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EXERCISE

ABSTRACT & COMMENTARY

Exercise Intervention for Improving Metabolic Associated Fatty Liver

By Sebastian Gallego, MD, and Nancy Selfridge, MD

Dr. Gallego is Clinical Skills Facilitator, Clinical Foundations Department, Ross University School of Medicine, Barbados, West Indies.

Dr. Selfridge is Professor, Clinical Foundations Department at Ross University School of Medicine, Barbados, West Indies.

SYNOPSIS: A small interventional study assessed the histological appearance of liver biopsies from patients with metabolic associated fatty liver disease (MAFLD) who completed 12-weeks of structured and supported aerobic exercise. Compared to biopsies from a nonexercising control group, the intervention arm demonstrated some reversal of histopathologic changes caused by MAFLD.

SOURCE: O'Gorman P, Naimimohasses S, Monaghan A, et al. Improvement in histological endpoints of MAFLD following a 12-week aerobic exercise intervention. *Aliment Pharmocol Ther* 2020;52:1387-1398.

Metabolic dysfunction caused by insulin resistance, type 2 diabetes mellitus, and obesity is associated with an increased risk of cardiovascular disease and metabolic (dysfunction) associated fatty liver disease (MAFLD), previously referred to as non-alcoholic fatty liver disease.

MAFLD has a global prevalence estimated at 25% and is a major contributor to morbidity and mortality from chronic liver disease worldwide.[1]

The natural history of MAFLD includes potential progression of this chronic liver inflammation to non-alcoholic steatohepatitis (NASH), liver cirrhosis, and hepatocellular carcinoma. There is no known pharmacologic treatment or cure for MAFLD, although both aerobic and resistance exercise have been shown to achieve histological benefit in MAFLD when associated with 7% to 10% weight loss. These strategies comprise the current evidence-based recommendations for management of this condition.

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Summary Points

- Exercise with accompanying weight loss has been shown to improve histopathologic changes associated with metabolic associated fatty liver disease (MAFLD).
- Aerobic and resistance exercise without weight loss have been shown to reduce intrahepatic lipid content, assessed noninvasively.
- In this non-randomized controlled trial, 12 weeks of aerobic exercise reduced histopathologic changes characteristic of MAFLD, namely hepatocyte fibrosis and hepatocyte ballooning.
- Twelve weeks of aerobic exercise also increased cardiorespiratory fitness, an independent predictor of reduced all-cause mortality in patients.

Exercise has been associated with a reduction in morbidity and mortality for several inflammatory conditions, such as cancer, type 2 diabetes mellitus, arthritis, and atherosclerotic cardiovascular disease. Therefore, it makes sense that it might be a helpful intervention for MAFLD. A recent meta-analysis of the effect of exercise interventions without weight loss on MAFLD demonstrated significant improvement in liver steatosis, measured noninvasively, after both aerobic and resistance exercise training interventions.[2] However, other recent studies have shown no histologic improvement in MAFLD after exercise interventions.[3,4] Thus, O'Gorman et al investigated the effect of a 12-week aerobic exercise program without dietary intervention or weight loss on improving MAFLD histological endpoints and explored the optimal dose, frequency, and type of exercise necessary for that outcome.

The authors further determined the effect of the prescribed exercise intervention on participant cardiorespiratory fitness, physical activity levels, and measures of cardiometabolic health, including body composition, vascular health, glucose metabolism, lipid metabolism, and circulating inflammatory markers. Sustainability of the exercise intervention was determined at 12 weeks and 52 weeks post-exercise intervention.

Twenty-eight participants with biopsy-confirmed MAFLD, all patients attending an outpatient hepatology clinic, were divided into a treatment group (n = 18) and a control group (n = 10), based upon participant preference. Of these, four participants dropped out before the completion of the first follow-up assessment in week 13, two in the treatment group and two in the control group, leaving 16 in the intervention group and eight in the control group for the week 13 data analysis. The age range of the participants was 46 to 77 years (mean 61), the male-to-female ratio was 7:17, and the average body mass index (BMI) was 35.7 kg/m^2.

Inclusion criteria for participants included:

- age > 18 years;
- biopsy-proven MAFLD;
- ability to attend bi-weekly, clinic-based exercise classes for the full 12 weeks.

Exclusion criteria for the participants included:

- contraindications to exercise testing or prescription;
- significant orthopedic or neuromuscular limitations;
- unwillingness to participate;
- alcohol consumption > 40 g/day (males);
- Alcohol consumption > 20 g/day (females);
- coexisting liver disease.

All participants were assessed at baseline and at week 13 for the following: dietary intake using a four-day diet diary, hepatic elastography (a noninvasive assessment of hepatic steatosis and fibrosis), and cardiorespiratory fitness using a modified Bruce protocol and estimates of VO_2 max. Cardiometabolic analysis measures included fat mass, skeletal muscle mass, waist and hip circumference, liver function tests (LFTs), lipid profile, fasting glucose, hemoglobin A1C, and circulating inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], tumor necrosis factor alpha [TNF-alpha], interleukin 6 [IL-6], and

interleukin 1 beta [IL-1 beta]). Additionally, the treatment group underwent follow-up liver biopsies at 13 weeks to assess changes in liver histological architecture. Statistical analysis using independent *T* tests and Mann-Whitney *U* tests found no differences in means for baseline measures for the control and treatment groups nor differences in baseline liver histology measures. Standard tests for multivariate analysis were applied to assess within-group differences in repeated measures for both continuous and categorical data. Effect size was calculated using eta squared, and statistical significance was set at $P < 0.05$.

The treatment intervention consisted of a 12-week moderate-to-intense aerobic exercise program, three to five sessions/week (two supervised by an exercise specialist and one to three unsupervised sessions). The exercise program was individualized and graduated in duration and intensity. Supervised group sessions consisted of five to seven minutes of warm-up, 21-42 minutes of moderate-intensity aerobic exercise (increasing over the 12-week study period), followed by a five- to seven-minute cool-down. For unsupervised sessions, participants were sent phone text messages to encourage them to repeat the same format of the supervised sessions and reminding them of the specific duration and intensity of the exercise prescription for the week. Unsupervised sessions were prompted once weekly for the first three weeks, and prompts increased to three per week in weeks 8-12. For the supervised sessions, participants were provided heart rate monitors to gauge exercise intensity, starting at 40% to 59% of heart rate reserve (HRR) and increasing to 55% to 75% HRR by week 9. Participants were trained to use the Borg scale to rate perceived exertion in order to duplicate the same intensity exercise for their unsupervised sessions. The control group was provided standard care. Diet was not changed during the study period in either group.

An assessment at week 13 showed statistically significant increased cardiorespiratory fitness in the treatment group, with the mean VO_2 max increasing by 17% compared to the control group ($P = 0.027$). VO_2 max also improved between baseline and week 13 within the treatment group. The treatment group also demonstrated improved cardiometabolic markers, including body mass (2.1% mean reduction, $P = 0.038$), waist circumference (4.0% mean reduction, $P = 0.015$), and fat mass (4.9% mean reduction, $P = 0.007$) compared to controls.

Additional improvements were noted within the treatment group compared to baseline measures for waist-to-hip ratio (2.4% mean reduction, $P = 0.008$) and increased skeletal muscle mass (3.8% mean increase, $P = 0.034$), weight loss, and BMI. No patient achieved 7% to 10% weight loss, although 19% of participants in the treatment group achieved 5% weight loss by the end of the intervention period. Histological changes in liver biopsy specimens were assessed for 12 of the 16 patients from the treatment group (four participants declined repeat liver biopsy). Those changes included improvement in liver fibrosis by one stage in 58% ($P = 0.034$) of patients and decreased hepatocyte ballooning (a characteristic histopathologic finding of steatohepatitis) by one stage in 67% ($P = 0.020$) of patients. Improvements in liver fibrosis and hepatocyte ballooning were associated with increases in estimated VO_2 max by 25% ($P = 0.020$) and 26% ($P = 0.010$), respectively. The treatment group demonstrated no changes in hepatic steatosis ($P = 1.000$), lobular inflammation ($P = 0.739$), or non-alcoholic fatty liver disease (NAFLD) activity score ($P = 0.172$). Furthermore, there were no significant changes in LFTs, nor changes in measured circulatory inflammatory markers (CRP, ESR, TNF-alpha, IL-6, IL-1 beta), lipid profiles, or measures of glycemic control. Although participants were encouraged to continue exercising after the 12-week prescribed and supervised exercise intervention, none of these beneficial changes was sustained at a one-year follow-up.

■ COMMENTARY

The results from this study supported the existing evidence that exercise alone may improve pathologic liver changes characteristic of the metabolic dysfunction associated with obesity, insulin resistance, and type 2 diabetes. The limitations of the study methodology included a small sample size, nonrandomization of study participants, and an invasive and potentially risky biopsy procedure as part of the baseline and post-intervention assessment that likely limited recruitment. The control group was not subjected to liver biopsy after 12 weeks, and medication checks were not performed for either group after study participants were recruited. Thus, there was no control for changes in biopsy findings caused by non-exercise-related variables. Both conditions introduce a possibility of type II statistical error. Despite histologic improvement in hepatic fibrosis and hepatocyte ballooning noted in the treatment group, no other histologic changes met statistical significance; therefore, it is difficult to judge the clinical significance of the improvement without a longer study period.

The strengths of this study included intervention and control groups with no significant baseline differences despite nonrandomization and a superbly structured group exercise intervention that included a supervised component and had a high level of reported adherence by participants (93%) during the 12-week implementation period. In fact, it is likely that the structure of the intervention program (graduated moderate- to vigorous-intensity aerobic exercise, a supervised group setting, and text message prompts for unsupervised sessions) influenced the positive liver histology endpoints noted in this study that were not apparent in previous exercise intervention studies by Hickman et al and Eckard et al.[3,4]

Clinicians can capitalize on the findings from this study in clinical practice, citing an additional possible salubrious effect of a committed exercise program. First, this study suggests that adherence to exercise is easier and more likely in a set of patients with metabolic disorder and associated conditions when the exercise program includes a group setting, supervision, and structured encouragement. These are conditions for clinicians to promote when creating exercise prescriptions for patients. Although exercise with moderate weight loss remains the goal and foundation of lifestyle-change counseling for patients with metabolic disorder and MAFLD, patients who have repeatedly struggled with weight loss can be encouraged that exercise alone, performed with sufficient consistency and at least moderate intensity, can improve cardiometabolic risk profile and appears to improve associated fatty liver changes. ■

REFERENCES

A complete list of references can be found online at http://bit.ly/3cMlV9h.

STROKE

ABSTRACT & COMMENTARY

Employing Technology and Exergames to Improve Balance Post-Stroke

By Ellen Feldman, MD

Altru Health System, Grand Forks, ND

SYNOPSIS: This small pilot study reveals potential for exergames (activity-based video games) to be used as a telemedicine rehabilitation intervention in improving balance and function in patients six to eight weeks post-stroke.

SOURCE: Burgos PI, Lara O, Lavado A, et al. Exergames and telerehabilitation on smartphones to improve balance in stroke patients. *Brain Sci* 2020;10:773.

Strokes leave more than one-half of survivors older than 65 years of age with reduced mobility. Rehabilitation is a standard practice to improve functional impairment associated with stroke. Typically, balance training is a later intervention, but recent studies suggest that addressing balance in early post-stroke periods may be safe and effective.[1,2]

Burgos et al noted that some health systems hesitate to use remote balance training interventions out of concern for fall risk in post-stroke patients. However, they noted growing literature in the field supporting the use of technology to check posture remotely and perhaps mitigate this risk. With a goal of developing a remote intervention for balance training in the early phases of the post-stroke period, this team devised a series of movements linked to a game (exergames) delivered via a conventional smartphone and sensors. Exergames generally are defined as technology-driven physical activities, such as video games, requiring body motion and physical movement to participate. While exergames such as Dance Dance Revolution and games for Microsoft's Kinect initially were developed to motivate youth to become more active, there is exciting potential for use of this modality in other populations.[3]

Patients were recruited from two physical therapy rehabilitation centers in Santiago, Chile. Ten volunteers, six to eight weeks post-stroke, enrolled and qualified for the study. Each was randomly assigned to either the control or intervention group. Inclusion criteria for the study included having at least one caregiver at home and showing evidence of impaired balance (as measured on the Berg Balance Scale [BBS]).[4] All study participants continued to receive standard rehabilitation (three sessions of 40 minutes weekly) at the physical therapy site throughout the four weeks of the study. The intervention group received additional remote balance training of nine 30-minute sessions weekly. These sessions used smartphone exergames to motivate and direct movement along with inertial movement sensors (IMU) designed to measure stability.

The study protocol included an initial balance assessment at the physical therapy site followed by a home visit where the participant and caregiver were trained on exercise safety and sensor placement and calibration. Six different exergames were introduced over the four weeks of the study. These games targeted balance improvement in multiple areas, including sit-to-stand, side-to-side, and front-to-back. The games also used music and dance aimed at improving anticipatory postural control. The games were designed to allow modification of difficulty as the participants progressed. With remote monitoring in place, an assigned physical therapist reviewed videos of games, kept in touch daily via phone, and problem-solved any technical difficulties. Several scales and tests

Summary Points

- With a goal of developing a low-cost, effective, and safe telerehabilitation intervention for balance training in the early post-stroke period, this Chilean group recruited 10 patients from a physical therapy center.
- Six post-stroke patients received nine sessions of 30 min/week of the telemedicine intervention in addition to conventional hospital-based rehabilitation, while four patients made up the randomly selected control group (conventional treatment only).
- The intervention included specially designed exergames (activity-based video games) delivered via a conventional smartphone along with sensor monitoring and remote supervision.
- After four weeks, one measure of balance and a measure of functional independence showed significant improvement in the intervention group when compared with the control; a second measure of balance did not show significant difference between the groups.

were used to measure outcomes. The BBS and the Mini Balance Evaluation Systems Test (MBT) were employed to assess initial and final balance.[5] The Barthel Index (BT) ranked the ease of performing activities of daily living (ADLs) and helped to determine functional independence.[6] The System Usability Scale (SUS), a 10-item questionnaire regarding ease of use (higher scores reflect greater satisfaction), was used to evaluate participants' user experience.[7]

RESULTS

Control and intervention group participants all showed improvement on both measures during the four weeks of the study. The difference between the intervention and control groups was significantly stronger as measured by the BBS, but not by the MBT:

- BBS: average improvement 20.20% ± 6.36 for the intervention group vs. 12.5% ± 8.63 ($P = 0.019$);
- MBT: average improvement 29.7% ± 10.75 for the intervention group vs. 16.96% ± 9.39 ($P = 0.245$).

Significant improvement in functional independence (BT score) was seen in the intervention vs. the control group: 17.50 ± 9.87 vs. 3.75 ± 8.53 ($P = 0.025$). Finally, the average SUS score was 87.5 (± 11.61), indicating high to excellent user satisfaction.

■ COMMENTARY

Burgos et al presented a pilot study regarding the efficacy and feasibility of enhancing rehabilitation efforts via remote intervention in the subacute phase of stroke recovery. Taking an innovative approach, this group demonstrates that a relatively low-cost solution using a conventional cell phone and sensors may have promise in delivering remote, individualized physical therapy.

There are many areas of this study that limit generalizability. Certainly, the low number of participants is a barrier to broad generalizations. Additionally, the lack of a sham control makes it difficult to fairly compare results between the intervention and control groups, since both groups continued to receive conventional rehabilitation. Given that the intervention group received significantly more rehabilitation minutes weekly, it may be that factors such as the frequency of intervention alone, scheduled time to focus on movement, or even scheduled interaction with a caregiver around movement was more significant than progression through the exergame series. Expanding the control group to include a physical activity with frequency matched for time to the active intervention can help in defining these relationships. No negative outcomes linked to the use of the exergames were described in this paper.

Future studies that investigate the limits and applicability of exergames (or similar remote physical therapy interventions) in specific populations will help clarify the usefulness and relative risk of these techniques. Finally, it is difficult to understand why one measure of balance (BBS) in the intervention group showed a significant improvement vs. control, while the other measure (MBT) did not show a significant difference. Further studies with larger number of participants are needed to more fully delineate the advantages and disadvantages of this type of remote intervention.

Interestingly, in 2019 another group (Arienti et al) published a meta-analysis covering 51 systematic reviews regarding interventions for balance improvement post-stroke. This team concluded that methodology in the majority of the studies was poor (only 22% of the studies were considered high quality), thus no firm conclusions could be drawn. Stroke is one of the main causes of long-term disability in the developed world; high quality, robust investigations in this field can help develop a path to lessen the effect of this neurological insult.

For now, the take-home message from this study is clear: technology has a role and future in medical practice. It is notable that Burgos et al adapted exergames — a technology developed primarily for youth — to a high-medical-risk older adult population. Thinking outside the box

and broadening medical teams to include persons with expertise in technological fields may open new doors and encourage novel approaches. ■

REFERENCES

A complete list of references can be found online at http://bit.ly/3tFEuD7.

OSTEOPOROSIS

ABSTRACT & COMMENTARY

Dairy, Bone Health, and Menopause

By Ghazaleh Barghgir, MD, and Nancy Selfridge, MD

Dr. Barghgir is Clinical Skills Facilitator, Department of Clinical Foundations at Ross University School of Medicine, Barbados, West Indies.

Dr. Selfridge is Professor, Department of Clinical Foundations at Ross University School of Medicine, Barbados, West Indies.

SYNOPSIS: An analysis of data from the Study of Women's Health Across the Nation cohort did not reveal a significant association between daily dairy intake frequency, femoral and spine bone mineral density loss, and non-traumatic fracture risk among women transitioning to menopause.

SOURCE: Wallace TC, Jun S, Zou P, et al. Dairy intake is not associated with improvements in bone mineral density or risk of fractures across the menopause transition: Data from the Study of Women's Health Across the Nation. *Menopause* 2020;27:879-886.

Osteoporosis is a disease characterized by an increase in osteoclastic bone resorption not balanced by osteoblastic bone formation, resulting in low bone mass and an increased risk of fractures. Osteoporosis often is diagnosed via dual-energy X-ray absorptiometry (DEXA) scans and defined as a bone mineral density (BMD) 2.5 standard deviations or more below the norm for healthy young women (T score of < -2.5 standard deviations). Osteoporosis has been estimated to affect 53.6 million people, representing approximately 54% of the adult United States population aged 50 years and older.[1]

Osteoporosis is more prevalent in postmenopausal women and in the United States (25% to 30% of global prevalence).[2] In 2010-2011, there were 131,443 osteoporosis-attributable fractures, resulting in 64,884 acute care admissions and 983,074 acute hospital days. Acute care costs were $1.5 billion, an 18% increase since 2008.[3] Risk factors associated with osteoporosis include age, female sex, ethnicity, family history of osteoporosis, smoking, vitamin D or calcium deficiency, high caffeine intake, immobilization, late menarche, early menopause, and being underweight.[4] Bone loss is accelerated during menopause; thus, prevention strategies aimed at age-related bone loss are important potential interventions.

One potential modifiable risk factor is dietary dairy product intake, since these foods are rich in nutrients (calcium, magnesium, phosphorus, vitamin D, zinc, and protein) beneficial for bone health maintenance.[5,6] Currently, the 2015-2020 Dietary Guidelines for Americans (DGA) recommend that adults consume three servings/day of fat-free or low-fat dairy, with one serving equivalent to one cup of milk (e.g, 1 cup of low-fat yogurt or half an ounce of hard cheese).[7] No long-term clinical data presently exist assessing the relationship between bone health and dairy intake for women transitioning into menopause.

Thus, the authors aimed to help fill this gap by examining dairy intake and bone health outcomes using publicly available data from the Study of Women's Health Across the Nation (SWAN). SWAN data collection began in 1996 for 3,302 pre- and perimenopausal women 42 to 53 years of age.

Criteria for inclusion were having an intact uterus and at least one ovary and no hormone usage within the three months prior to screening. Five clinical sites in the United States included Oakland, CA; Los Angeles, Boston, Detroit, and Pittsburgh. Enrolled participants were followed annually to gather information on their demographics, clinical data, and anthropomorphic data. There were 2,335 women with complete baseline femoral neck and/or lumbar spine BMD data. Of these, women with osteoporosis, diabetes, unknown menopausal status, and missing information on dairy intake, physical activity, and smoking status were eliminated. Ultimately, 1,955 participants were included in this BMD and fracture analysis. Loss of femoral neck bone density mass over 10 years was calculated using the following formula: ([BMD at visit 10 - BMD at baseline] / BMD at baseline) x 100.

Menopausal status was determined on annual questionnaires and characterized as premenopause (menstrual bleeding within the past three months and no change in bleeding pattern during the last year), early perimenopause (bleeding in the past three months with decreased menstrual regularity during the past year), late

Summary Points

- The authors found no significant differences in bone mineral density changes over a 10-year period in perimenopausal women with different daily dairy product intake.
- The risk ratio and hazard ratio values for non-traumatic fractures showed no significant association with amount of daily dairy intake.
- Participants with higher daily dairy intake were more likely to be premenopausal, heavier, and taller than the mean, nonsmokers, alcohol consumers and somewhat more physically active at baseline compared to peers.

perimenopause (no bleeding for the past three to 11 months), and postmenopause (no bleeding in the past 12 months). Participants missing data on their femoral neck bone density measurement at baseline (n = 7) and for visit 10 (n = 587) and those missing a final menstrual period date (n = 252) were excluded from the analysis, leaving 1,109 women with adequate data for the study cohort analysis.

BMD of the femoral neck and spine was assessed at each annual follow-up visit using DEXA scanning. The occurrence of fractures was entirely self-reported for visits 1-7 but confirmed at visits 7-10 by a review of medical records and radiology reports. The investigators excluded face, toe, and digit fractures not typically seen in osteoporosis and fractures caused by significant trauma (fall from a height > 6 inches, motor vehicle accident, sports activity-related falls, and fractures when struck by a heavy object).

A modified block food frequency questionnaire assessing the average intake of 137 food items was administered at baseline, visit 5, and visit 9 to collect data on eating habits and dairy product consumption. In the analysis, the average number of dairy servings were used, and any missing dietary data in the questionnaires were imputed using the last observation carried forward method. Study subjects then were classified into four groups based upon their cumulative average daily dairy intake: < 0.5 servings, 0.5-1.5 servings, 1.5-2.5 servings, and ≥ 2.5 servings. Characteristics of study participants related to average daily dairy intake category are shown online at https://bit.ly/3f5Z9vM (Table 1 at source). Linear trend estimations were used for participants in each dairy-intake group to assess differences in continuous variables, such as weight, body mass index (BMI), age, and BMD. Chi-square tests were similarly applied to the groups to analyze difference in categorical variables. The statistical significance was set at $P < 0.01$.

The association of dairy intake with 10-year BMD loss rate was analyzed using a general linear model. A Cox proportional hazard model was applied to calculate hazard ratios (HR) for non-traumatic fractures with 95% confidence intervals. Because of the small number of fractures reported in the cohort, hazard ratios between only the < 1.5 dairy serving per day and ≥ 1.5 dairy serving per day groups were used. The study used several different models in the analysis, adjusting for a variety of variables. The fully adjusted models controlled for race, baseline height, age, activity level, smoking status, time-varying weight, menopausal status, alcohol use, calcium supplementation, and caloric intake. The results can be seen online at https://bit.ly/3f5Z9vM (Tables 2 and 4 at source).

The final analysis yielded some noteworthy associations. Women consuming more dairy at baseline also were more likely to be premenopausal, heavier, taller, nonsmokers, alcohol consumers, and somewhat more physically active. Compared to Chinese, African-American, and Japanese participants, non-Hispanic white individuals were more likely to have a higher daily intake of dairy. There were no significant differences between the dairy intake groups at baseline for age, BMI, bone density measurements of femoral neck and lumbar spine, use of calcium supplements, or history of fractures. Despite adjustment for potential confounding variables and sensitivity analysis, no significant differences in changes in bone mineral density were found among the four dairy intake groups. No differences in hazard ratios and relative risks for non-traumatic fractures were observed based on daily dairy intake group in fully adjusted models, available online at https://bit.ly/3f5Z9vM (Table 2 at source).

■ COMMENTARY

This analysis contributes to the current body of knowledge concerning dairy food intake associations with bone density and fracture risk or prevention. A significant strength of this study was that the SWAN cohort data collection was designed to assess changes in BMD and occurrence of fractures and also included data for many potential confounding variables that strengthened the ultimate data analyses. A major weakness of the study is that the cohort did not include any Hispanic women. A significant factor to consider while interpreting results of this study is that dairy intake was low overall among SWAN participants, with 65% of participants consuming < 1.5 servings per day (well below the three servings/day recommended in the DGA) and was notably lower for

ethnic groups other than non-Hispanic whites. In fact, only 7% of the SWAN cohort met the DGA dairy intake recommendations. This low overall dairy consumption in the cohort may have been insufficient to affect BMD loss and fracture outcomes. Further, the study did not explore associations according to different types of dairy food consumption (e.g., yogurt vs. cheese vs. milk), only focusing on a derived composite of total dairy intake. This is noteworthy given the varying nutritional content and inflammatory potential in different dairy products.[8] Potential bias in data collection would be present in all self-reported data, including food and supplement intake and fracture occurrence before visit 5. Although the investigators adjusted all analyses for confounding variables, residual confounding remains a source of potential bias.

Although this study found no association between higher dairy intake and reduced risk of bone mineral loss and fracture occurrence in perimenopausal women, physicians can and should continue to recommend adequate dietary calcium intake, which can be accomplished through consumption of green leafy vegetables (spinach, collard greens, and kale), canned fish with bones (salmon, sardines), tofu, edamame, beans, lentils, and, only if their patients can tolerate them, dairy products (milk, fortified soy milk, etc.). Additional high-quality research is needed, assessing larger cohorts with higher daily dairy intake, accounting for early life nutritional and dairy intake adequacy, differentiating types of dairy products consumed (fermented vs. non-fermented), including data on exercise volume/type, and extending investigation into the post-menopausal period to determine the best evidence-based recommendations for optimizing bone density before menopause, preserving bone density, and reducing fracture risk thereafter. ■

REFERENCES

A complete list of references can be found online at http://bit.ly/2P22d18.

CME QUESTIONS

1. **Which of the following histological endpoints of metabolic associated fatty liver disease were observed in liver biopsies after 12 weeks of aerobic exercise intervention?**
   a. Decreased hepatic steatosis, hepatocyte ballooning, and liver fibrosis
   b. Decreased hepatic steatosis only
   c. Decreased liver fibrosis and hepatocyte ballooning
   d. Decreased hepatic steatosis, hepatocyte ballooning, liver fibrosis, and lobular inflammation
2. **Based on the results of the analysis by Wallace et al, which of the following statements about the effect of daily dairy consumption on non-traumatic fractures and bone mineral density (BMD) in perimenopausal women is correct?**
   a. No significant difference was found between any of the four dairy intake groups (between < 0.5 servings to ≥ 2.5 servings a day) for either non-traumatic fractures or BMD.
   b. Perimenopausal women consuming more than ≥ 2.5 servings a day had a significant lower hazard ratio and risk ratio for non-traumatic fractures and change in BMD.
   c. The risk reduction for non-traumatic fractures was significant only in the ≥ 2.5 servings/day dairy intake group.
   d. Bone mineral density was preserved in the > 2.5 servings/day dairy intake group, although fracture risk was not affected.
3. **Regarding the study about exergames and stroke rehabilitation, which of the following is true?**
   a. This large-scale prospective study showed significant improvement in balance and independent function with the intervention.
   b. This small pilot randomized controlled study showed significant promise in one measure of balance and improvement in independent function, but firm conclusions are limited by small numbers and other factors.
   c. This small pilot prospective trial showed significant promise in improvement in independent function, but not in balance; firm conclusions are limited by study design.
   d. This large-scale randomized controlled study showed clear and significant improvement in multiple measures of balance and independent function with the intervention.

[IN FUTURE ISSUES]

Obesity, Food Insecurity, and Depression in Women

Vitamin D and Mental Health

Rheumatoid Arthritis and Diet