of the 2 single variables. The odds of having cancer with these combined exposures is 10.14 times the odds of those with normal vitamin D and less than 8 sensitive trigger points (95% confidence interval [CI], 5.08, 20.25, $p < 0.001$). For adenomatous colon polyps, the OR was 7.24 (95% CI, 3.83, 13.69, $p < 0.001$), and for tendon rupture, the OR was 8.65 (95% CI, 3.76, 19.94, $p < 0.001$) with combined exposures.

Colonoscopy results and pathology reports from the subjects' gastroenterologists were evaluated. Ninety-five individuals in the study population had one or more incidence of adenomatous colon polyps found on colonoscopy. The percentage of colonoscopies performed on subjects with both exposures ($N = 80$) was 88%, and for all others ($N = 189$) it was 83%. Forty-two subjects did not have a colonoscopy, and all but 10 were less than 50 years old. The average age of 10 subjects who did not have a colonoscopy and were more than 50 years old was 53.

Of the 80 subjects who had both myofascial pain and 25(OH)D deficiency, 74 had an RBC magnesium test drawn at some point in the previous 10 months (reference range for RBC magnesium 4.0–6.4 mg/dL). Some of these subjects had started taking a magnesium supplement before a baseline concentration was obtained. The mean and median RBC magnesium concentration for the 74 study subjects with both myofascial pain and 25(OH)D deficiency was 4.6 mg/dL (range 2.9–6.5 mg/dL). Eighteen (23%) had an RBC magnesium concentration less than 4.0 mg/dL. The mean total blood calcium for this group was 9.2 mg/dL, with a range of 8.5–9.9 mg/dL. None had a diagnosis of hyperparathyroidism. Regression analysis on this subpopulation of 80 subjects showed that for cancer and colon polyps, RBC magnesium levels were not significantly correlated. But with an RBC magnesium < 4.0 mg/dL, the OR for tendon rupture was 6.43 (CI, 2.03, 20.39, $p < 0.002$).

Discussion

This cross-sectional retrospective study shows a significant association of myofascial pain and total serum 25(OH)D deficiency with cancer, adenomatous colon polyps, and tendon rupture, and the odds increase when both variables are present.

Of particular interest in our San Francisco and Bay Area communities is that there is an elevated incidence of breast cancer. For Marin County, which is a soft water municipal region just north of San Francisco where some of the study subjects reside, recent research has shown a high frequency of the VDR *Apa1 A2/A2* homozygous polymorphism in a population of breast cancer patients. Additionally, alcohol consumption and hormone replacement therapy, both of which can contribute to a magnesium deficiency state, were common among the breast cancer patients [28]. Alcohol and hormone use was also true for our study population, as well as having low-magnesium drinking water from the tap, reverse osmosis, or bottled sources. In addition, because vitamin D and magnesium are involved in many important pathways, including DNA repair, the combination of 25(OH)D deficiency and magnesium deficiency may lead to a higher susceptibility to environmental toxicants. How individuals with vitamin D polymorphisms respond in the setting of low magnesium intake and/or reduced sun exposure warrants further investigation.

In this study, 79% of the subjects with known vitamin D status had a 25(OH)D concentration of <30 ng/mL. Many of the subjects were outdoors for extended periods without sunscreen yet still had levels <30 ng/mL. Many populations in the United States and around the world have also demonstrated vitamin D deficiency at unexpected high prevalence, even in geographic areas of abundant and intense sunshine. In areas of the world where 25(OH)D deficiency would be expected, such as northern latitudes above the 48th parallel, there can be much variation in 25(OH)D concentrations in the population. In Sweden, 56–67° N, the drinking water is also low in magnesium. In measurements made on 76 municipal water supplies across Sweden, the median content of magnesium in the household water was 3.3 mg/L in the west (range 0.7–14.3) and 5.4 mg/L in the east (range 0.1–13.5) [53]. Two surveys conducted in Sweden demonstrate the differences in adaptation to low sun availability and low magnesium in the water in regard to vitamin D concentrations. In a survey of 1622 randomly selected subjects aged 25–74 years in northern Sweden (latitude 63° N), the mean 25(OH)D concentration was 27.24 ng/mL, and 65% had values < 30 ng/mL. All but 53 of the study subjects were born in Sweden or Finland [54]. In contrast, in a study of recent immigrants to Sweden from the Middle East and Africa, including Afghanistan, Iran, Iraq, Pakistan, Turkey, Burundi, Eritrea, Ethiopia, and Somalia, the mean 25(OH)D was 16.4 ng/mL and 96.3% had values less than 30 ng/mL [55]. It was concluded that traditional dress that limited sun exposure to the skin, as well as diet, were correlated with 25(OH)D deficiency within the immigrant population. Those immigrants who consumed fatty fish more than once per week and those who consumed vitamin D–fortified milk daily had higher levels of 25(OH)D. Fatty fish and fortified milk contain both vitamin D and magnesium. It has been shown that taking magnesium plus a vitamin D supplement will raise 25(OH)D levels in the body greater than either supplement taken alone [14]. Dietary and supplement intervention through clean healthy sources of magnesium and vitamin D could improve the 25(OH)D status of populations where sun exposure is greatly reduced and the drinking water or diet is low in magnesium.

The subjects in this study had a prevalence of tendon ruptures, hernias, knee anterior cruciate ligament and meniscus tears, frozen shoulders, osteoarthritis, degenerative disc disease, and vascular aneurysms. For the 269 study subjects, 25(OH)D < 30 ng/mL or tendon tenderness increased the odds of a tendon rupture, and the odds increased further when both variables were present. Magnesium is important for the integrity of these tissues and the production of collagen type I, elastin, fibronectin, and integrin, as demonstrated in magnesium-deficient dogs [56]. VDR polymorphisms have also been associated with degenerative disc disease and osteoarthritis, but the results have been inconsistent for osteoarthritis [57–59].

Among the 80 study subjects who had combined myofascial pain and 25(OH)D deficiency, half had RBC

magnesium concentrations that were low normal or less, and nearly 25% had concentrations below the reference range. However, many subjects were well within the reference range yet still had severe tender trigger points along with low 25(OH)D. In addition, some individuals had started taking magnesium supplements before a baseline level was obtained; therefore, caution should be used in interpretation of the RBC magnesium results. Furthermore, how RBC magnesium concentrations interact with tissue concentrations is unclear, because blood levels may not reflect tissue concentrations. Regardless, the finding that an RBC magnesium level < 4.0 mg/dL increased the odds of having a tendon rupture is important to further investigate.

Although nearly all of the study subjects had white-collar occupations or were retirees or homemakers, many exercised regularly and participated in outdoor activities without sunscreen. Many also participated in competitive sports at some time in their life. The odds of tendon rupture increased with either 25(OH)D < 30 ng/mL or tendon tenderness, and the odds increased further with the combined exposures. Though magnesium has been found to be essential for the production of collagen type I, elastin, fibronectin, and integrin [56], vitamin D was determined to be important for maintenance of muscle mass, strength, and tendon to bone healing [60]. 1-Alpha, 25-dihydroxyvitamin D binds to vitamin D receptors on myocytes to stimulate growth and proliferation, and 25 (OH)D is important for initiating myocyte healing [60]. However, it is important to also recognize that the vitamin D binding protein and the 3 enzymes that determine the 25(OH)D and 1-alpha, 25-hydroxyvitamin D concentrations are dependent on magnesium as a cofactor [14,15,27–37].

For individuals who have increased strain to their tendons because of their occupation or physical activities, the risk of tendon tears or rupture is increased. A review of the literature by Volpe showed that insufficient magnesium intake in professional athletes is common [61]. A 25[OH]D level < 30 ng/mL is also common in professional athletes, even in regions where there is an abundance of ultraviolet B sunshine [62]. In a survey of 269 players participating in the National Basketball Association Combines (2009 through 2013), 79.3% had 25(OH)D <30 ng/mL [63]. For the National Football League, a study using a team of 80 players during the off season, which would have been during the time of ample sunshine, compared vitamin D levels and injury reports. Sixty-seven of the players were black and had significantly lower 25(OH)D than white players. In addition, 68.8% of the 80 players had 25(OH)D < 32 ng/mL. Vitamin D levels were lower in those who suffered a bone fracture and those who were released from the team. The authors assumed that their release was due to poor performance [64]. However, even though vitamin D deficiency is associated with muscle weakness and myalgia, treatment using vitamin D only or with calcium has met with inconsistent results [65]. Studies using both vitamin D and magnesium need to be conducted to determine whether this combination will increase muscle strength and reduce tendonosis, injury, and disability.

One of the outliers among the vitamin D in athlete studies involved those from the Middle East, where despite adequate sun, the prevalence of deficiency was very high [62]. In a study of 342 male professional outdoor soccer players in Qatar (25° N and 220–350 sunshine hours per month), 84% had levels < 30 ng/mL and 12% had levels < 10 ng/mL [66]. Because Qatar is a desert country with very little rain and cloud cover throughout the year, it relies heavily on desalination for drinking water, which is devoid of magnesium [67]. Screening for magnesium intake, especially in those with low vitamin D levels, is warranted, especially when there is an unexpected 25 (OH)D deficiency despite adequate sun exposure.

In the study population, 95 subjects had one or more incidences of adenomatous polyps found on colonoscopy. Adenomatous colon polyps were associated with 25(OH)D deficiency as well as myofascial pain, and the odds increased when both variables were present. The screening rate was high in this population, with only 10 individuals over the age of 50 not having a colonoscopy. Had the preventive measure of screening colonoscopy not been so high, an increase incidence of colon cancer would have been expected.

Soft water, low magnesium intake, vitamin D deficiency, and VDR polymorphisms have all been associated with colon cancer [16,18,19,21,22,24,27,46]. In 3 recent studies, prospective cohorts were used to evaluate the role of dietary magnesium in colorectal cancer in women. All 3 concluded that dietary magnesium intake was inversely associated with colon cancer occurrence. Unfortunately, these studies did not include magnesium intake from water. In the Larsson et al. study, the subjects resided in Sweden, where the water is known to be soft and have low magnesium (1–14 mg/L) [22,57]. For the Folsom and Hong study, the subjects resided in Iowa, where magnesium concentrations in drinking water can be as high as 30–50 mg/L, and demineralizing water softeners could have been implemented sporadically within the study population [18,68]. For the Gorczyca et al. study, the subjects were from all over the United States [19]. The omission of magnesium consumption from drinking water by the study subjects could have impacted the studies' strength of the conclusions. In contrast, 2 other studies showed that vitamin D3 supplementation and calcium did not reduce the incidence of colorectal adenomas [69] or colon cancer [70], but magnesium intake through food or water was not addressed. The finding that vitamin D and calcium supplements did not reduce colon adenomas or cancer supports the magnesium hypothesis, because calcium supplementation does not resolve vitamin D deficiency, and supplementing vitamin D3 does not resolve a possible magnesium deficiency. More research is needed to determine whether optimizing 25(OH)D and magnesium status can reduce the incidence of adenomatous polyps and colon cancer.

A limitation of this study is temporality—in this case, whether the 3 medical conditions of interest (cancers, colon polyps, and tendon rupture) resulted from myofascial pain and low 25(OH)D levels or vice versa.

The strength of this study is that it is the first to use tender trigger points and total serum 25(OH)D concentrations < 30 ng/mL found in individuals in an internal medicine practice to assess the prevalence of disease. The article itself is the first to discuss the importance of both magnesium and vitamin D and their association to myofascial pain and apply the concepts to clinical medicine. It is also the first study to investigate a clinical population living in a low-magnesium soft water community in the United States.

Conclusion

Having both total serum 25(OH)D deficiency and myofascial pain assessed by tender trigger points showed a significant association with cancer, adenomatous colon polyps, and tendon rupture. The odds of having cancer with these combined exposures is 10.14 times the odds of not having these exposures (95% CI, 5.08, 20.25, $p < 0.001$). For colon polyps, the OR was 7.24 (95% CI, 3.83, 13.69, $p < 0.001$), and for tendon rupture, the OR was 8.65 (95% CI, 3.76, 19.94, $p < 0.001$). Further studies to verify these results are needed, especially in areas where there is low magnesium in the drinking water.

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