Taylor & Francis
Taylor & Francis Group

Journal of Nutrition in Gerontology and Geriatrics

ISSN: 2155-1197 (Print) 2155-1200 (Online) Journal homepage: http://www.tandfonline.com/loi/wjne21

Nutritional Risk is Associated with Chronic Musculoskeletal Pain in Community-dwelling Older Persons: The PAINEL Study

Aline Bárbara Pereira Costa MSc, Luciana Andrade Carneiro Machado PhD, João Marcos Domingues Dias PhD, Adriana Keller Coelho de Oliveira MSc, Joana Ude Viana PhD candidate, Sílvia Lanziotti Azevedo da Silva PhD, Flávia Gonçalves Pereira Couto BappSc, Juliana Lustosa Torres PhD candidate, Liliane P. Mendes MSc & Rosangela Correa Dias PhD

To cite this article: Aline Bárbara Pereira Costa MSc, Luciana Andrade Carneiro Machado PhD, João Marcos Domingues Dias PhD, Adriana Keller Coelho de Oliveira MSc, Joana Ude Viana PhD candidate, Sílvia Lanziotti Azevedo da Silva PhD, Flávia Gonçalves Pereira Couto BappSc, Juliana Lustosa Torres PhD candidate, Liliane P. Mendes MSc & Rosangela Correa Dias PhD (2016) Nutritional Risk is Associated with Chronic Musculoskeletal Pain in Community-dwelling Older Persons: The PAINEL Study, Journal of Nutrition in Gerontology and Geriatrics, 35:1, 43-51

To link to this article: http://dx.doi.org/10.1080/21551197.2015.1125325

JOURNAL OF NUTRITION IN GERONTOLOGY AND GERIATRICS
2016, VOL. 35, NO. 1, 43–51
http://dx.doi.org/10.1080/21551197.2015.1125325

Routledge
Taylor & Francis Group

Nutritional Risk is Associated with Chronic Musculoskeletal Pain in Community-dwelling Older Persons: The PAINEL Study

Aline Bárbara Pereira Costa, Msc[a], Luciana Andrade Carneiro Machado, PhD[a], João Marcos Domingues Dias, PhD[b], Adriana Keller Coelho de Oliveira, Msc[c], Joana Ude Viana, PhD candidate[b], Sílvia Lanziotti Azevedo da Silva, PhD[b,d], Flávia Gonçalves Pereira Couto, BappSc[b], Juliana Lustosa Torres, PhD candidate[a], Liliane P. Mendes, MSc[b], and Rosangela Correa Dias, PhD[b]

[a]Faculty of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; [b]Department of Physical Therapy, Federal University of Minas Gerais, Belo Horizonte, Brazil; [c]Institute of Biological and Health Sciences, Pontifical Catholic University of Minas Gerais, Belo Horizonte, Brazil; [d]Department of Physical Therapy, Federal University of Alfenas, Alfenas, Brazil

ABSTRACT

Malnutrition is a risk factor for noncommunicable diseases related to ageing, and it can also contribute to musculoskeletal health. This study investigated whether nutritional risk is associated with chronic musculoskeletal pain in community-dwelling older persons. Nutritional risk was assessed by the DETERMINE Checklist. Chronic musculoskeletal pain was defined as the presence of pain in the past six months that did not disappear for at least 30 consecutive days. Multivariate logistic regression including confounding variables was used for the analysis. The sample was comprised of 383 participants (age 75.6 ± SD 6.1); the majority were at moderate-to-high nutritional risk (69%) and approximately one third presented chronic musculoskeletal pain (30%). The nutritional risk score was independently associated with chronic musculoskeletal pain: adding one unit in the risk score produces an 11% increment in the odds of presenting pain (OR 1.109, 95% CI 1.022–1.204). Individuals classified into moderate- or high-risk categories also had substantially higher odds (~90%) of presenting chronic musculoskeletal pain when compared to those in the low-risk category, although our findings were only marginally significant. This is the first study to demonstrate the association between nutritional risk and chronic musculoskeletal pain above and beyond the contributed effects from relevant confounders.

KEYWORDS

Ageing; chronic pain; community-dwelling elders; malnutrition; musculoskeletal disorders

Introduction

The World Health Organization (WHO) recognizes older persons as particularly vulnerable to malnutrition. The identification of community-dwelling older persons at risk of malnutrition and the awareness of the factors associated with this risk are crucial for the development of strategies to

CONTACT Luciana AC Machado machadolac@hotmail.com Centro de Investigação ELSA-Brasil-MG, Hospital Borges da Costa, Rua Professor Alfredo Balena 190 Santa Efigênia Belo Horizonte, MG 30130-100, Brazil.

promote nutritional health and to reduce adverse health outcomes in later life. Malnutrition is a risk factor for multiple chronic noncommunicable diseases (CND) related to aging, such as cardiovascular diseases, diabetes, and cancer (1), and it can also contribute to the musculoskeletal health. The relationship between malnutrition and musculoskeletal health has mainly been acknowledged through the role of obesity (overnutrition) in producing excessive joint loads that can trigger the development of degenerative joint diseases (2–4). On the other hand, the reduction in the quantity of food intake among older persons put them at higher risk of nutrient deprivation (undernutrition) and this can also affect their musculoskeletal health through the loss of lean mass and skeletal muscle function (5–7).

Despite the extensive body of literature supporting the link between malnutrition and musculoskeletal health, to our knowledge, no previous study has focused on the relationship between nutritional risk and chronic musculoskeletal pain. The present study investigated whether nutritional risk is independently associated with chronic musculoskeletal pain in Brazilian community-dwelling older persons.

Methods

Study design

This cross-sectional study is part of a population-based survey on the prevalence of musculoskeletal disorders in Brazilian community-dwelling older persons, namely, the Pain in the Elderly (PAINEL) Study. The sample was derived from the FIBRA Network Study (Frailty among Brazilian Older Adults), Federal University of Minas Gerais (UFMG) pole. Recruitment was based on a probability sample of 1640 households located in 15 clusters (census regions) distributed across the city of Belo Horizonte (8). Belo Horizonte is the third largest capital city of the Southeast of Brazil, currently comprising 2.4 million inhabitants (http://www.ibge.gov.br). The study was approved by the Research and Ethics Committee of Federal University of Minas Gerais (process number ETIC 187/07).

Participants

Eligible subjects were community-dwelling older persons of both sexes, aged 65 years or older, who were actively enrolled in FIBRA Network Study and consented to participate in the PAINEL Study. Individuals were excluded if they presented any of the following conditions: severe cognitive impairment; transient or permanent bedridden status; wheelchair confinement; severe sequelae of stroke; or neurological disorders that could hinder their performance on tests. Those who did not provide data on chronic musculoskeletal pain were also excluded from the present analysis.

Measurements

From April 2010 to March 2012, the following variables were collected through telephone interviews or face-to-face examinations: age, sex, Body Mass Index (BMI), depression, cardiovascular disease, diabetes, cancer, chronic musculoskeletal pain and nutritional risk. BMI was calculated from directly measured weight and height (weight, kg/ [height, m]^2). Depressive symptoms were assessed through the Geriatric Depression Scale (GDS-15), which had been translated to Portuguese-Brazil and validated to the Brazilian population (9). Cardiovascular disease, diabetes, and cancer were identified through the self-report of a diagnosis by a doctor in the past 12 months. Chronic musculoskeletal pain was identified through the question: "In the past six months, did you feel any pain that did not disappear for at least 30 consecutive days?" Nutritional risk was assessed by the DETERMINE Your Nutritional Health Checklist from the Nutrition Screening Initiative (NSI) (10). The overall risk score from the DETERMINE checklist ranges from 0 to 21 points and consists of assigning different risk weights to 10 items covering the following aspects: diseases or use of medications that affect dietary intake, problems shopping for food (including access and financial difficulties), frequency of eating, specific component intake (e.g., fruits, vegetables, milk, alcohol), history of rapid weight change, and social isolation. Scores from 0–2 points identify elders at low nutritional risk, from 3–5 points identify elders at moderate nutritional risk, and scores of 6 or more points identify those at high nutritional risk (10).

Statistical analysis

Frequencies, means, and standard deviations were calculated for descriptive analyses. Student's t-test and Chi-squared test were used to investigate the association between sociodemographic or clinical characteristics and chronic musculoskeletal pain. Characteristics associated at $p < 0.15$ were considered potential confounders and entered into the multivariate logistic regression analysis investigating the independent association between the overall nutritional risk score and chronic musculoskeletal pain (dependent variable). Nutritional risk categories (low, moderate, or high) were also assessed in a separate multivariate analysis to contribute to the clinical interpretation of findings. Continuous predictors (BMI and GDS) were not categorized to avoid loss of power and residual confounding (11). Statistical significance was set at $p < 0.05$ for the final multivariate regression analysis. SPSS 19.0 (SPSS Inc., Chicago, USA) was used.

Results

A total of 383 participants, 272 (71.0%) women and 111 (29.0%) men, with mean age of 75.6 (SD $\pm$ 6.1) years, were included in the study. BMI was above

Table 1. Relationship between participants' characteristics and chronic musculoskeletal pain, $n = 383$.

Characteristics	Chronic musculoskeletal pain		*P*-value
	No ($n = 268$)	Yes ($n = 115$)	
Age, years, mean ± SD	76.0 ± 6.3	74.5 ± 5.5	0.023*
Sex, n (%)			0.002†
Female	178 (66.4)	94 (81.7)	
Male	90 (33.6)	21 (18.3)	
BMI, kg/m^2, mean ± SD	26.4 ± 4.5	29.4 ± 5.2	<0.001*
Overweight or obese (BMI ≥ 25 kg/m^2)	160 (59.7)	93 (80.9)	<0.001†
GDS, 0–15, mean ± SD	7.0 ± 1.7	7.6 ± 2.0	0.003*
Cardiovascular disease, n (%)	25 (9.3)	15 (13.0)	0.276†
Diabetes, n (%)	36 (13.4)	23 (20.0)	0.103†
Cancer, n (%)	7 (2.6)	4 (3.5)	0.642†
Nutritional risk			
Overall risk score, 0–21, mean ± SD	3.8 ± 2.8	5.4 ± 3.3	<0.001*
Categories of risk			0.001†
Low risk, 0–2 points	97 (36.2)	22 (19.1)	
Moderate risk, 3–5 points	99 (36.9)	45 (39.1)	
High risk, >6 points	72 (26.9)	48 (41.7)	

Note. BMI, Body Mass Index; GDS, Geriatric Depression Scale; *Student's t-test; †Chi-square test.

the WHO cut-off point for overweight (BMI ≥25 kg/m^2) in 253 (66.1%) participants. The prevalence of chronic musculoskeletal pain was 30.0%. Nutritional risk statuses of the participants were as follows: 119 (31.1%) were at low risk; 144 (37.6%) were at moderate risk; 120 (31.3%) were at high risk. The mean nutritional risk score was 4.3 points (SD ± 3.1, range 0–14). Table 1 displays the results of univariate analyses on the relationship between sociodemographic or clinical characteristics and chronic musculoskeletal pain. The following characteristics were associated with chronic musculoskeletal pain below the selected significance threshold and were thus entered into the multivariate models: age, sex, BMI, GDS score, and diabetes. In the final regression model controlling for confounders, the nutritional risk score was significantly associated with chronic musculoskeletal pain (odds ratio, OR 1.109, 95% CI 1.022–1.204, $p = 0.013$). The analysis considering nutritional risk categories (with low risk as the reference) found marginally significant associations: moderate risk, OR 1.819, 95% CI 0.979–3.380, $p = 0.058$;

Table 2. Independent association between nutritional risk and chronic musculoskeletal pain, $n = 383$.

Multivariate analysis	Overall risk score *0–21*			Categories of risk *low, moderate, high**		
	Exp(B)	95% CI	*P*-value	Exp(B)	95% CI	*P*-value
Age, years	0.970	0.931–1.011	0.145	0.966	0.927–1.007	0.100
Sex, female	1.674	0.952–2.943	0.074	1.763	1.002–3.100	0.049
BMI, kg/m^2	1.105	1.050–1.164	<0.001	1.110	1.054–1.168	<0.001
GDS, 0–15	1.138	0.992–1.306	0.065	1.167	1.018–1.338	0.027
Diabetes	0.997	0.527–1.884	0.992	0.979	0.518–1.851	0.949
Nutritional risk	1.109	1.022–1.204	0.013		N/A	
Moderate risk		N/A		1.819	0.979–3.380	0.058
High risk		N/A		1.910	0.998–3.655	0.051

Note. BMI, Body Mass Index; GDS, Geriatric Depression Scale; *Reference = low risk.

high risk, OR 1.910, 95% CI 0.998–3.655, $p = 0.051$). Table 2 presents the findings from both multivariate analyses.

Discussion

Malnutrition has a direct impact on CND associated with increased mortality and it is also an important contributor to the evolution of multimorbidity in later life (12). Painful musculoskeletal problems are an integral part of this multimorbidity scenario. Recent data from European cohort studies identified musculoskeletal problems as the most prevalent conditions among older adults with multimorbidity and the major contributor to their quality of life (13).

The majority of community-dwelling older persons in our study were at moderate to high nutritional risk (almost one third were at high risk). Previous epidemiological studies assessing the risk of malnutrition in Brazilian community-dwelling older persons reported prevalence estimates from 22%–31% (14–16). Worldwide prevalence estimates of malnourishment and risk of malnutrition among community-dwelling older persons show great variability, ranging from 1%–8% for malnourishment and from 4%–44% for risk of malnutrition (17–22). This large variability is probably due to geographical differences, use of different measurement instruments, and/or definitions. For example, there is currently a lack of consensus on how to define and operationalize malnutrition (23).

We found a significant association between nutritional risk score and chronic musculoskeletal pain: the odds of presenting chronic musculoskeletal pain were 11% higher by adding one unit in the nutritional risk score. One key aspect was that the association between nutritional risk and chronic musculoskeletal pain was independent from the contributed effects from other CND. As expected, BMI was strongly associated with chronic musculoskeletal pain: the odds of presenting chronic musculoskeletal pain were 10% to 11% higher for each additional BMI unit. We also found marginally significant results indicating that individuals classified into moderate or high risk categories have up to 91% higher odds of presenting chronic musculoskeletal pain, when compared to those in the low-risk category.

Concurrent associations between obesity and chronic musculoskeletal pain, and between nutritional risk and chronic musculoskeletal pain, may be viewed as counterintuitive at first glance, since higher scores on the DETERMINE Checklist relate to low nutrient intakes in comparison with Recommended Dietary Allowances (RDA) standards (10). However, these associations possibly refer to distinct etiologic pathways, where increased joint load and inflammation may constitute shared underlying mechanisms. When it comes to obesity, increments in body weight can produce pain by directly imposing abnormal mechanical loads to articular surfaces (particularly in

large weight-bearing joints such as hip and knee) (2), while obesity-related systemic factors, such as proinflammatory cytokines secreted by the adipose tissue, can further contribute to musculoskeletal pain through a direct sensitization of nociceptive afferent nerve fibers (24). On the other hand, undernutrition can also increase mechanical joint loads by a depletion in skeletal muscle mass that produce a reduction in the "muscle corset" protective role against joint impact loading (25).

Lebreton and colleagues have recently described an inflammatory mechanism triggered by undernutrition that may also produce pain by the sensitization of nociceptors. They found that undernutrition causes mesenteric vascular dysfunction due to smooth muscle impairment, which can lead to a systemic inflammatory response (26). Additionally, the synergistic interrelationships between increased joint load and inflammation introduce more complexity to these casual pathways. First, imbalances between protein synthesis and breakdown (e.g., up-regulation of proteolytic enzymes) triggered by inflammation can contribute to significant loss of muscle mass (27) and to increased degradation of cartilaginous joint structures (28, 29), which in turn lead to an increased mechanical loading. Second, mechanical joint load is known as one of the key factors responsible for regulating the cartilaginous matrix metabolism and the production of proinflammatory mediators (30). The shared mechanisms and the relationships between malnutrition (obesity or undernutrition) and pain are described in Figure 1.

Lee and colleagues have demonstrated that the odds of having painful degenerative joint disease are higher in individuals with sarcopenic obesity, when compared to nonsarcopenic nonobese, sarcopenic nonobese, or nonsarcopenic obese individuals (29). This finding suggests that the combination of obesity and low musculoskeletal mass may yield a double burden to older persons, by increasing their risk of developing chronic musculoskeletal pain. A large proportion of participants in our sample (48.8%) were both overweight/obese and at moderate to high nutritional risk. We have explored the potential joint effect of BMI and nutritional risk on the prevalence of chronic musculoskeletal pain through a post-hoc multivariate logistic regression

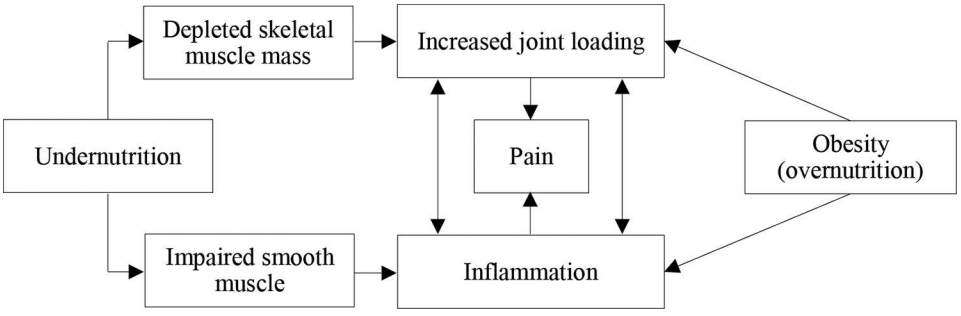

Figure 1. Shared mechanisms and relationships between malnutrition and pain.

analysis including the interaction term *BMI x nutritional risk score*. However, we could not find evidence for any relevant joint effect (data not shown).

This is the first study to demonstrate the association between nutritional risk and chronic musculoskeletal pain above and beyond the contributed effects from relevant confounders. Taken together, our findings highlight the need for raising the awareness of the mutual contribution of nutritional and musculoskeletal health among older persons. This is particularly important in developing countries such as Brazil, where the rapid demographic transition represents an anticipated challenge to societies and public health systems when it comes to handling age-related adverse health consequences (31). Future longitudinal studies must clarify the direction of the complex relationships between nutritional risk and chronic musculoskeletal pain, given that reverse causation cannot be ruled by the cross-sectional nature of our analysis.

Take away points

- We investigated the association between nutritional risk and chronic musculoskeletal pain.
- Although the assessment of nutritional risk has mainly focused on institutionalized elders, we found high rates of nutritional risk (~70%) among community-dwelling older persons.
- Malnutrition and chronic musculoskeletal pain are known to affect an important proportion of older persons, but the knowledge on the relationship between these comorbidities is still limited.
- Our study is the first to demonstrate a significant and independent association between nutritional risk and chronic musculoskeletal pain.

Funding

The PAINEL study was supported by FAPEMIG (Grant BPD-I 00149) and CNPq (Grant 555078/2006-0). L.A. Machado is a Postdoctoral Research Fellow supported by CAPES.

References

1. von Ruesten A, Feller S, Bergmann MM, Boeing H. Diet and risk of chronic diseases: results from the first 8 years of follow-up in the EPIC-Potsdam study. Eur J Clin Nutr. 2013; 67(4):412–9.
2. Messier SP, Gutekunst DJ, Davis C, DeVita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. Arthritis Rheum. 2005; 52(7):2026–32.
3. Powell A, Teichtahl AJ, Wluka AE, Cicuttini FM. Obesity: a preventable risk factor for large joint osteoarthritis which may act through biomechanical factors. Br J Sports Med. 2005; 39(1):4–5.

4. Butterworth PA, Landorf KB, Smith SE, Menz HB. The association between body mass index and musculoskeletal foot disorders: a systematic review. Obes Rev. 2012; 13(7):630–42.
5. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab. 2003; 88(12):5766–72.
6. Kim J, Lee Y, Kye S, Chung YS, Kim KM. Association of vegetables and fruits consumption with sarcopenia in older adults: the Fourth Korea National Health and Nutrition Examination Survey. Age Ageing. 2015; 44(1):96–102.
7. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr. 2008; 87(1):150–5.
8. Vieira RA, Guerra RO, Giacomin KC, Vasconcelos KS, Andrade AC, Pereira LS, et al. [Prevalence of frailty and associated factors in community-dwelling elderly in Belo Horizonte, Minas Gerais State, Brazil: data from the FIBRA study]. Cad Saude Publica. 2013; 29(8):1631–43.
9. Almeida O, Almeida S. Reliability of the Brazilian version of the abbreviated form of Geriatric Depression Scale (GDS) short form Arq Neuropsiquiatr. 1999; 57:421–6.
10. Posner BM, Jette AM, Smith KW, Miller DR. Nutrition and health risks in the elderly: the nutrition screening initiative. Am J Public Health. 1993; 83(7):972–8.
11. Royston P, Altman DG, Sauerbrei W. Dichotomizing continuous predictors in multiple regression: a bad idea. Stat Med. 2006; 25(1):127–41.
12. Ruel G, Shi Z, Zhen S, Zuo H, Kroger E, Sirois C, et al. Association between nutrition and the evolution of multimorbidity: the importance of fruits and vegetables and whole grain products. Clin Nutr. 2014; 33(3):513–20.
13. Forjaz MJ, Rodriguez-Blazquez C, Ayala A, Rodriguez-Rodriguez V, de Pedro-Cuesta J, Garcia-Gutierrez S, et al. Chronic conditions, disability, and quality of life in older adults with multimorbidity in Spain. Eur J Intern Med. 2015; 26(3):176–81.
14. Delacorte RR, Moriguti JC, Matos FD, Pfrimer K, Marchinil JS, Ferriolli E. Mini-nutritional assessment score and the risk for undernutrition in free-living older persons. J Nutr Health Aging. 2004; 8(6):531–4.
15. Cabrera MA, Mesas AE, Garcia AR, de Andrade SM. Malnutrition and depression among community-dwelling elderly people. J Am Med Dir Assoc. 2007; 8(9):582–4.
16. Klee Oehlschlaeger MH, Alberici Pastore C, Schuler Cavalli A, Gonzalez MC. Nutritional status, muscle mass and strength of elderly in Southern Brazil. Nutr Hosp. 2014; 31(1):363–70.
17. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. Clin Geriatr Med. 2002; 18(4):737–57.
18. Margetts BM, Thompson RL, Elia M, Jackson AA. Prevalence of risk of undernutrition is associated with poor health status in older people in the UK. Eur J Clin Nutr. 2003; 57(1):69–74.
19. Krzyminska-Siemaszko R, Mossakowska M, Skalska A, Klich-Raczka A, Tobis S, Szybalska A, et al. Social and economic correlates of malnutrition in Polish elderly population: the results of PolSenior study. J Nutr Health Aging. 2015; 19(4):397–402.
20. Kvamme JM, Gronli O, Jacobsen BK, Florholmen J. Risk of malnutrition and zinc deficiency in community-living elderly men and women: the Tromso Study. Public Health Nutr. 2014:1–7.
21. Chavarro-Carvajal D, Reyes-Ortiz C, Samper-Ternent R, Arciniegas AJ, Gutierrez CC. Nutritional assessment and factors associated to malnutrition in older adults: a cross-sectional study in Bogota, Colombia. J Aging Health. 2015; 27(2):304–19.

22. Isenring E, Baker J, Kerr G. Malnutrition and falls risk in community-dwelling older adults. J Nutr Health Aging. 2013; 17(3):277–9.
23. Meijers JM, van Bokhorst-de van der Schueren MA, Schols JM, Soeters PB, Halfens RJ. Defining malnutrition: mission or mission impossible? Nutrition. 2010; 26(4):432–40.
24. Sommer C, Kress M. Recent findings on how proinflammatory cytokines cause pain: peripheral mechanisms in inflammatory and neuropathic hyperalgesia. Neurosci Lett. 2004; 361(1–3):184–7.
25. Cole GK, Nigg BM, van Den Bogert AJ, Gerritsen KG. The clinical biomechanics award paper 1995 Lower extremity joint loading during impact in running. Clin Biomech (Bristol, Avon). 1996; 11(4):181–93.
26. Lebreton G, Tamion F, Coeffier M, Richard V, Bubenheim M, Bessou JP, et al. Modulation of mesenteric vasoreactivity and inflammatory response by protein undernutrition in cardiopulmonary bypass. Nutrition. 2013; 29(1):318–24.
27. Meng SJ, Yu LJ. Oxidative stress, molecular inflammation and sarcopenia. Int J Mol Sci. 2010; 11(4):1509–26.
28. McNulty AL, Miller MR, O'Connor SK, Guilak F. The effects of adipokines on cartilage and meniscus catabolism. Connect Tissue Res. 2011; 52(6):523–33.
29. Lee S, Kim TN, Kim SH. Sarcopenic obesity is more closely associated with knee osteoarthritis than is nonsarcopenic obesity: a cross-sectional study. Arthritis Rheum. 2012; 64(12):3947–54.
30. Guilak F, Fermor B, Keefe FJ, Kraus VB, Olson SA, Pisetsky DS, et al. The role of biomechanics and inflammation in cartilage injury and repair. Clin Orthop Relat Res. 2004; 423:17–26.
31. United Nations—Department of Economic and Social Affairs—Population Division. World Population Ageing 2013. ST/ESA/SER.A/348; 2013.