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ORIGINAL ARTICLE

Prunes preserve cortical density and estimated strength of the tibia in a 12-month randomized controlled trial in postmenopausal women: The Prune Study

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Abstract

Summary Non-pharmacological therapies, such as whole-food interventions, are gaining interest as potential approaches to prevent and/or treat low bone mineral density (BMD) in postmenopausal women. Previously, prune consumption preserved two-dimensional BMD at the total hip. Here we demonstrate that prune consumption preserved three-dimensional BMD and estimated strength at the tibia.

Purpose Dietary consumption of prunes has favorable impacts on areal bone mineral density (aBMD); however, more research is necessary to understand the influence on volumetric BMD (vBMD), bone geometry, and estimated bone strength.

Methods This investigation was a single center, parallel arm 12-month randomized controlled trial (RCT; NCT02822378) to evaluate the effects of 50 g and 100 g of prunes vs. a Control group on vBMD, bone geometry, and estimated strength of the radius and tibia via peripheral quantitative computed tomography (pQCT) in postmenopausal women. Women (age 62.1 ± 5.0yrs) were randomized into Control ($n = 78$), 50 g Prune ($n = 79$), or 100 g Prune ($n = 78$) groups. General linear mixed effects (LME) modeling was used to assess changes over time and percent change from baseline was compared between groups.

Results The most notable effects were observed at the 14% diaphyseal tibia in the Pooled (50 g + 100 g) Prune group, in which group × time interactions were observed for cortical vBMD ($p = 0.012$) and estimated bone strength (SSI; $p = 0.024$); all of which decreased in the Control vs. no change in the Pooled Prune group from baseline to 12 months/post.

Conclusion Prune consumption for 12 months preserved cortical bone structure and estimated bone strength at the weight-bearing tibia in postmenopausal women.

Keywords Bone geometry · Bone strength · Dried plum · Menopause · Prune

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Introduction

Osteoporosis, a condition affecting over 10 million adults (~80% female) in the United States, is characterized by age-related decline in bone strength due to reduced bone mineral density (BMD) and impaired bone quality contributing to increased fracture risk [1, 2]. Most studies investigating bone health utilize dual energy X-ray absorptiometry (DXA), the current gold-standard method for clinically evaluating areal BMD (aBMD) and diagnosing osteoporosis. However, DXA is unable to differentiate between cortical and trabecular compartments or measure the structural properties of bone, all of which may influence bone strength independently of aBMD [3]. Alternatively, peripheral quantitative computed tomography (pQCT), can allow for three-dimensional

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assessments of volumetric BMD (vBMD), bone structure, and estimated bone strength within the trabecular and cortical bone compartments, and therefore, may provide additional insight regarding components of bone strength and fracture risk.

Currently, pharmacological therapies to treat low aBMD are limited by low compliance, in which many individuals who should receive pharmacological treatment are not prescribed or taking medications [4, 5]. As such, alternative therapies, including whole-food interventions, are gaining traction for their potential role in preventing and/or treating postmenopausal osteoporosis and osteopenia [6–13]. Prunes (i.e., dried plums), in particular, are one such whole-food nutritional strategy that may have promising effects on bone health [11, 14, 15], potentially due to the presence of bioactive polyphenols that may target anti-inflammatory pathways to mitigate bone loss [11, 16, 17]. In preclinical animal models, prune supplementation improved trabecular bone health following ovariectomy [9, 14, 18–20], and also had pronounced effects on the cortical compartment of long bones [21]. In postmenopausal women, declines in trabecular and cortical density at the tibia and radius can range from -1.1% to -2.6% and -3.5% to -4.3%, respectively, over a 5 year period [22]. To date, however, despite previous randomized controlled trials (RCTs) examining the effect of prunes on aBMD and bone biomarkers [23–25] [26], investigators have not assessed the influence of prune consumption on pQCT-assessed changes in vBMD, geometry, and estimated bone strength in postmenopausal women prospectively.

Recently, we have demonstrated that a 12-month RCT designed to evaluate the effects of two dosages of prunes (50 g/d and 100 g/d) on aBMD in postmenopausal women was sufficient to preserve total hip aBMD and prevent increased fracture risk development as assessed by FRAX score [13, 27]. Herein, as a secondary analysis of the dataset, we examine the effect of a 12-month dietary intervention of prune intake on vBMD, geometry, and estimated bone strength in postmenopausal women. Both 50 g/d and 100 g/d dosages of prunes are hypothesized to effectively prevent age-related declines in trabecular and cortical vBMD, geometry, and estimated bone strength in postmenopausal women.

Methods

Subjects and methods

Study design

The Prune Study (Clinical Trials NCT02822378,) is a single center, parallel arm 12-month RCT to compare dietary supplementation with 50 g (i.e., 4–6 prunes) and 100 g of prunes (i.e., 10–12 prunes) per day vs. a no-prune Control group (Control) in postmenopausal women aged 55 to 75 yrs with a BMD T-score of < 0.0 and > -3.0 at any site and determine effects on aBMD at the total body, lumbar spine, total hip, or femoral neck that took place in the Women's Health and Exercise Laboratory at Pennsylvania State University [27]. The study duration was increased for 23 participants (10 Control, 10 50 g, 3 100 g) during the COVID university closure (Fig. 1). Detailed study procedures are outlined in Fig. 2 and published elsewhere [27]. Body weight

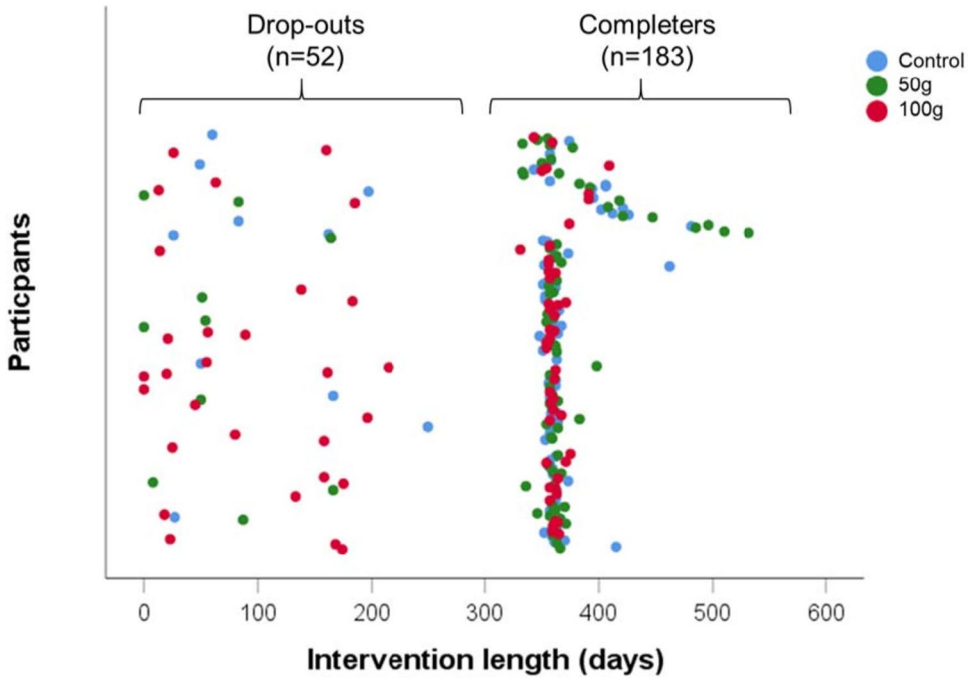

Fig. 1 Duration of intervention for the Prune Study. Due to the high dropout rate in the 100-g prune group, the average length of time in the intervention group for all participants (completers and those who dropped out) was significantly shorter compared with control and 50-g prune groups ($P < 0.001$). Duration of intervention extended for some participants due to COVID-19 disruption of the clinic. In those who completed the full 12-mo intervention, the average length of time in the intervention was comparable ($P = 0.410$)

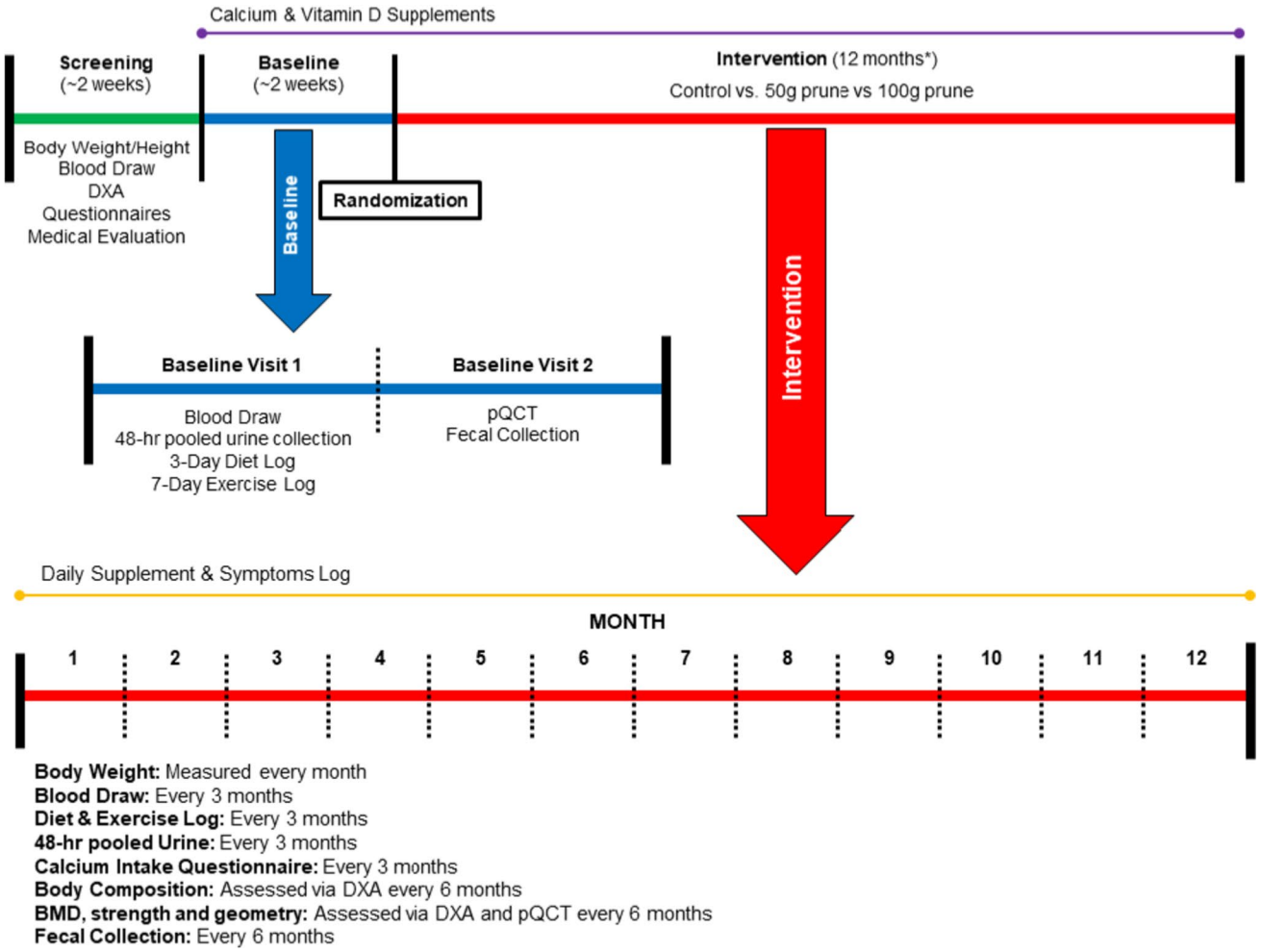

Fig. 2 An overview of the type and timing of measurements collected during this randomized controlled trial. DXA, dual-energy X-ray absorptiometry; pQCT, peripheral quantitative computed tomography. *Due to COVID-19 university closure impacting the timing of 12-month visit, 23 women (10 Control, 10 50 g, 3 100 g) completed a post visit upon university opening and IRB approval beyond the 12-month intended study duration (mean measurement timing of 14 months). Reprinted from De Souza et al. *Contemp Clin Trials Commun* 2022 (CC-BY-NC-ND 4.0) and De Souza et al. Am J Clin Nutr 2022 with permission.

and review of symptoms occurred monthly for 12 months. Body composition, aBMD, vBMD, bone geometry and bone strength measurements were assessed every 6 months.

Recruitment and screening

Recruitment occurred through fliers, e-mail announcements, information sessions, and advertisements initiated in June 2016 and completed February 2021. Preliminary screening was completed via phone. If initial criteria were met, a physical exam and evaluation of medical health history, aBMD, and results from the fasted blood draw were reviewed to determine eligibility. Eligibility criteria are detailed elsewhere [27] and summarized below. The study was approved by the PSU Institutional Review Board, and participants signed an approved informed consent.

Eligibility

Preliminary screening was completed via phone. If eligibility criteria were met, a physical exam and evaluation of medical health history, aBMD, and results from the fasted blood draw were reviewed. Eligibility criteria were as follows [27]: 1) postmenopausal women aged 55–75 yrs; 2) not severely obese [BMI (in kg/m^2) < 40]; 3) healthy (determined by a screening questionnaire, complete metabolic panel); 4) willing to include prunes in their daily diet; 5) not taking any natural dietary supplement containing phenolics or < 1 cup/d of blueberries or apples for at least 2 mo prior to study entry; 6) nonsmoking; 7) ambulatory; and 8) had eligible aBMD as measured by DXA. Eligible aBMD values (T-scores) for DXA measures of the lumbar spine, total hip, and/or femoral neck corresponded

to T-scores between 0.0 and –3.0. Participants were not on any hormonal, osteoporosis, or other medications within a year of study participation that would interfere with bone health during the study. Specifically, participants could not have taken intravenous bisphosphonates at any time, fluoride within 24 mo, denosumab at any time, oral bisphosphonates within 12 mo, selective estrogen receptor modulators within 12 mo, hormone therapy within 3 mo, or glucocorticosteroids within 3 mo of enrollment.

Randomization

Randomized allocation was achieved using a computer-generated list of random numbers with a 1:1:1 group allocation using randomly permuted blocks with fixed sizes of 3. It was not possible to blind participants and study staff to the allocated treatment arm; however, outcome assessors and data analysts were kept blinded to the allocation. A total of 235 participants were randomized into 1 of 3 groups: 1) Control ($n = 78$; no prunes), 2) 50 g Prune ($n = 79$; 4–6 prunes daily), or 3) 100 g Prune ($n = 78$; 10–12 prunes daily). Participants were supplemented as necessary to meet the required intake of 1200 mg of calcium and 800 IU vitamin D_3 daily from diet plus supplements (Nature Made Pharmavite LLC, West Hills, CA). Participants randomly allocated to a prune group consumed California prunes of the "Improved French" variety, which are a type of La Petite D'Agen native to southwest France (Supplemental Table 1). The prunes were provided by the California Prune Board. Participants underwent a "run-in" period to slowly increase prune consumption, as follows [27]: the 50-g prune run-in plan included 2 prunes/d for 3 d (1 prune after breakfast and 1 prune after dinner), followed by 4 prunes/d for 4 d (1 prune after breakfast, 1 prune after lunch, and 2 prunes after dinner), followed by 5 prunes/d for 4 d (2 prunes after breakfast, 1 prune after lunch, and 2 prunes after dinner), followed by the desired dose of 6 prunes/d (2 prunes after breakfast, 2 prunes after lunch, and 2 prunes after dinner) for the remainder of the 12-mo study duration. The 100-g prune run-in plan included 2 prunes/d for 3 d (1 prune after breakfast and 1 prune after dinner), followed by 4 prunes/d for 4 d (1 prune after breakfast, 1 prune after lunch, and 2 prunes after dinner), followed by 6 prunes/d for 4 d (2 prunes after breakfast, 2 prunes after lunch, and 2 prunes after dinner), followed by 9 prunes/d for 4 d (3 prunes after breakfast, 3 prunes after lunch, and 3 prunes after dinner), and, last, an increase to the desired dose of 12 prunes/d for the remainder of the 12-mo study duration (4 prunes after breakfast, 4 prunes after lunch, and 4 prunes after dinner). After the "run-in" period, participants were instructed to eat the assigned daily number of prunes, and record time and number of prunes consumed each day.

Anthropometric assessment

Height was measured in centimeters using a stadiometer. Total body weight was measured to the nearest 0.5 kg on a physician's scale (Seca, Model 770, Hamburg, Germany). BMI was calculated as the body mass divided by height squared (kg/m^2).

Medical and health history assessment

Participants completed questionnaires to detail medical history, exercise, and dietary practices.

Body composition assessment & DXA assessment

Every 6 months, a DXA scan was performed to assess body composition and aBMD. Participants were scanned on a Hologic QDR4500 system (Hologic, Bedford, MA) by an International Society for Clinical Densitometry (ISCD) certified technologist. Laboratory precision is $\leq 1.1\%$ coefficient of variation (CV) for body composition and $< 0.8\%$ CV at all sites (total body, spine, and hip). Participants were classified as osteopenic if T-scores were < -1.0 but > -2.5 at any site, or osteoporotic if T-scores were ≤ -2.5 at any site.

Bone quality and strength assessment

Every 6 months, a pQCT scan (XCT3000, Stratec Germany) was performed to assess vBMD, bone geometry, and bone strength estimates at the non-dominant radius and opposite tibia [Stratec XCT3000 (Orthometrix, White Plains, NY, USA)], unless the participant reported history of fracture or metal implants in those limbs. Radial length was measured to the nearest millimeter from the styloid process to the olecranon process, with measurements obtained at 4% and 66% of radial length from the distal endplate. Tibial length was measured to the nearest millimeter from the tibial plateau to the medial malleolus, with measurements done at 4%, 14%, and 66% of tibial length from the distal endplate. An initial scout view scan was conducted to identify tibial and radial endplates. The 4% (metaphyseal) sites were assessed for total and trabecular vBMD (mg/cm^3), and bone strength index (BSI; mg^2/mm^4), and the 14% and 66% (diaphyseal) sites were assessed for total and cortical vBMD (mg/cm^3), periosteal/endosteal perimeter (mm), and strength estimates (strength strain index (SSI); mm^3) [28, 29]. Each region was assessed as a single slice, with all modes and thresholds utilized for analysis in this study implemented according to expert recommendations (Bone Diagnostic

LLC, Spring Branch, TX). The unit is a 12-detector unit, voxel size 0.4 mm, slice thickness 2.2 mm, and scan speed of 20-50 mm/s. Quality assurance scans using cortical and cone phantoms (Bone Diagnostic LLC, Spring Branch, TX) were conducted prior to scanning each day and scans were analyzed with Stratec software v6.00B.

Compliance assessment

To monitor compliance, prune and/or calcium + vitamin D_3 consumption logs were completed daily and adverse symptoms recorded (bloating, cramping, gas, diarrhea, etc.). Compliance was calculated as the reported prunes consumed divided by the prescribed number of prunes to be consumed each month (%). The self-report compliance measure was supported by urinary assessments of total phenolics and a targeted set of phenolic metabolites associated with phenolic rich food consumption. Three particular metabolites were found to be most robust in response and associated with prune dosage including 4-hydroxybenzoic acid, hippuric acid, and 3-hydroxyhippuric acid [27]. Analysis was completed in 48-h pooled urinary samples every 3 mo on which quantitative measurement was performed to determine total phenolics (Folin–Ciocalteu assay), normalized by creatinine (colorimetric assay kit 500,701; Cayman Chemical) and phenolic metabolites by LC–MS/MS as described previously [27].

Statistics

Analyses were first based on Intent-to-Treat (ITT) principle, in that the analysis set included all study subjects who were randomly allocated. To compare the effects of the intervention on radial and tibial pQCT outcomes, we used a general linear mixed effects (LME) model fit to the longitudinal observations at three time points (baseline, 6 months, 12 months/post) during the study. An unadjusted model was run to include random subject-level intercept, and fixed effects of time, study group, and study group × time interaction. Additionally, an adjusted model was run that included baseline body weight, time since menopause, compliance, and minutes of high magnitude loading exercise as covariates based on previous investigations demonstrating relevance to bone-related outcomes in postmenopausal women [13, 30–32] and changes over the course of the study [13]. For all longitudinal analyses, model based 95% confidence intervals are presented, and for variables with a significant group × time interaction, simple contrasts using sequential Bonferroni correction were performed. As a sensitivity analysis for those who completed the intervention (i.e., completers only), percent changes from baseline were also calculated and independent t-tests or Mann–Whitney U tests, based on the distribution of the data as assessed by the Shapiro–Wilk test, were used to determine group differences. Percent change were then compared with the same, previously described, covariates based on LME. Models were run comparing Control vs. 50 g Prune groups only and control vs. 100 g Prune groups only. Due to a higher-than-expected dropout rate in the 100 g Prune group (41% vs. 10–15%, $p < 0.001$), a parallel analysis was also run comparing the Control vs. Pooled (50 g + 100 g) Prune groups, to maximize statistical power.

Little's missing completely at random (MCAR) test was performed on main pQCT variables to assess if data were missing completely at random. If Little's MCAR test was significant (indicating data were not missing completely at random), t-tests would be used to determine if there were baseline differences between those with and without missing data for the dependent variables in the study. No data were imputed.

Sample size calculations were determined for the primary outcomes of percent change of total hip and lumbar spine aBMD, in which sample sizes of 50 and 55 women per group, respectively, provide 80% power at a significant level of 5%, as described previously [27]. Outcomes from pQCT assessments were secondary outcomes. IBM SPSS Statistics for Windows (Version 28.0. Armonk, NY: IBM Corp.) was used for analyses. Baseline descriptive characteristics were reported as mean ± SD and counts and proportion (%), and longitudinal outcomes reported as estimated marginal means ± SEM (95% Confidence Interval). All tests were two-sided, and a difference with a $p < 0.05$ was considered significant.

Results

Demographics

Descriptive characteristics were balanced among the three randomized groups as shown in Table 1, consistent with previous investigation in this cohort [13]. The participants were 62.1 ± 5.0 years old with an average age of menopause of 50.2 ± 4.8 years. Participants were primarily Caucasian (227/235, 97%) and 51.4% of participants had overweight/obesity. Regarding aBMD classification with T-scores, 14.5% had normal aBMD, 67.7% had osteopenia, and 17.9% had osteoporosis (Table 1). A majority of participants reported no previous hormone therapy (75%) or previous osteoporosis medication use (83%).

After screening 638 women, 322 women were screened in-person, and 250 entered baseline. In total, 235 women were randomized into one of 3 groups: 1) Control Group ($n = 78$), 2) 50 g Prune Group ($n = 79$), or 3) 100 g Prune Group ($n = 78$) (Fig. 3). 160 women completed 12 months (60 in the Control Group, 57 in the 50 g Group, 43 in the

Table 1 Baseline characteristics of randomization groups

	Control ($n=78$)	Pooled (50 g + 100 g) Prune ($n=157$)	50 g Prune ($n=79$)	100 g Prune ($n=78$)
Demographics				
Age (yrs)	62.0 ± 4.8	62.2 ± 5.1	62.0 ± 4.7	62.3 ± 5.4
Age of menopause (yrs)	50.1 ± 4.9	50.3 ± 4.8	50.6 ± 4.8	49.9 ± 4.8
Time since menopause (yrs)	11.9 ± 6.9	11.7 ± 7.0	11.2 ± 6.7	12.2 ± 7.4
Height (cm)	163.6 ± 5.8	162.4 ± 6.0	162.3 ± 5.8	162.5 ± 6.2
Body Mass (kg)	67.2 ± 11.1	68.8 ± 10.9	69.1 ± 11.4	68.4 ± 10.4
BMI (kg/m^2)	25.1 ± 4.0	26.1 ± 4.2	26.3 ± 4.5	25.9 ± 3.8
Fat Mass (kg)	26.9 ± 8.4	28.3 ± 7.2	28.6 ± 7.7	28.0 ± 6.7
Lean Body Mass (kg)	36.9 ± 4.0	37.2 ± 4.4	37.3 ± 4.6	37.1 ± 4.3
Body Fat (%)	40.0 ± 6.7	41.4 ± 5.0	41.5 ± 5.4	41.3 ± 4.6
Bone mineral density				
Total Body BMD (g/cm^2)	1.054 ± 0.077	1.059 ± 0.087	1.051 ± 0.082	1.067 ± 0.091
Total Body T-score	-0.7 ± 1.0	-0.6 ± 1.1	-0.7 ± 1.0	-0.5 ± 1.2
Lumbar L1-4 BMD (g/cm^2)	0.880 ± 0.090	0.910 ± 0.110	0.893 ± 0.105	0.927 ± 0.113
Lumbar L1-4 T-score	-1.5 ± 0.8	-1.2 ± 1.0	-1.4 ± 1.0	-1.1 ± 1.0
Femoral Neck BMD (g/cm^2)	0.675 ± 0.078	0.679 ± 0.083	0.672 ± 0.087	0.686 ± 0.077
Femoral Neck T-score	-1.6 ± 0.7	-1.5 ± 0.7	-1.6 ± 0.8	-1.5 ± 0.7
Total Hip BMD (g/cm^2)	0.803 ± 0.076	0.812 ± 0.090	0.807 ± 0.100	0.818 ± 0.078
Total Hip T-score	-1.1 ± 0.6	-1.1 ± 0.7	-1.1 ± 0.8	-1.0 ± 0.6
vBMD, geometry & strength				
Tibia 4%	Control ($n=78$)	Pooled (50 g + 100 g) Prune ($n=155$)	50 g Prune ($n=79$)	100 g Prune ($n=76$)
Tt.vBMD (mg/cm^3)	264.3 ± 36.7	265.9 ± 34.6	263.6 ± 36.2	268.2 ± 32.9
Tb.vBMD (mg/cm^3)	224.8 ± 33.6	223.7 ± 31.5	220.8 ± 33.3	226.8 ± 29.5
BSI (mg^2/mm^4)	71.0 ± 16.3	71.5 ± 16.7	70.5 ± 17.9	72.5 ± 15.4
Tibia 14%	Control ($n=78$)	Pooled (50 g + 100 g) Prune ($n=155$)	50 g Prune ($n=79$)	100 g Prune ($n=76$)
Tt.vBMD (mg/cm^3)	483.8 ± 83.1	486.3 ± 81.2	488.9 ± 83.3	483.6 ± 79.4
Ct.vBMD (mg/cm^3)	1073.0 ± 43.2	1076.7 ± 44.6	1075.5 ± 43.2	1077.9 ± 46.3
PPm (mm)	72.7 ± 5.4	72.5 ± 5.3	72.0 ± 5.3	73.1 ± 5.3
EPm (mm)	58.8 ± 7.2	58.6 ± 7.1	58.0 ± 7.0	59.2 ± 7.1
SSI (mm^3)	1179.9 ± 175.8	1180.7 ± 177.4	1166.2 ± 182.1	1195.8 ± 172.2
Tibia 66%	Control ($n=76$)	Pooled (50 g + 100 g) Prune ($n=151$)	50 g Prune ($n=78$)	100 g Prune ($n=73$)
Tt.vBMD (mg/cm^3)	652.7 ± 88.8	669.9 ± 89.1	666.2 ± 90.7	673.8 ± 87.8
Ct.vBMD (mg/cm^3)	1095.2 ± 38.2	1099.5 ± 35.9	1097.1 ± 34.9	1102.0 ± 37.1
PPm (mm)	79.2 ± 5.6	78.0 ± 5.1	78.0 ± 4.9	78.0 ± 5.4
EPm (mm)	54.4 ± 8.0	52.5 ± 7.6	52.6 ± 7.3	52.4 ± 8.0
SSI (mm^3)	1974.7 ± 309.4	1928.4 ± 303.2	1918.2 ± 311.9	1939.0 ± 295.6
Radius 4%	Control ($n=78$)	Pooled (50 g + 100 g) Prune ($n=152$)	50 g Prune ($n=78$)	100 g Prune ($n=74$)
Tt.vBMD (mg/cm^3)	291.1 ± 48.0	300.4 ± 53.0	296.6 ± 55.7	304.5 ± 50.1
Tb.vBMD (mg/cm^3)	185.1 ± 32.4	183.2 ± 33.0	179.2 ± 31.8	187.3 ± 33.8
BSI (mg^2/mm^4)	26.0 ± 6.0	27.2 ± 7.5	26.4 ± 7.7	28.1 ± 7.3
Radius 66%	Control ($n=74$)	Pooled (50 g + 100 g) Prune ($n=140$)	50 g Prune ($n=71$)	100 g Prune ($n=69$)
Tt.vBMD (mg/cm^3)	673.5 ± 107.4	696.4 ± 128.8	691.1 ± 123.4	701.8 ± 134.9
Ct.vBMD (mg/cm^3)	1101.3 ± 44.0	1104.6 ± 47.1	1104.8 ± 43.4	1104.4 ± 50.8
PPm (mm)	38.1 ± 2.8	37.6 ± 3.4	37.5 ± 3.6	37.7 ± 3.2
EPm (mm)	25.4 ± 3.8	24.6 ± 4.9	24.7 ± 4.9	24.5 ± 5.0
SSI (mm^3)	245.4 ± 48.3	241.9 ± 53.7	238.7 ± 54.3	245.2 ± 53.4

Data are mean ± SD. *Tt.vBMD* Total volumetric bone mineral density; *Tb.vBMD* Trabecular volumetric bone mineral density; *BSI* Bone strength index; *Ct.vBMD* Cortical volumetric bone mineral density; *Ct.Th* Cortical thickness; *PPm* Periosteal perimeter; *EPm* Endosteal perimeter; *SSI* Strength strain index

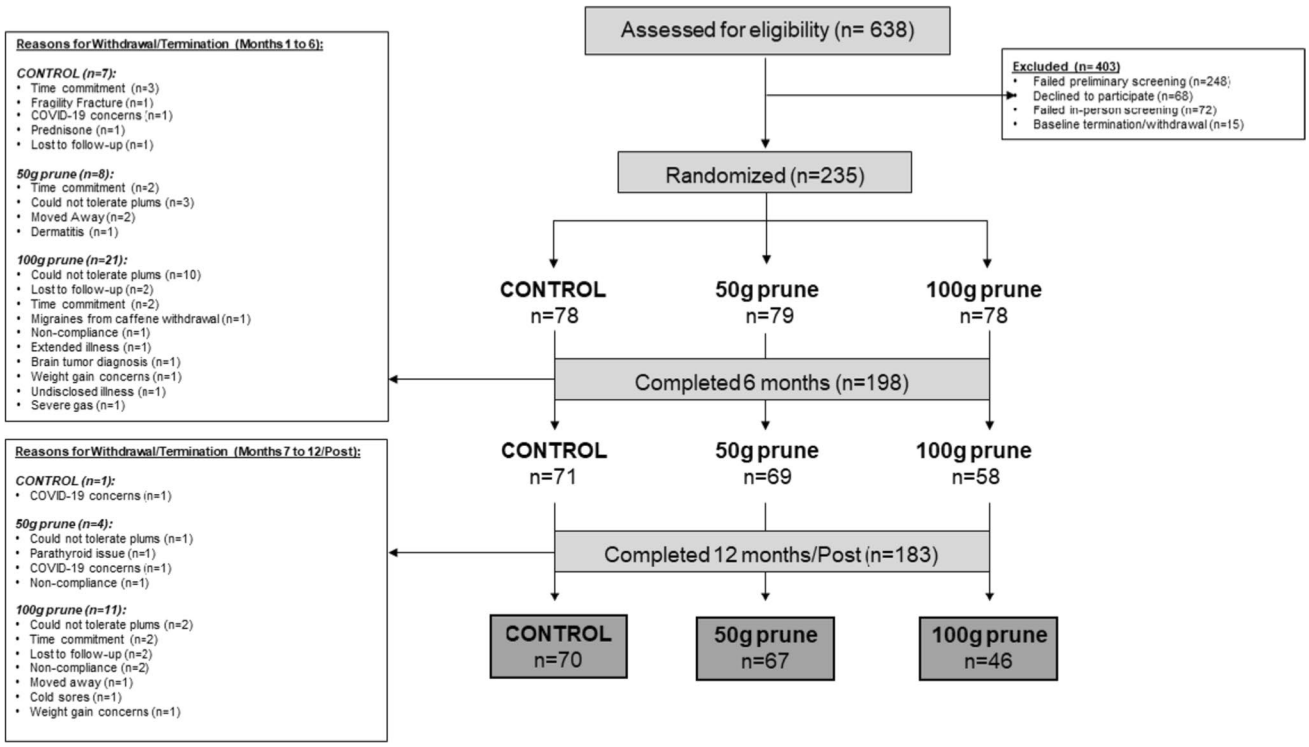

Fig. 3 Consolidated Standards of Reporting Trials (CONSORT) diagram depicting number of participants enrolled at each study phase and the reasons for dropout. Reprinted from De Souza et al. *Contemp Clin Trials Commun* 2022 (CC-BY-NC-ND 4.0) and De Souza et al. *Am J Clin Nutr* 2022 with permission

100 g Group) and 23 women (10 in the Control Group, 10 in the 50 g Group, 3 in the 100 g Group) completed a post-visit upon university re-opening (after COVID-19 university closure) and IRB approval beyond the 12-month intended study duration (mean measurement timing of 14 months). A total of 183 women completed 12-month/post study visits (70 in the Control Group, 67 in the 50 g Prune Group, and 46 in the 100 g Prune Group), with an overall dropout/early termination rate of 22% [13]. Specific details regarding dropout/early termination and compliance have been previously reported [13].

For the main outcomes of this manuscript, radial pQCT scans were completed in 229 participants at baseline (Control Group = 77, 50 g Prune Group = 78, 100 g Prune Group = 74), 183 participants at 6-months (Control Group = 67, 50 g Prune Group = 65, 100 g Prune Group = 51), and 176 participants at 12-months/post (Control Group = 67, 50 g Prune Group = 66, 100 g Prune Group = 43). Tibia scans were completed in 233 participants baseline (Control Group = 78, 50 g Prune Group = 79, 100 g Prune Group = 76), 186 participants at 6-months (Control Group = 67, 50 g Prune Group = 66, 100 g Prune Group = 53), and 179 participants at 12-months/post (Control Group = 67, 50 g Prune Group = 67, 100 g Prune Group = 45). Little's MCAR test indicated that data were missing completely at random.

Body composition and aBMD

Body composition and aBMD outcomes have been previously reported [13]. Briefly, body fat percentage increased during the intervention in both the 50 g and Control groups (main effect of time, $p = 0.042$), and Pooled Prune and Control groups (main effect of time, $p = 0.011$), whereas the 100 g Prune group increased body fat percentage at 6 Months compared to Baseline (group × time interaction, $p = 0.050$). For total hip aBMD, the Control group experienced a decrease in total hip aBMD at both 6 months and 12-month/post compared to baseline (group × time interaction, $p = 0.030$) and the Pooled Prune group preserved aBMD at both the 6 months and 12-month/post intervention timepoints (group × time interaction, $p = 0.047$).

Intent to treat analyses of pQCT outcomes

The following results are for the ITT analyses of pQCT outcomes at the tibia and radius, which incorporates data

from all study timepoints (Baseline, 6 months, 12 months/Post) in all participants that were randomly allocated.

Pooled (50 g + 100G) Prune group vs Control group

To maximize statistical power, results are first presented for the Control vs. Pooled (50 g + 100 g) Prune groups and data are presented in Supplemental Table 2 and Table 2, respectively.

No significant interaction or main effects were observed at the 4% tibial metaphysis for either the unadjusted model or after adjusting for covariates. At the 14% tibial diaphysis, in the unadjusted model, a group × time interaction was observed for SSI ($p = 0.041$), in which SSI decreased in the Control group compared to no change in the Pooled Prune group. When adjusting for covariates, the group × time interaction remained significant for SSI ($p = 0.024$) and an interaction effect was also evident for cortical vBMD ($p = 0.012$), both of which decreased in the Control group compared to no change in the Pooled Prune group and indicates an effect of prune consumption for preserving cortical vBMD and estimated strength. A main effect of time was also observed at the 14% tibia, only in the adjusted model, wherein total vBMD ($p = 0.029$) decreased in the total sample. At the 66% diaphyseal tibia, main effects of time were also observed in both models, such that total vBMD ($p < 0.001$) decreased and endosteal perimeter increased ($p < 0.001$). Additionally, a main effect of group was evident for endosteal perimeter in the basic model ($p = 0.050$), but not after adjusting for covariates ($p = 0.053$).

At the radius, there were no significant interaction effects in either model. Main effects of time were observed at the 66% diaphyseal radial site in the basic and adjusted models such that total vBMD ($p < 0.001$, $p < 0.001$) and cortical vBMD ($p < 0.001$, $p < 0.001$) decreased, and endosteal perimeter increased ($p = 0.001$, $p = 0.004$).

50 g Prune group vs Control group

Results for the Control vs. low dose (50 g) Prune group are presented in Supplemental Table 3 and 4. No significant interaction or main effects were observed at the 4% metaphyseal tibia in either model. At the 14% diaphyseal tibia, main effects of time were observed in the basic and adjusted models, such that cortical vBMD ($p < 0.001$, $p < 0.001$) and SSI ($p < 0.001$. $p = 0.003$) decreased. At the 66% diaphyseal tibia, a main effect of time indicates decreased total vBMD ($p < 0.001$, $p < 0.001$) and an increase in endosteal perimeter ($p < 0.001$, $p < 0.001$) in both models.

At the radius, no significant effects were observed at the 4% metaphyseal site. A significant group × time interaction was observed for SSI at the 66% ($p = 0.030$) diaphyseal site, only after adjusting for covariates, but with no post-hoc significance. Main effects of time were also observed at the 66% diaphyseal site indicative of a general deterioration in vBMD and geometry throughout the intervention. Specifically, declines in total vBMD ($p < 0.001$, $p < 0.001$) and cortical vBMD ($p < 0.001$, $p < 0.001$), and an increase in endosteal perimeter ($p = 0.009$, $p = 0.013$) were observed at the 66% diaphyseal site in the unadjusted and adjusted models, respectively.

100 g Prune group vs Control group

Results for the Control vs. high dose (100 g) Prune group are presented in Supplemental Table 5 and 6. No significant interaction effects were observed at the 4% tibial metaphysis. A main effect of time was observed at the 4% tibial metaphysis, such that BSI decreased in the basic model ($p = 0.013$) and after adjusting for covariates ($p = 0.028$). At the 14% tibial diaphysis, no significant interaction effects were observed in the basic model, but a group × time interaction was observed for cortical vBMD ($p = 0.009$) after adjusting for covariates, which decreased in the Control group compared to no change in the 100 g Prune group, thereby suggesting a potential protective effect of high dose prune consumption on vBMD. However, a main effect of time was observed at the 14% diaphysis in the basic and adjusted models such that SSI decreased ($p = 0.002$, $p = 0.001$). At the 66% tibial diaphysis, main effects of time were observed for the basic and adjusted models such that total vBMD ($p = 0.002$, $p = 0.003$) decreased and endosteal perimeter ($p = 0.009$, $p = 0.019$) increased. Together, such decrements over time suggest a general worsening of cortical bone parameters during the intervention.

At the 4% metaphyseal radius, no significant interaction effects were evident. In the basic model, BSI decreased over time ($p = 0.028$), but this was no longer significant after adjusting for covariates ($p = 0.149$).There were also main effects of time such that, in both the basic and adjusted models at the 66% diaphyseal radius, total vBMD ($p < 0.001$, $p < 0.001$) and cortical vBMD ($p = 0.012$, $p = 0.015$) decreased, and endosteal perimeter increased ($p = 0.001$, $p = 0.003$).

Completers only

As a sensitivity analysis, only those who completed the 12 month intervention were included. Due to attrition, fewer subjects are analyzed, but all had a similar exposure time to allow adequate time for changes to be detected. Percent change data for all groups are presented in Table 3 and Supplemental Table 7 and 8.

Pooled (50 g + 100G) Prune group vs Control group

In the unadjusted analyses (Supplemental Table 7), the Control group had greater decreases in SSI (-1.4 vs -0.5; $p = 0.025$;

Table 2 Intent-to-treat results for control vs. pooled (50 g + 100 g) Prune Group, adjusted for covariates

	Control			Pooled 50 g + 100 g Prune			*P*-values		
Tibia 4%	BL	6 mo	Post	BL	6 mo	Post	Group	Time	Group *time
Tt.vBMD (mg/cm^3)	265.4 ± 4.0 (257.5, 273.3)	265.4 ± 4.2 (257.2, 273.6)	263.6 ± 4.1 (255.5, 271.7)	265.0 ± 3.0 (259.2, 270.9)	263.5 ± 3.2 (257.3, 269.7)	267.0 ± 3.2 (260.8, 273.2)	0.933	0.912	0.455
Tb.vBMD (mg/cm^3)	225.2 ± 3.7 (217.9, 232.6)	224.9 ± 3.7 (217.5, 232.2)	224.1 ± 3.7 (216.7, 231.4)	222.8 ± 2.8 (217.3, 228.2)	222.8 ± 2.8 (217.3, 228.3)	223.5 ± 2.8 (218.0, 229.0)	0.717	0.936	0.223
BSI (mg^2/mm^4)	71.6 ± 1.8 (68.1, 75.2)	71.3 ± 1.8 (67.7, 74.9)	70.5 ± 1.8 (66.9, 74.0)	70.9 ± 1.3 (68.2, 73.5)	70.7 ± 1.4 (68.0, 73.3)	71.1 ± 1.4 (68.4, 73.7)	0.906	0.403	0.117
Tibia 14%									
Tt.vBMD (mg/cm^3)	486.2 ± 9.9 (466.8, 505.5)	484.1 ± 9.9 (464.7, 503.5)	481.8 ± 9.9[a] (462.4, 501.2)	484.9 ± 7.4 (470.5, 499.3)	483.8 ± 7.4 (469.3, 498.3)	483.2 ± 7.4[a] (468.7, 497.7)	0.997	**0.029**	0.491
Ct.vBMD (mg/cm^3)	1074.0 ± 5.0 (1064.1, 1083.9)	1074.2 ± 5.1 (1064.3, 1084.1)	1068.6 ± 5.0[b] (1058.7, 1078.5)	1076.5 ± 3.7 (1069.1, 1083.9)	1075.8 ± 3.8 (1068.4, 1083.2)	1075.2 ± 3.8 (1067.8, 1082.6)	0.569	**< 0.001**	**0.012**
PPm (mm)	72.7 ± 0.6 (71.5, 73.8)	72.7 ± 0.6 (71.5, 73.9)	72.7 ± 0.6 (71.5, 73.8)	72.4 ± 0.4 (71.6, 73.3)	72.3 ± 0.4 (71.4, 73.2)	72.5 ± 0.4 (71.6, 73.3)	0.704	0.850	0.584
EPm (mm)	58.7 ± 0.8 (57.1, 60.3)	58.8 ± 0.8 (57.2, 60.4)	58.8 ± 0.8 (57.2, 60.4)	58.5 ± 0.6 (57.3, 59.7)	58.5 ± 0.6 (57.3, 59.7)	58.6 ± 0.6 (57.4, 59.8)	0.821	0.813	0.862
SSI (mm^3)	1186.3 ± 18.1 (1150.7, 1221.9)	1181.2 ± 18.2 (1145.4, 1216.9)	1167.6 ± 18.2[b] (1131.9, 1203.3)	1171.4 ± 13.5 (1144.9, 1198.0)	1166.7 ± 13.6 (1140.0, 1193.5)	1166.4 ± 13.6 (1139.7, 1193.1)	0.651	**< 0.001**	**0.024**
Tibia 66%									
Tt.vBMD (mg/cm^3)	652.6 ± 10.8 (631.5, 673.7)	652.0 ± 10.8 (630.8, 673.2)	644.6 ± 10.8[a] (623.4, 665.7)	672.4 ± 7.9 (656.9, 688.0)	672.0 ± 8.0 (656.4, 687.6)	668.2 ± 7.9[a] (652.6, 683.8)	0.113	**< 0.001**	0.345
Ct.vBMD (mg/cm^3)	1095.0 ± 4.1 (1086.9, 1103.2)	1095.2 ± 4.2 (1087.0, 1103.4)	1093.6 ± 4.2 (1085.4, 1101.7)	1101.1 ± 3.0 (1095.1, 1107.1)	1101.5 ± 3.1 (1095.5, 1107.5)	1100.5 ± 3.1 (1094.4, 1106.5)	0.208	0.292	0.878
PPm (mm)	79.3 ± 0.6 (78.1, 80.5)	79.2 ± 0.6 (78.0, 80.4)	79.4 ± 0.6 (78.2, 80.6)	77.8 ± 0.4 (77.0, 78.7)	77.8 ± 0.5 (76.9, 78.7)	77.9 ± 0.4 (77.0, 78.8)	0.055	0.111	0.764
EPm (mm)	54.5 ± 0.9 (52.6, 56.3)	54.5 ± 0.9 (52.6, 56.3)	55.0 ± 0.9[a] (53.2, 56.9)	52.3 ± 0.7 (50.9, 53.6)	52.3 ± 0.7 (51.0, 53.7)	52.6 ± 0.7[a] (51.3, 54.0)	0.053	**< 0.001**	0.475
SSI (mm^3)	1981.1 ± 33.0 (1916.3, 2045.8)	1972.8 ± 33.0 (1907.9, 2037.7)	1974.3 ± 33.0 (1909.5, 2039.2)	1925.1 ± 24.6 (1876.8, 1973.4)	1920.8 ± 24.7 (1872.4, 1969.3)	1927.3 ± 24.7 (1878.8, 1975.7)	0.210	0.213	0.459
Radius 4%									
Tt.vBMD (mg/cm^3)	291.4 ± 6.0 (279.6, 303.2)	293.9 ± 6.1 (281.9, 305.9)	293.2 ± 6.1 (281.3, 305.1)	298.4 ± 4.5 (289.6, 307.2)	294.7 ± 4.6 (285.6, 303.7)	297.2 ± 4.6 (288.1, 306.2)	0.591	0.894	0.269
Tb.vBMD (mg/cm^3)	186.6 ± 3.8 (179.1, 194.0)	184.0 ± 3.9 (176.4, 191.5)	183.7 ± 3.8 (176.2, 191.2)	183.3 ± 2.8 (177.8, 188.9)	185.3 ± 2.9 (179.6, 191.0)	184.3 ± 2.9 (178.6, 190.0)	0.925	0.732	0.127
BSI (mg^2/mm^4)	26.1 ± 0.8 (24.6, 27.7)	26.1 ± 0.8 (24.5, 27.7)	26.0 ± 0.8 (24.4, 27.5)	26.9 ± 0.6 (25.8, 28.1)	26.6 ± 0.6 (25.4, 27.8)	26.9 ± 0.6 (25.7, 28.1)	0.448	0.773	0.618
Radius 66%									
Tt.vBMD (mg/cm^3)	679.4 ± 14.2 (651.6, 707.2)	667.5 ± 14.3[a] (639.4, 695.7)	658.9 ± 14.3[a] (630.9, 687.0)	695.7 ± 10.7 (674.6, 716.9)	691.3 ± 10.9[a] (669.9, 712.6)	683.7 ± 10.9[a] (662.3, 705.1)	0.220	**< 0.001**	0.315
Ct.vBMD (mg/cm^3)	1102.3 ± 5.6 (1091.4, 1113.3)	1096.8 ± 5.8[a] (1085.5, 1108.1)	1091.8 ± 5.7[a] (1080.6, 1103. 1)	1106.4 ± 4.2 (1098.1, 1114.7)	1100.8 ± 4.4[a] (1092.2, 1109.3)	1100.2 ± 4.4[a] (1091.6, 1108.7)	0.421	**< 0.001**	0.485
PPm (mm)	37.9 ± 0.4 (37.1, 38.6)	38.0 ± 0.4 (37.3, 38.8)	38.0 ± 0.4 (37.2, 38.8)	37.4 ± 0.3 (36.8, 38.0)	37.2 ± 0.3 (36.7, 37.8)	37.5 ± 0.3 (37.0, 38.1)	0.210	0.499	0.454
EPm (mm)	25.2 ± 0.5 (24.1, 26.2)	25.6 ± 0.5 (24.6, 26.7)	25.8 ± 0.5[a] (24.7, 26.9)	24.5 ± 0.4 (23.7, 25.3)	24.5 ± 0.4 (23.7, 25.4)	25.0 ± 0.4[a] (24.2, 25.8)	0.202	**0.004**	0.399
SSI (mm^3)	243.9 ± 5.8 (232.6, 255.3)	246.0 ± 5.9 (234.5, 257.6)	241.8 ± 5.8 (230.3, 253.3)	239.4 ± 4.4 (230.7, 248.1)	237.5 ± 4.5 (228.7, 246.4)	239.0 ± 4.5 (230.2, 247.8)	0.462	0.588	0.166

Values are reported as estimated marginal mean ± SEM (Model-based 95% Confidence Interval). *Tt.vBMD* Total volumetric bone mineral density; *Tb.vBMD* Trabecular volumetric bone mineral density; *BSI* Bone strength index; *Ct.vBMD* Cortical volumetric bone mineral density; *PPm* Periosteal perimeter; *EPm* Endosteal perimeter; *SSI* Strength strain index

[a]Indicates significant main effect of time vs. baseline

[b]Indicates significant change from baseline within group

Table 3 Percent change from baseline for pQCT measures in those who completed the full 12-month intervention for Control vs. Pooled Group, adjusted for covariates

	Control group	Pooled prune group	*P*-value Control vs. pooled
Tibia 4%			
Tt.vBMD (mg/cm^3)	0.5 ± 1.5 (-2.4, 3.4)	0.8 ± 1.1 (-1.5, 3.1)	0.862
Tb.vBMD (mg/cm^3)	-0.7 ± 0.3 (-1.3, -0.2)	-0.05 ± 0.2 (-0.5, 0.4)	0.053
BSI (mg^2/mm^4)	-2.0 ± 0.5 (-3.0, -1.0)	-0.7 ± 0.4 (-1.4, 0.1)	**0.037**
Tibia 14%			
Tt.vBMD (mg/cm^3)	-0.7 ± 0.4 (-1.4, 0.1)	-0.2 ± 0.3 (-0.8, 0.4)	0.342
Ct.vBMD (mg/cm^3)	-0.3 ± 0.1 (-0.6, -0.1)	-0.1 ± 0.1 (-0.3, 0.1)	0.224
PPm (mm)	-0.2 ± 0.2 (-0.5, 0.1)	0.1 ± 0.1 (-0.3, 0.2)	0.509
EPm (mm)	-0.1 ± 0.3 (-0.7, 0.4)	-0.1 ± 0.2 (-0.5, 0.4)	0.897
SSI (mm^3)	-1.4 ± 0.4 (-2.2, -0.7)	-0.3 ± 0.3 (-0.9, 0.2)	**0.018**
Tibia 66%			
Tt.vBMD (mg/cm^3)	-1.1 ± 0.4 (-1.9, -0.3)	-0.7 ± 0.3 (-1.3, -0.0)	0.372
Ct.vBMD (mg/cm^3)	-0.1 ± 0.1 (-0.3, 0.2)	0.0 ± 0.1 (-0.2, 0.2)	0.717
PPm (mm)	0.1 ± 0.2 (-0.2, 0.4)	0.1 ± 0.1 (-0.1, 0.4)	0.991
EPm (mm)	1.1 ± 0.4 (0.4, 1.9)	0.8 ± 0.3 (0.2, 1.4)	0.508
SSI (mm^3)	-0.3 ± 0.3 (-0.9, 0.3)	0.0 ± 0.2 (-0.5, 0.5)	0.407
Radius 4%			
Tt.vBMD (mg/cm^3)	0.7 ± 1.1 (-1.4, 2.7)	-0.5 ± 0.8 (-2.2, 1.1)	0.377
Tb.vBMD (mg/cm^3)	-1.6 ± 1.4 (-4.4, 1.2)	1.2 ± 1.1 (-1.0, 3.5)	0.129
BSI (mg^2/mm^4)	-0.8 ± 1.7 (-4.1, 2.6)	0.6 ± 1.3 (-2.1, 3.2)	0.543
Radius 66%			
Tt.vBMD (mg/cm^3)	-2.8 ± 0.7 (-4.2, -1.3)	-1.8 ± 0.6 (-3.0, -0.7)	0.323
Ct.vBMD (mg/cm^3)	-0.8 ± 0.3 (-1.4, -0.3)	-0.6 ± 0.2 (-1.0, -0.1)	0.509
PPm (mm)	0.9 ± 0.6 (-0.3, 2.1)	0.3 ± 0.5 (-0.6, 1.3)	0.457
EPm (mm)	2.8 ± 1.0 (0.8, 4.7)	1.9 ± 0.8 (0.4, 3.5)	0.519
SSI (mm^3)	-0.2 ± 0.9 (-1.9, 1.4)	-0.1 ± 0.7 (-1.6, 1.3)	0.932

Data are mean ± SEM (Model-based 95% Confidence Interval). *Tt.vBMD* Total volumetric bone mineral density; *Tb.vBMD* Trabecular volumetric bone mineral density; *BSI* Bone strength index; *Ct.vBMD* Cortical volumetric bone mineral density; *PPm* Periosteal perimeter; *EPm* endosteal perimeter; *SSI* Strength strain index

effect size: -0.31 (-0.61, -0.004)) than the Pooled group at the 14% diaphysis. At the 66% tibial diaphysis, total vBMD (-1.1% vs -0.5%; $p=0.043$; effect size: -0.18 (-0.49, 0.12)) also declined more in the Control than the Pooled Prune group. After adjusting for covariates (Table 3), the effect on SSI at the 14% diaphysis remained significant ($p=0.018$), although total vBMD at the 66% diaphysis was no longer significant ($p=0.372$). Additionally, after adjusting for covariates, BSI at the 4% tibial metaphysis decreased to a greater extent in the Control vs. Pooled Prune group (-2.0% vs -0.7%; $p=0.037$). Potentially beneficial effects of prune consumption on mitigating declines in estimated strength are thus indicated. There were no significant differences in percent changes at any radial sites in Control vs Pooled Prune group completers.

50 g Prune group vs Control group

No differences in percent change between groups were present at the 4% tibial metaphysis (Supplemental Table 7 and 8). Age-related declines in SSI were attenuated in the 50 g Prune group compared to the Control group (-0.4% vs -1.4%; $p=0.047$; effect size: -0.35 (-0.70, -0.01)). Results remained significant after adjusting for covariates ($p=0.022$). There were no significant differences in percent change of radial outcomes at any site ($p>0.05$).

100 g Prune group vs Control group

In the participants who completed the full 12-month intervention, no significant effects were observed at the tibia or radius in the basic model (Supplemental Table 7); however, after adjusting for covariates (Supplemental Table 8), trabecular vBMD at the 4% tibial metaphysis decreased more in the Control group compared to the 100 g Prune group ($p=0.050$).

Discussion

This is the first RCT to test the effects of two doses (50 g/d and 100 g/d) of prune consumption on pQCT indices of vBMD, geometry, and estimated bone strength for 12 months in postmenopausal women. Herein, we demonstrate that the pooled 50 + 100 g Prune group successfully preserved cortical vBMD in the total ITT sample and estimated bone strength in both the total ITT and completers only samples. The 50 g dose of daily prune consumption yielded no significant findings in the total ITT sample, but the percent decline in estimated strength was attenuated at the weight-bearing tibia (14% site) in women who completed the 12-month intervention compared to the Control group. The 100 g dose also demonstrated promising results at the 14% tibia site by preserving cortical vBMD in the total ITT sample, although estimated bone strength was not preserved.

Maintenance of cortical vBMD and estimated strength is important because peripheral measures of bone structure and strength have been associated with fracture risk independently of aBMD in older adults [33].

Previously, prune consumption has been demonstrated to preserve [13, 26], or even improve [23, 24], aBMD in postmenopausal women, but effects on bone structure and estimated strength were either not measured or not reported. Utilization of pQCT analysis in the current investigation may allow for greater insight on the localized effects of prune consumption on trabecular and cortical vBMD and estimates of bone strength, all of which may impact fracture risk. To our knowledge, the only study to utilize such methodology to examine potential effects of prune consumption on bone structure and estimated strength in humans was conducted in older men [34]. During the 12 month intervention in men, no changes in aBMD were observed, and endosteal perimeter actually increased at the 66% tibia site in the prune group (100 g/d) compared to no change in the Control group [34]. Endosteal resorption, and the ensuing increase in endosteal perimeter, is a typical aging-related consequence that is observed in both men and women [35]. Indeed, in our current sample of postmenopausal women, endosteal perimeter also increased at the 66% tibia site. Notably, a majority of the men in the aforementioned investigation [34] had T-scores within the healthy range, which may have reduced the likelihood of observing a significant protective effect of prunes compared to a sample of postmenopausal women.

The most notable findings in the current investigation indicate a potential protective effect of prunes on vBMD and strength at the 14% tibia site, a site that is predominantly cortical bone and that was not assessed by Hooshmand et al. [34]. In the ITT analysis, compared to no change in the 100 g Prune group, cortical vBMD declined in the Control group; although, estimated strength was similarly reduced in both groups. Alternatively, no declines in cortical vBMD or strength occurred in the Pooled Prune group compared to significant reductions in the Control group. In completers of the 12-month intervention, percent declines in estimated strength were reduced in the 50 g and Pooled Prune groups compared to the Control group, but no difference was present for the 100 g Prune group. Due to the higher than expected dropout rate in the 100 g dose group (41% vs. 10–15%, $p < 0.001$) [13], the 50 g and Pooled Prune groups may have been more adequately powered to identify differences between groups, if present.

With respect to predominantly trabecular sites (4%), in the current investigation, the only significant effect was observed for percent change in trabecular vBMD of the tibia between the 100 g dose group compared to the Control group. Previously, declines in trabecular vBMD of the tibial metaphysis have been reported as ~ 0.2%/year in postmenopausal women [22], whereas we saw a greater decline of approximately -0.7% during the 12-month study in the Control group compared to no change in the 100 g Prune group. There were no significant effects observed for the non-weight bearing radius (4% site). In older men, no significant effects of prune consumption were observed at the metaphysis of the tibia or radius [34]. In animal models of postmenopausal osteoporosis, prune consumption improved trabecular measures, including increased bone volume/total volume [9, 14, 20], trabecular number [9, 14, 20], and decreased trabecular spacing [21]. Differences among studies may be due to the resolution of the methods used, as standard pQCT can quantify vBMD of the trabecular compartment but not specific trabecular microarchitecture, as well as differences between human and animal models, and/or differences in the dosage of plum consumption.

A 50 g daily dose of prune consumption has now been demonstrated to preserve total hip aBMD and moderate intakes of prunes ≥ 50 g daily potentially mitigate losses to estimated bone strength as assessed by pQCT in postmenopausal women with T-scores between 0.0 and − 3.0. Although some beneficial effects were found for the 100 g group, the dosage was associated with poor compliance and a significantly higher dropout rate than the other groups [13], thereby demonstrating limited feasibility. Specifically, among the 100 g Prune group, the primary reason for study withdrawal was poor tolerance; however, the 50 g per day dose was associated with good compliance and retention. The pooled analysis of the 50 + 100 g group was associated with preservation of estimated bone strength as assessed by both pQCT and FRAX, suggesting that doses of prune consumption ≥ 50 g daily may be beneficial for reducing fracture risk in postmenopausal women.

Strengths of this investigation include a large cohort of postmenopausal women to explore the effects of two dosages of prunes and the incorporation of novel measurements to assess three-dimensional vBMD, bone structure, and estimated strength. Limitations include a largely Caucasian sample, which may limit the generalizability of results, and the monitoring time of only 12 months, which may require longer time intervals for detecting significant changes [36]. Additionally, the common region of longitudinal scans was not assessed, which may influence precision estimates of the changes observed.

In conclusion, long term consumption of prunes protected against aging-related declines in bone geometry and estimated bone strength at the weight-bearing tibial diaphysis in postmenopausal women. A daily 100 g dose of prunes preserved cortical density at the tibia, but did not translate to effects on bone strength. Additionally, this high dose of prunes (100 g/d) had a low retention rate, which reduces its feasibility as a treatment strategy. Alternatively, greater declines in estimated strength of the diaphyseal tibia were observed in the Control group compared to the 50 g and

Pooled (50 g + 100 g) prune groups suggesting that a moderate dosage of daily prune consumption (6/day) may represent a valuable non-pharmacological treatment strategy that can be used to preserve bone strength and possibly reduce the risk of fracture in postmenopausal women.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00198-024-07031-6.

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Data availability Data described in the manuscript, code book, and analytic code will be made available upon reasonable request pending application.

Declarations

Conflict of interest None.

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