
Interactions of Dietary Patterns, Systemic Inflammation, and Bone Health

2

Adrian D. Wood and Helen M. Macdonald

Abstract

Examination of combinations of foods, as described by dietary patterns in relation to health indices, may be an important approach to further our understanding of chronic disease prevention. Bone loss is a common factor in many chronic inflammatory conditions, although it is unclear whether low-grade systemic inflammation may have similar long-term effects. In this chapter we summarize current evidence relating dietary patterns and chronic low-grade systemic inflammation to bone health. Consideration is then given to potential mechanisms whereby dietary eating patterns may affect inflammatory status. Dietary patterns rich in fruits and vegetables consistently appear to have a protective effect on bone mineral density, likely due to their abundance of micronutrients, minerals, and bioactive compounds. Current evidence relating low-grade systemic inflammation to indices of bone health is limited and contradictory, although modification of dietary eating habits (increasing intakes of plant-based foods and reducing the omega-6 to omega-3 fatty acid ratio) may be important in the management of chronic inflammatory status. Longitudinal studies assessing dietary patterns in relation to bone mineral density/fracture incidence and biomarkers of inflammation could further our understanding of these complex interactions.

Keywords

Dietary patterns • Systemic inflammation • Bone mineral density • Fracture
• Chronic disease prevention

Introduction

Nutritional research in relation to chronic disease prevention has historically focused on the effects of single nutrients, foods, or food groups on incident disease events or surrogate markers of risk. Poor nutrition may play a role in the pathogenesis

A.D. Wood, BSc, MSc, PhD (✉)
H.M. Macdonald, BSc, MSc, PhD
Department of Musculoskeletal Research,
University of Aberdeen, Health Sciences Building
Foresterhill, Aberdeen AB25 2ZD, UK
e-mail: a.d.wood@abdn.ac.uk

of osteoporosis. Research in relation to bone health has tended to focus on vitamin D and calcium, with adequate intake of these nutrients required for the prevention and cure of rickets in children [1]. Convincing evidence for dietary supplementation of calcium alone or in combination with vitamin D to reduce fracture incidence in older adults remains somewhat equivocal [2]. In studies of other nutrients and food groups such as fruits and vegetables [3–5], potassium [5], vitamin K [6], caffeine [7, 8], and protein [9] in relation to bone health, clear relationships have not yet been elucidated.

The majority of foods and nutrients are typically consumed in combinations, of which, many are likely to be interactive or have synergistic effects [10]. It is possible that discrepancies from single nutrient studies may relate in part to inherent imprecision associated with food composition databases or that the extent of effect of a single nutrient or food on disease risk/outcome may be too small to overcome potential confounding factors [11]. We would suggest it may therefore be appropriate to examine combinations of foods as described by dietary patterns [10, 12]. Such combinations, which reflect dietary preferences of the individual, are influenced by a mixture of socioeconomic, cultural, environmental, and lifestyle factors [13].

Dietary patterns can be generated using *a priori* knowledge (under which circumstances the dietary patterns are generated by the investigator), or empirically. In *a priori* analyses, the investigator may utilize national dietary guidelines from which to base a dietary pattern and score foods according to how much they represent a particular “healthy eating” pattern. Empirical analyses employ data reduction techniques such as cluster analysis and factor analysis, using commonly available statistical software packages. Details of the different methodologies employed in dietary pattern analysis, covering the advantages and disadvantages of the general approach, have been reviewed previously [14]. Such methods appear to consistently derive similar dietary patterns reflective of differences in diets which are nutrient poor and nutrient rich [15].

Chronic inflammatory diseases are frequently associated with bone loss [16]. A comprehensive explanation of the mechanisms behind these associations has yet to be established although interactions of inflammatory cells, cytokines, and bone cells affecting the bone remodeling cycle may be important. While associations between chronic inflammatory diseases and bone loss are well recognized, it is less clear whether low-grade systemic inflammation has similar effects. In this chapter we summarize current evidence relating dietary patterns to bone health. We discuss chronic low-grade systemic inflammation as it relates to bone physiology and indices of bone health, with particular reference to bone mineral density. Consideration is given to potential mechanisms whereby dietary eating patterns may affect inflammatory status. Finally we present evidence from a recent cross-sectional study assessing associations of dietary patterns with chronic low-grade systemic inflammation.

Dietary Patterns and Bone Health

There have been relatively few studies to date investigating the impact of dietary patterns on BMD, bone mineral content (BMC), or fracture incidence [17–25]. The results of these studies, which vary markedly in terms of size, participant population, and analysis methodology, are summarized in Table 2.1. Food types included in dietary patterns which appear to be associated with greater BMD at various sites are fruits and vegetables [17–19, 21], oily fish [18, 19], and meat [25]. It has been suggested that fruits and vegetables may be beneficial because of the alkaline salts they provide by balancing excessive dietary acidity [26], although we have previously reported no effect of supplementary potassium citrate (high dose, 55.6 mmol/day ($n=56$); low dose, 18.5 mmol/day ($n=54$); placebo ($n=55$)) on BMD or markers of bone turnover in a 2-year parallel group RCT of postmenopausal women [5]. Potentially beneficial effects of this food group on bone health are more likely to be related to their micronutrient (vitamin C, K, and B vitamins), phytochemical (including flavonoids and phytoestrogens), and dietary fiber

Table 2.1 Studies assessing association of dietary patterns with BMD, BMC, or fracture incidence

Study, year [reference]	Cohort (country)	Women (%)	Participants, <i>n</i> ; mean age, years (SD)	Main dietary patterns (ascertainment method)	Association with BMD/fracture risk	Covariates ^a
Tucker et al., 2002 [14]	Framingham Osteoporosis Study (USA)	62	Elderly women, 345; 75.1 (4.9) Elderly men, 562; 75.3 (4.8)	1. Fruit, veg, cereal 2. Candy (CA)	1. Greater BMD at RF in men ($P < .05$) 2. Lower BMD at radius in women ($P < .01$) and RF in men ($P < .05$)	1–8
Okubo et al., 2006 [15]	JMETS Study (Japan)	100	Premenopausal women, 291; 46.4 (3.7)	1. Healthy – fruit, veg, fish 2. Western – fats/oils, processed meat (FA)	1. Positive association with FA BMD ($P < .05$)	1, 3, 6, 7, 9, 11
Kontogianni et al., 2009 [16]	(Greece)	100	Premenopausal women, 100; 38.0 (8.7) Peri-/postmenopausal women, 96; 56.7 (6.4)	1. Mediterranean type – fish and olive oil, low red meat (PCA)	1. Positive association with LS BMD ($P = .017$) and total body BMC ($P = .05$)	1, 3–6, 12
Langsetmo et al., 2010 [17]	Canadian Multicentre Osteoporosis Study (Canada)	71	Women, 4,611; 61.2 (12.2) Men, 1,928; 58.8 (13.5)	1. Nutrient dense – fruit, veg, whole grains 2. Energy dense (FA)	1. No association with primary outcome (FN BMD)	
Hardcastle et al., 2011 [18]	APOSS (United Kingdom)	100	Women, 3,236; 55.1 (2.2)	1. Fruit, veg, rice/pasta 2. Processed food 3. Snack food (PCA)	1. Negative association with FN BMD ($P < .001$) 2. Positive association with FN BMD ($P < .001$)	2, 3, 5, 6, 12, 14, 17
Langsetmo et al., 2011 [19]	Canadian Multicentre Osteoporosis Study (Canada)	68	Women, 3,539; 67.6 (8.6) Men, 1,649; 64.6 (10.0)	1. Nutrient dense – fruit, veg, whole grains 2. Energy dense (FA)	1. Lower risk of fracture per 1SD in women (HR: 0.86; 95 % CI: 0.76, 0.98). Similar trend in men (HR: 0.83; 95 % CI: 0.64, 1.08)	1, 6, 7, 10, 15, 16
McNaughton et al., 2011 [20]	Twin and Sister Bone Research Program (Australia)	100	Women, 527; 39.4 (10.2)	1. Legumes, seafood, seeds, wine, rice, veg 2. Processed meat/ cereals, fats/oils (FA)	1. Positive association with BMC (TB $P = .016$) and BMD (total hip $P = .042$; LS $P < .0001$) 2. Negative association with BMC (TB $P = .01$)	2–7, 14

(continued)

Table 2.1 (continued)

Study, year [reference]	Cohort (country)	Women (%)	Participants, <i>n</i> ; mean age, years (SD)	Main dietary patterns (ascertainment method)	Association with BMD/fracture risk	Covariates ^a
Karamati et al., 2012 [21]	(Iran)	100	Postmenopausal women, 154; 60.0 (8.4)	1. High-fat dairy, organ/red/processed meat 2. French fries, oils, mayo, sweets/desserts (PCA)	Those in high category for pattern 1 and 2 had greater probability of below median BMD at LS (OR 2.29; 95 % CI: 1.05–4.96) and FN (OR 2.83; 95 % CI: 1.31–6.09)	1, 3–7, 10, 11, 13, 14
Whittle et al., 2012 [22]	Young Hearts Project (Northern Ireland)	49	Women, 238; 22.8 (1.7) Men, 251; 22.4 (1.6)	1. Nuts and meat – nuts, chocolate, meat dishes 2. Refined – desserts, snack food, soft drinks (PCA)	1. Greater FN BMD for women in top vs. bottom quintile (<i>P</i> = .05) 2. Lower FN BMC for men in top vs. bottom quintile (<i>P</i> = .05)	1, 3–6, 14

BMD bone mineral density, BMC bone mineral content, TB total body, RF right femur, FA forearm, LS lumbar spine, FN femoral neck, CA cluster analysis, FA factor analysis, PCA principal components analysis

^a 1 BMI, 2 height, 3 age, 4 energy intake, 5 physical activity level, 6 smoking status, 7 medication and supplement use, 8 season, 9 grasping power, 10 falls/fracture history, 11 age at menarche, 12 menopausal status, 13 parity, 14 social deprivation category/education, 15 BMD, 16 milk consumption, 17 weight

content [27]. Beneficial effects of oily fish and meat in nutrient-dense dietary patterns may be related to vitamin D (particularly at northerly latitudes) and protein (to adequately support bone remodeling), respectively, although the relationship between dietary protein and bone health is controversial with high dietary protein traditionally thought to act negatively on bone via an increased acid load [26]. In a relatively recent review of the literature in relation to dietary protein and bone health interactions, the authors conclude that this macronutrient has a modest beneficial effect on bone density, although recommendations about its use should be reserved for groups at higher risk of bone loss (such as the elderly) and that consideration of the interaction between dietary protein and other components in a mixed diet, such as calcium and fruits and vegetables, may be important [28].

Inflammatory Disease and Bone Loss

Conditions which include rheumatoid arthritis [29, 30], inflammatory bowel disease [31, 32], systemic lupus erythematosus [33], ankylosing spondylitis [34], and chronic obstructive pulmonary disease [35] share common mechanisms by which bone can be lost. For example, in osteoblasts and bone marrow stromal cells, a wide variety of cytokines have been found to impact on the osteoprotegerin (OPG)/receptor activator of nuclear factor- κ B ligand (RANKL) (involved in signaling of osteoblasts to osteoclasts) system to affect osteoclastogenesis and bone resorption. Cytokines with stimulatory effects on osteoclastogenesis include tumor necrosis factor- α (TNF- α), interleukin (IL)-1 β , IL-6, IL-11, and IL-17. Cytokines with predominantly inhibitory effects include interferon (IFN)- γ , IL-4, and transforming growth factor (TGF)- β [36]. A variety of other important signaling mechanisms (beyond the scope of this chapter) may be involved in bone loss during inflammatory disease [16] with an uncoupling of bone formation from resorption in favor of excess bone resorption most commonly attributable to the pathogenic damage to bone.

C-reactive protein (CRP) is an acute-phase reactant produced mainly by the liver that increases in response to inflammatory stimuli [37], with biochemical testing widely used to detect immediate-phase responses to tissue injury, and in infectious and autoimmune diseases. Developments in assay methodologies towards the end of the 1990s allowed for more accurate and precise measurement of this protein at the lower end of its distribution. Serum concentrations of high-sensitivity C-reactive protein (hsCRP) markedly below those associated with an acute-phase response (indicative of chronic low-grade systemic inflammation) have been shown to be associated with prediction of the risk of developing major chronic conditions such as cardiovascular disease [38]. Many other surrogate markers of systemic inflammation such as IL-6, TNF- α , homocysteine, fibrinogen, E-selectin, and serum amyloid A (SAA) have been positively associated with cardiovascular disease risk and events in observational studies [39], although the role for these systemic biomarkers in risk assessment and appropriate prevention interventions is not yet well defined [40].

Synthesis of CRP is induced by IL-6, IL-1, and TNF- α . Concentrations of hsCRP in serum may therefore be an appropriate surrogate marker of the broad extent of chronic low-grade systemic inflammation. The results of recent observational studies assessing the association of serum hsCRP concentration with BMD are summarized in Table 2.2 [41–48]. These data are somewhat conflicting with some studies demonstrating an inverse association between hsCRP concentration and BMD at various skeletal sites [41, 46, 47] and others showing mixed results or no association [42–45, 48]. Two of these studies showed positive associations of hsCRP concentration with fracture risk [43, 44], while another study observed no such association [48]. Substantial variation with regard to participant populations, confounding effects, and BMD measurement methodology may partly explain divergent results.

It has been suggested that longitudinal studies may be warranted to confirm the association of chronic low-grade systemic inflammation (assessed by hsCRP) with BMD. Strategies to modify systemic inflammation could then be tested to

Table 2.2 Studies assessing association of serum hsCRP concentration with BMD or fracture incidence

Study, year [reference]	Cohort (country)	Women (%)	Participants, <i>n</i> ; mean age, years (SD)	hsCRP association with BMD/ incident fracture	Covariates ^a
Koh et al., 2005 [41]	(Korea)	100	Premenopausal women, 3,662; 42.6 (5.1) Postmenopausal women, 1,031; 57.6 (5.3)	Lower FN BMD in highest vs. lowest quintile of hsCRP ($P= .003$) Lower FN BMD in highest vs. lowest quintile of hsCRP ($P< .001$)	1–6
Ganesan et al., 2005 [42]	NHANES Survey (USA)	100	Postmenopausal women, 2,807; >65years	No association with total hip BMD	
Pasco et al., 2006 [43]	Geelong Osteoporosis Study (Australia)	100	Elderly women, 444; 77.0 (71.2–82.3) (median (IQR))	24–32 % increase in fracture risk for each SD increase in hsCRP (data collected between 1994 and 2002)	1, 2, 7–11
Schett et al., 2006 [44]	Bruneck Study (Italy)	50.9	Men and women, 906; 40–79 years	Incidence of nontraumatic fractures varied from 1.3 to 13.9 per 1,000 person-years in the lowest vs. highest tertile of hsCRP (data collected every 5 years between 1990 and 2005)	1, 2, 5, 6, 10, 12–15
Bhupathiraju et al., 2007 [45]	SIRBL (USA)	100	Postmenopausal women, 184; 54.2 (3.1)	No association with trabecular BMD	
Ding et al., 2008 [46]	Tasmanian Older Adult Cohort Study (Tasmania)	48.2	Men, 100; 63.3 (7.2) Women, 93; 61.9 (6.9)	Baseline hsCRP and hsCRP change negatively associated with Total body BMD change (over 2.9 years; $P< .05$)	1, 4, 7, 10, 12, 16, 17
de Pablo et al., 2012 [47]	NHANES Survey (USA)	49.8	Men, 5,261; 51 [18] Women, 5,214; 51 [19]	BMD (total, subtotal, extremities, ribs, trunk subregions) negatively associated with hsCRP quintiles (total BMD P for trend: <.001 for men and women)	1, 2, 4–6, 9, 10, 12, 14, 18–23

Cauley et al., 2007 [48]	Health Ageing and Body Composition Study (USA)	51.5	Men and women, 2,985; 70–79 years	1, 4–6, 9, 10, 12, 16, 18, 24
--------------------------	--	------	-----------------------------------	-------------------------------

No association of hsCRP with fracture incidence (data collected over 5.8 ± 1.6 years) although in a composite measure of inflammation, ≥3 elevated systemic inflammatory biomarkers were associated with RR (95 % CI) of fracture; 2.65 (1.44–4.89) compared with no elevation ($P < .001$)

BMD bone mineral density, *FN* femoral neck, *hsCRP* high-sensitivity C-reactive protein
^a1 age, 2 BMI, 3 years since menopause, 4 smoking status, 5 alcohol intake, 6 physical activity level, 7 BMD, 8 prevalent fracture, 9 medication and supplement use, 10 disease status, 11 lifestyle, 12 sex, 13 income, 14 serum creatinine, 15 bone turnover markers, 16 weight, 17 height, 18 race/ethnicity, 19 education, 20 socioeconomic status, 21 blood lipids, 22 serum 25(OH)D, 23 blood pressure, 24 falls history

determine their effects on the risk of bone loss over the longer term [47].

Dietary Patterns and Inflammation

One potential strategy to protect against inflammation and chronic disease development is via modification of dietary eating patterns [49]. A Western-type diet, common in industrialized nations, which is characterized by high intakes of refined grains, red meat, sweetened beverages, added fats (including trans fats generated from the processing of polyunsaturated fatty acids in food production), and low intakes of fresh and dried fruits, nuts, vegetables, whole grains, insoluble fiber, and foods rich in omega-3 fatty acids [50], has been identified as a major contributing factor to the promotion of chronic inflammation. High dietary intakes of trans fats may promote inflammation via direct effects on cell surface receptors to trigger proinflammatory signals (elevated CRP, IL-6, E-selectin, and soluble intracellular adhesion molecules (sICAM-1 and sVCAM-1)) [51]. Dietary patterns with a high glycemic index or glycemic load are also associated with inflammation. Excessive glucose intake may induce oxidative stress and upregulate inflammatory processes [52].

Nutrient-dense dietary patterns which tend to contrast with those of the Western-type are associated with a reduced risk for the development of many chronic conditions and diseases [53] and may act to reduce inflammation via a variety of mechanisms. Plant-based foods contain a vast array of secondary metabolites (phytochemicals) [54] ranging from structurally simple alkaloids to more complex polyphenols and steroids, many of which have been shown to have potent anti-inflammatory effects. For example, polyphenols may act to modulate inflammatory processes via inhibition of proinflammatory enzyme activation [55, 56], modulation of the production of proinflammatory cytokines [56, 57], inhibition of proinflammatory cell adhesion molecules [58, 59], and scavenging effects towards reactive oxygen species [60, 61]. Omega-3 fatty acids from fish or plant sources may also be particularly important,

acting via inhibitory effects on the arachidonic acid content of cell membranes, alteration of eicosanoid production, and modulation of nuclear receptor activation [62]. Contrastingly, omega-6 fatty acids are found predominantly in grain crops and vegetable oils, and a diet disproportionately high in omega-6 compared to omega-3 fatty acids has been associated with a shift towards proinflammatory processes [63, 64]. Finally, high intakes of dietary fiber from plant sources have consistently been shown to be associated with a reduced inflammatory status [65]. Mechanisms to explain these anti-inflammatory effects are not yet clear, although they may be associated with effects on glycemia [66].

Creating a healthy eating pattern which emphasizes a balanced intake of energy and nutrients tending towards substantial intakes of plant-based foods and reduced ratio of omega-6 to omega-3 fatty acids may be important in the management of chronic systemic inflammation.

Cross-Sectional Analysis of Dietary Patterns and Chronic Low-Grade Systemic Inflammation

Against this background, we explored the relationship between dietary patterns and systemic inflammation, assessed by serum concentrations of hsCRP and BMD. Data collected from the Aberdeen Prospective Osteoporosis Screening Study [67] cohort were used for this investigation. Diet was examined by validated Food Frequency Questionnaire [68] (FFQ) ($n=3,238$) during study visits conducted between 1997 and 2000, when the mean (SD) age of participants was 55 [2] years. Dietary patterns were generated by principal components analysis. Concentrations of hsCRP from stored serum collected during 1997–2000 study visits were recently measured ($n=2,013$) using standardized automated procedures (ADIVA 1800 Chemistry System). Inter/intra-assay coefficients of variation were $<4\%$ across the range of concentrations tested. Potential confounding factors (weight, national deprivation category, smoking status, physical activity level, and menopausal status) were measured as described previously [21].

Table 2.3 Characteristics of our study cohort from 1997 to 2000 study visit who completed both dietary questionnaires and provided serum for hsCRP analysis

	N	Mean (SD)
Height (cm)	2,010	160.5 (5.9)
Weight (kg)	2,010	68.5 (12.5)
Age (years)	2,012	54.8 (2.2)
BMI (kg/m ²)	2,010	26.6 (4.6)
PAL (MET.h/week)	2,011	1.83 (0.32)
		Percent
Current smoker	369	18.4
Nonsmoker	1,634	81.6
HRT use and menopausal status		
Postmenopausal	588	29.4
Perimenopausal	126	6.3
Premenopausal	69	3.4
Past HRT user	445	22.2
Present HRT user	775	38.7
National deprivation category ^a		
I	520	26.0
II	873	43.7
III	151	7.6
IV	281	14.1
V–VI	173	8.6

BMI body mass index (calculated as weight in kilograms divided by height in meters squared), *PAL* physical activity level, *HRT* hormone replacement therapy

^aBased on postcode classification, where I represents the most affluent and VI represents the most deprived

Table 2.4 Concentrations of CLSI biomarkers across quintiles of dietary score for dietary patterns generated from principal components analysis^a

Diet descriptor	Q1 (n 396)	Q2 (n 400)	Q3 (n 384)	Q4 (n 414)	Q5 (n 419)	P ^b	P ^c
“Healthy”							
hsCRP mg/L	1.9 (3.5)	1.2 (2.4)	1.1 (2.6)	1.1 (2.3)	1.2 (2.3)	.001	.01
“Bread and butter, low red meat and alcohol”							
hsCRP mg/L	1.6 (3.3)	1.3 (2.4)	1.3 (2.4)	1.2 (2.4)	1.2 (2.4)	.01	.12
“High fat and white fish”							
hsCRP mg/L	1.0 (1.9)	1.3 (2.8)	1.3 (2.8)	1.4 (2.9)	1.6 (2.9)	.009	.45

^aData presented as median (IQR) for each quintile of dietary pattern score

^bBased on ANOVA with inflammatory marker as the independent variable (unadjusted)

^cBased on ANCOVA with inflammatory marker as the independent variable, dietary pattern quintiles as the fixed factor, and adjustment for the following potential confounding covariates: weight, national deprivation category, smoking status, and physical activity level

ANOVA was used to test the relationship between dietary pattern scores and hsCRP measurements with ANCOVA to control for lifestyle covariates (weight, national deprivation category, smoking status, physical activity level, and menopausal status).

Characteristics of our study cohort who completed both dietary questionnaire and provided

serum for hsCRP analysis are shown in Table 2.3. Five dietary patterns (accounting for 26 % of the variance in the diet) were identified [21], three of which were associated with serum hsCRP concentrations (Table 2.4). Women in the highest quintile of the “healthy” dietary pattern (rich in fruits and vegetables, lean meat, and with negative

loadings for high-sugar foods) had lower median serum hsCRP concentration compared with those in the lowest quintile (Table 2.4). This relationship remained significant after confounding adjustment. Concentrations of hsCRP decreased with increasing quintiles of the dietary pattern with positive factor loadings for bread and butter and negative factor loadings for red meat and alcohol (Table 2.4). Finally, hsCRP concentration increased with increasing quintiles of the high-fat/whitefish dietary pattern (Table 2.4). However, these relationships were no longer significant after adjustment for confounding covariates.

Our data confirm that healthy dietary patterns rich in fruits, vegetables, and lean protein appear to suppress chronic low-grade systemic inflammation assessed by the biomarker hsCRP independently of weight and physical activity level.

Conclusions

Dietary components may influence bone health and chronic inflammatory status via both positive and negative effects on inflammatory pathways. A dietary pattern approach may help to further our understanding the role of nutrition on disease processes. Future studies assessing diet in relation to indices of bone health and both traditional and novel biomarkers of inflammation longitudinally may be particularly informative.

References

- Wharton B, Bishop N. Rickets. *Lancet*. 2002;362:1389–400.
- Bischoff-Ferrari HA, Willett WC, Orav EJ, Lips P, Meunier PJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention. *N Engl J Med*. 2012;367:40–9.
- New SA, Robins SP, Campbell MK, Martin JC, Garton MJ, et al. Dietary influences on bone mass and bone metabolism: further evidence of a positive link between fruit and vegetable consumption and bone health? *Am J Clin Nutr*. 2000;71:142–51.
- Macdonald HM, New SA, Golden MH, Campbell MK, Reid DM. Nutritional associations with bone loss during the menopausal transition: evidence of a beneficial effect of calcium, alcohol, and fruit and vegetable nutrients and of a detrimental effect of fatty acids. *Am J Clin Nutr*. 2004;79:155–65.
- Macdonald HM, Black AJ, Aucott L, Duthie G, Duthie S, et al. Effect of potassium citrate supplementation or increased fruit and vegetable intake on bone metabolism in healthy postmenopausal women: a randomized controlled trial. *Am J Clin Nutr*. 2008;88:465–74.
- Cockayne S, Adamson J, Lanham-New S, Shearer MJ, Gilbody S, et al. Vitamin K and the prevention of fractures: systematic review and meta-analysis of randomized controlled trials. *Arch Intern Med*. 2006;166:1256–61.
- Hegarty VM, May HM, Khaw KT. Tea drinking and bone mineral density in older women. *Am J Clin Nutr*. 2000;71:1003–7.
- Tucker KL, Morita K, Qiao N, Hannan MT, Cupples LA, et al. Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: the Framingham Osteoporosis Study. *Am J Clin Nutr*. 2006;84:936–42.
- Hannan MT, Tucker KL, Dawson-Hughes B, Cupples LA, Felson DT, et al. Effect of dietary protein on bone loss in elderly men and women: the Framingham Osteoporosis Study. *J Bone Miner Res*. 2000;15:2504–12.
- Jacobs Jr DR, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. *Am J Clin Nutr*. 2003;78:508S–13.
- Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13:3–9.
- Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr*. 2001;73:1–2.
- Kant AK. Dietary patterns and health outcomes. *J Am Diet Assoc*. 2004;104:615–35.
- Macdonald HM, Hardcastle AC. Dietary patterns and bone health. In: Burckhardt P, Dawsonhughes B, Weaver C, editors. Nutritional influences on bone health. London: Springer; 2002.
- Newby PK, Tucker KL. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev*. 2004;62:177–203.
- Hardy R, Cooper MS. Bone loss in inflammatory disorders. *J Endocrinol*. 2009;201:309–20.
- Tucker KL, Chen H, Hannan MT, Cupples LA, Wilson PW, et al. Bone mineral density and dietary patterns in older adults: the Framingham Osteoporosis Study. *Am J Clin Nutr*. 2002;76:245–52.
- Okubo H, Sasaki S, Horiguchi H, Oguma E, Miyamoto K, et al. Dietary patterns associated with bone mineral density in premenopausal Japanese farmwomen. *Am J Clin Nutr*. 2006;83:1185–92.
- Kontogianni MD, Melistas L, Yannakoulia M, Malagaris I, Panagiotakos DB, et al. Association between dietary patterns and indices of bone mass in a sample of Mediterranean women. *Nutrition*. 2009;25:165–71.
- Langsetmo L, Poliquin S, Hanley DA, Prior JC, Barr S, et al. Dietary patterns in Canadian men and women ages 25 and older: relationship to demographics, body mass index, and bone mineral density. *BMC Musculoskeletal Disord*. 2010;11:20.

21. Hardcastle AC, Aucott L, Fraser WD, Reid DM, Macdonald HM. Dietary patterns, bone resorption and bone mineral density in early post-menopausal Scottish women. *Eur J Clin Nutr*. 2011;65:378–85.
22. Langsetmo L, Hanley DA, Prior JC, Barr SI, Anastassiades T, et al. Dietary patterns and incident low-trauma fractures in postmenopausal women and men aged ≥ 50 y: a population-based cohort study. *Am J Clin Nutr*. 2011;93:192–9.
23. McNaughton SA, Wattanapenpaiboon N, Wark JD, Nowson CA. An energy-dense, nutrient-poor dietary pattern is inversely associated with bone health in women. *J Nutr*. 2011;141:1516–23.
24. Karamati M, Jessri M, Shariati-Bafghi SE, Rashidkhani B. Dietary patterns in relation to bone mineral density among menopausal Iranian women. *Calcif Tissue Int*. 2012;91:40–9.
25. Whittle CR, Woodside JV, Cardwell CR, McCourt HJ, Young IS, et al. Dietary patterns and bone mineral status in young adults: the Northern Ireland Young Hearts Project. *Br J Nutr*. 2012;108:1494–504.
26. Wachman A, Bernstein DS. Diet and osteoporosis. *Lancet*. 1968;1:958–9.
27. Macdonald H. Influence of organic salts of potassium on bone health: possible mechanisms of action for the role of fruit and vegetables. In: Burckhardt P, Weaver C, Dawsonhughes B, editors. *Nutritional aspects of osteoporosis*. London: Elsevier/Academic Press; 2007. p. 268–81.
28. Jesudason D, Clifton P. The interaction between dietary protein and bone health. *J Bone Miner Metab*. 2011;29:1–14.
29. Gough AK, Lillie J, Eyre S, Holder RL, Emery P. Generalised bone loss in patients with early rheumatoid arthritis. *Lancet*. 1994;344:23–7.
30. Spector TD, Hall GM, McCloskey EV, Kanis JA. Risk of vertebral fracture in women with rheumatoid arthritis. *BMJ*. 1993;306:558.
31. Bernstein CN, Blanchard JF, Leslie W, Wajda A, Yu BN. The incidence of fracture among patients with inflammatory bowel disease. A population-based cohort study. *Ann Intern Med*. 2000;133:795–9.
32. Loftus Jr EV, Crowson CS, Sandborn WJ, Tremaine WJ, O'Fallon WM, et al. Long-term fracture risk in patients with Crohn's disease: a population-based study in Olmsted County, Minnesota. *Gastroenterology*. 2002;123:468–75.
33. Lane NE. Therapy insight: osteoporosis and osteonecrosis in systemic lupus erythematosus. *Nat Clin Pract Rheumatol*. 2006;2:562–9.
34. Geusens P, Vosse D, van der Linden S. Osteoporosis and vertebral fractures in ankylosing spondylitis. *Curr Opin Rheumatol*. 2007;19:335–9.
35. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J*. 2009;33:1165–85.
36. Lorenzo J, Horowitz M, Choi Y. Osteoimmunology: interactions of the bone and immune system. *Endocr Rev*. 2008;29:403–40.
37. Du Clos TW. Function of C-reactive protein. *Ann Med*. 2000;32:274–8.
38. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *N Engl J Med*. 2000;342:836–43.
39. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, et al. Inflammatory markers and the risk of coronary heart disease in men and women. *N Engl J Med*. 2004;351:2599–610.
40. Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women – 2011 update: a guideline from the American Heart Association. *Circulation*. 2011;123:1243–62.
41. Koh JM, Khang YH, Jung CH, Bae S, Kim DJ, et al. Higher circulating hsCRP levels are associated with lower bone mineral density in healthy pre- and postmenopausal women: evidence for a link between systemic inflammation and osteoporosis. *Osteoporos Int*. 2005;16:1263–71.
42. Ganesan K, Tekleahmanot S, Tran TH, Asuncion M, Norris K. Relationship of C-reactive protein and bone mineral density in community-dwelling elderly females. *J Natl Med Assoc*. 2005;97:329–33.
43. Pasco JA, Kotowicz MA, Henry MJ, Nicholson GC, Spilbury HJ, et al. High-sensitivity C-reactive protein and fracture risk in elderly women. *JAMA*. 2006;296:1353–5.
44. Schett G, Kiechl S, Weger S, Pederiva A, Mayr A, et al. High-sensitivity C-reactive protein and risk of nontraumatic fractures in the Bruneck study. *Arch Intern Med*. 2006;166:2495–501.
45. Bhupathiraju SN, Alekel DL, Stewart JW, Hanson LN, Shedd KM, et al. Relationship of circulating total homocysteine and C-reactive protein to trabecular bone in postmenopausal women. *J Clin Densitom*. 2007;10:395–403.
46. Ding C, Parameswaran V, Udayan R, Burgess J, Jones G. Circulating levels of inflammatory markers predict change in bone mineral density and resorption in older adults: a longitudinal study. *J Clin Endocrinol Metab*. 2008;93:1952–8.
47. de Pablo P, Cooper MS, Buckley CD. Association between bone mineral density and C-reactive protein in a large population-based sample. *Arthritis Rheum*. 2012;64(8):2624–31.
48. Cauley JA, Danielson ME, Boudreau RM, Forrest KY, Zmuda JM, et al. Inflammatory markers and incident fracture risk in older men and women: the Health Aging and Body Composition Study. *J Bone Miner Res*. 2007;22:1088–95.
49. Haddad PS, Azar GA, Groom S, Boivin M. Natural health products, modulation of immune function and prevention of chronic diseases. *Evid Based Complement Alternat Med*. 2005;2:513–20.
50. Cordain L, Eaton SB, Sebastian A, Mann N, Lindeberg S, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr*. 2005;81:341–54.

51. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr.* 2005;135:562–6.
52. Yan SD, Schmidt AM, Anderson GM, Zhang J, Brett J, et al. Enhanced cellular oxidant stress by the interaction of advanced glycation end products with their receptors/binding proteins. *J Biol Chem.* 1994;269:9889–97.
53. Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am J Clin Nutr.* 2003;78:517S–20.
54. Acamovic T, Brooker JD. Biochemistry of plant secondary metabolites and their effects in animals. *Proc Nutr Soc.* 2005;64:403–12.
55. Guo W, Kong E, Meydani M. Dietary polyphenols, inflammation, and cancer. *Nutr Cancer.* 2009;61:807–10.
56. Garcia-Lafuente A, Guillamon E, Villares A, Rostagno MA, Martinez JA. Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. *Inflamm Res.* 2009;58:537–52.
57. Kim HP, Son KH, Chang HW, Kang SS. Anti-inflammatory plant flavonoids and cellular action mechanisms. *J Pharmacol Sci.* 2004;96:229–45.
58. Lee YH, Choi SJ, Ji JD, Song GG. Associations between ERAP1 polymorphisms and ankylosing spondylitis susceptibility: a meta-analysis. *Inflamm Res.* 2011;60:999–1003.
59. Park HJ, Jeong SK, Kim SR, Bae SK, Kim WS, et al. Resveratrol inhibits *Porphyromonas gingivalis* lipopolysaccharide-induced endothelial adhesion molecule expression by suppressing NF-kappaB activation. *Arch Pharm Res.* 2009;32:583–91.
60. Rahman I, Biswas SK, Kirkham PA. Regulation of inflammation and redox signaling by dietary polyphenols. *Biochem Pharmacol.* 2006;72:1439–52.
61. Gloire G, Legrand-Poels S, Piette J. NF-kappaB activation by reactive oxygen species: fifteen years later. *Biochem Pharmacol.* 2006;72:1493–505.
62. Visioli F, Poli A, Richard D, Paoletti R. Modulation of inflammation by nutritional interventions. *Curr Atheroscler Rep.* 2008;10:451–3.
63. Pischon T, Hankinson SE, Hotamisligil GS, Rifai N, Willett WC, et al. Habitual dietary intake of n-3 and n-6 fatty acids in relation to inflammatory markers among US men and women. *Circulation.* 2003;108:155–60.
64. Russo GL. Dietary n-6 and n-3 polyunsaturated fatty acids: from biochemistry to clinical implications in cardiovascular prevention. *Biochem Pharmacol.* 2009;77:937–46.
65. North CJ, Venter CS, Jerling JC. The effects of dietary fibre on C-reactive protein, an inflammation marker predicting cardiovascular disease. *Eur J Clin Nutr.* 2009;63:921–33.
66. Galland L. Diet and inflammation. *Nutr Clin Pract.* 2010;25:634–40.
67. Barr R, Macdonald H, Stewart A, McGuigan F, Rogers A, et al. Association between vitamin D receptor gene polymorphisms, falls, balance and muscle power: results from two independent studies (APOSS and OPUS). *Osteoporos Int.* 2010;21:457–66.
68. Masson LF, McNeill G, Tomany JO, Simpson JA, Peace HS, et al. Statistical approaches for assessing the relative validity of a food-frequency questionnaire: use of correlation coefficients and the kappa statistic. *Public Health Nutr.* 2003;6:313–21.



<http://www.springer.com/978-1-4471-2768-0>

Nutritional Influences on Bone Health

8th International Symposium

Burckhardt, P.; Dawson-Hughes, B.; Weaver, C.M. (Eds.)

2013, XVIII, 387 p. 68 illus., 23 illus. in color., Hardcover

ISBN: 978-1-4471-2768-0