Knee Osteoarthritis and Risk of Hypertension: A Longitudinal Cohort Study

Nicola Veronese^{1,2,*} Brendon Stubbs^{3-5,*} Marco Solmi^{2,6,7} Toby O. Smith⁸
Marianna Noale¹ Patricia Schofield⁵ and Stefania Maggi¹

Abstract

Although previous research has indicated an association between osteoarthritis (OA) and cardiovascular disease, it remains unclear whether people with OA are at greater risk of developing hypertension. The aim of this study was to answer this uncertainty. We used the data of the Osteoarthritis Initiative, an ongoing public and private longitudinal study including people at higher risk of OA or having knee OA. Knee OA was defined through radiological and clinical assessment. Incident hypertension was defined as a systolic blood pressure ≥ 140 mmHg and/or a diastolic value ≥ 90 mmHg. Multivariate Cox's regression analyses were constructed considering the presence of knee OA as the exposure and incident hypertension as the outcome during a 96-month follow-up interval. A total of 3558 people with normative blood pressure values at baseline were analyzed (1930 OA/1628 controls). Incidence of hypertension within the follow-up interval was significantly higher in people with knee OA than in those without (60/[1000 person-years] vs. 55/[1000 person-years]; $p < 0.0001$). After adjusting for 13 confounders, people with knee OA had a 13% higher chance of developing hypertension (hazard ratio = 1.13; 95% confidence interval: 1.01–1.26; $p = 0.03$). Propensity score analysis did not alter these conclusions. In conclusion, this is the first longitudinal data analysis to demonstrate that people with knee OA have a higher chance of developing hypertension than those without OA. Our data suggest that monitoring blood pressure and prescribing health promotion interventions may be warranted among people with OA to mitigate the potential onset and adverse consequences of hypertension.

Keywords: osteoarthritis, hypertension, cardiovascular disease, epidemiology

Introduction

OSTEoarthritis (OA) is one of the most common chronic musculoskeletal diseases worldwide.^{1,2} It has a high prevalence, estimated to be 10% in men and 20% in women over the age of 60 years.³ Previous research has demonstrated that people with OA have a higher prevalence of cardiovascular diseases (CVDs), as reported by a recent meta-analysis including more than one million participants.⁴ People with OA have a number of risk factors for CVD, such as low levels of physical activity,⁵ high levels of depressive and anxiety symptoms,⁶ and metabolic abnormalities, such as

diabetes and metabolic syndrome.⁷ Although cross-sectional data suggest increased prevalence of CVD in those with OA,⁴ considerably less is known about the incidence of CVD. Some recent studies have suggested that people with OA may be at increased risk of developing CVD, although with no univocal results.⁸⁻¹⁰ This is concerning because CVD is a leading cause of global mortality, particularly in the Western world.¹¹ Furthermore, people with OA may be at increased risk of premature death because of CVD.¹²

The heightened risk of CVD among people with OA has been hypothesized to be increased and potentially influenced through various mechanisms. First, OA is often characterized

¹National Research Council, Neuroscience Institute, Aging Branch, Padova, Italy.

²Geriatrics Unit, Department of Geriatric Care, OrthoGeriatrics and Rehabilitation, Ente Ospedaliero Galliera Hospital, National Rel-evance and High Specialization Hospital, Genova, Italy.

³Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, United Kingdom.

⁴Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, United Kingdom.

⁵Faculty of Health, Social Care and Education, Anglia Ruskin University, Chelmsford, United Kingdom.

⁶Department of Neurosciences, University of Padova, Padova, Italy.

⁷National Health Care System, Padua, Italy.

⁸Faculty of Medicine and Health Sciences, University of East Anglia, Norwich Research Park, Norwich, United Kingdom.

*These authors are joint first authors.

by some degree of low-grade inflammation, which is also a potential CVD risk factor.¹³ Second, OA is characterized by relevant modifications of extracellular matrix (ECM),¹⁴ which may also increase the risk of CVD.¹⁵ Finally, pain and disability associated with OA may result in physical inactivity, which, over time, may subsequently lead to CVD.¹⁶

Although a significant number of cross-sectional studies have reported the association between OA and hypertension,^{17–24} no longitudinal studies have to the best of our knowledge examined the incidence of hypertension in this population. This is an important omission given that it remains unclear whether there is a causal relationship between OA and hypertension, which may provide further insights into its pathophysiology for those with OA. Although longitudinal research cannot infer causality, it can enable some clarification of the directionality of the cross-sectional relationships observed. Moreover, such analyses would also provide greater insight into the magnitude of this comorbidity within this population, which has clinical relevance for preventing the sequelae of hypertension such as stroke and CVD.²⁵ It may also identify appropriate targeted interventions to prevent hypertension in people with OA if a relationship were observed.

Given this, the purpose of this study was to determine whether people with knee OA have an increased chance of developing hypertension over an 8-year follow-up period than people without knee OA.

Methods

Data source and subjects

All participants in this study were recruited as part of the ongoing, publicly and privately funded, multicenter Osteoarthritis Initiative (OAI) study, which is available for public access (www.oai.ucsf.edu). Patients were recruited from four clinical sites in the United States (Baltimore, MD; Pittsburgh, PA; Pawtucket, RI; and Columbus, OH) between February 2004 and May 2006.

The OAI study protocol was approved by the institutional review board of the OAI Coordinating Center, University of California at San Francisco. Specific data sets used were those recorded during baseline and screening evaluations (November 2008) and those evaluating the participants until the last evaluation (after 96 months from baseline evaluation).

Cases

The OA cohort was the “cases” and were defined as (1) having knee OA and reported knee pain in a 30-day period in the past 12 months or (2) at high risk of developing knee OA at baseline (*e.g.*, overweight/obese, knee injury/operation, parents/siblings with total knee replacement, frequent knee-bending activities that increase risk, and hand/hip OA). All participants provided written informed consent. Knee OA was defined as the combination in the clinical reporting and assessment of pain and stiffness (*i.e.*, pain, aching, or stiffness in or around the knee on most days during the past year) and radiographical evidence of OA on the baseline fixed-flexion radiograph defined as the presence of tibiofemoral osteophytes (correspondent to Osteoarthritis Research Society International atlas grades 1–3, clinical center reading²⁶). In the OAI, the presence of pain, stiffness, and physical functioning (or disability) because of OA was as-

sessed through the Western Ontario and McMaster Universities Arthritis Index.²⁷ In brief, the responses for each subscale (pain, stiffness, and disability) are categorized on a 5-point Likert scale ranging from none (0 points) to extreme (4 points). The maximum possible score is 68, and the final score was normalized to 100 (range 0–100), with higher scores reflecting greater activity limitations.²⁷

Outcomes

The assessment of blood pressure was made through a single measurement performed by a trained nurse at the right arm, unless contraindicated. Hypertension was defined as a value of systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mmHg in agreement with the guidelines suggested for this condition.²⁸ In the OAI data set, blood pressure was recorded at baseline and follow-up points of 12, 24, 36, 48, 72, and 96 months. Incident hypertension was defined as a normal blood pressure measurement at baseline but a measurement reaching the hypertensive threshold within a subsequent follow-up interval.

Covariates

Several candidate explanatory variables were identified to explore the possible association between OA and incident hypertension. These included race (“whites” vs. others), smoking habits (“previous/current” vs. never), educational level (“degree” vs. others), yearly income (missing data, < or $\geq \$50,000$), body mass index (BMI) measured by a trained nurse with a cutoff of equal/more than 30 kg/m^2 for defining obesity, and medical comorbidities assessed through the modified Charlson comorbidity index (CCI), where higher scores indicate a greater number of morbidities and poorer health²⁹; physical activity was evaluated through the validated Physical Activity Scale for the Elderly.³⁰ The scale covers 12 different activities, such as walking, sports, and housework, and is scored from 0 without a maximum score; any depressive symptoms were derived from the 20-item Center for Epidemiologic Studies-Depression (CES-D) instrument.³¹ The range of possible values for scale scores is 0–60, with the higher scores indicating more depressive symptoms.³¹ Specifically the diagnosis of diabetes, chronic obstructive pulmonary disease, cancer, or CVD (*i.e.*, the presence of heart failure, heart attack, peripheral artery disease, and/or stroke) were reported descriptively in our analyses. Finally, also the use of nonsteroidal anti-inflammatory drugs (NSAIDs) (prescribed or not by a doctor) was included as potential confounder.

Statistical analyses

For continuous variables, data normality was assessed and confirmed using the Kolmogorov-Smirnov test. Data are presented as mean and standard deviation (SD) values for quantitative measures, and as frequency and percentages for discrete variables by the presence of knee OA. *p*-Values were calculated for continuous variables using the independent Student's *t*-test, and for categorical parameters, the chi-square test, comparing people with knee OA with those without.

The incidence of cases who developed hypertension within the follow-up period was calculated as the number of

FIG. 1. Cohort flowchart.

new cases per 1000 person-years during the follow-up. Multivariate Cox's regression analyses were constructed using the presence of knee OA as the exposure and incident hypertension during the follow-up period as the outcome. The multivariate model included all confounding factors that were significantly different between participants with and without knee OA at baseline or were significantly associated with incident hypertension at follow-up (denoted as p -value <0.05 for both selections). Multicollinearity among covariates was assessed through variance inflation factor, taking a cutoff of two as reason for exclusion. No variable was excluded for this reason. The basic model was not adjusted for any confounders, whereas the fully

adjusted model adjusted for baseline values of age, gender, race, BMI, education, smoking habits, yearly income, CCI, baseline PASE score, baseline CES-D score, use of NSAIDs, and baseline values of systolic and diastolic BP. In a sensitivity analysis, to better control the role of possible confounding effects on the association between knee OA and incident hypertension, the propensity score matching methodology was applied.³² Data of Cox's regression analyses were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

Several sensitivity analyses were conducted for evaluating the interaction between the presence of knee OA and selected factors (*e.g.*, age $<$ or ≥ 65 years, obesity, presence of any disease, yearly income, gender, race, education, smoking habits, yearly income, and presence/absence of diabetes and CVD at baseline) in predicting hypertension at follow-up, although no factor was significant.

All analyses were performed using the SPSS 21.0 for Windows (SPSS, Inc., Chicago, IL). All statistical tests were two-tailed and statistical significance was assumed for a p -value <0.05 .

Results

Study participants

Among 4796 potentially eligible individuals, 1005 were excluded because of pre-existing hypertension at baseline assessment, 33 were excluded as there was insufficient information to confirm a diagnosis of knee OA, and 200 were lost at follow-up. Accordingly, 3558 participants were eligible for this study (Fig. 1).

TABLE 1. BASELINE CHARACTERISTICS CLASSIFIED ACCORDING TO PRESENCE OR NOT OF KNEE OSTEOARTHRITIS

Variable	Knee osteoarthritis (n = 1930)	No osteoarthritis (n = 1628)	p*
Age (years)	61.8 (9.1)	58.9 (8.8)	<0.0001
Females, n (%)	1125 (58.3)	993 (61.0)	0.11
White race, n (%)	1574 (81.6)	1340 (82.5)	0.48
BMI (kg/m ²)	29.2 (4.8)	27.1 (4.5)	<0.0001
Smoking [previous/current], n (%)	732 (45.4)	878 (46.0)	0.73
College and above, n (%)	598 (36.9)	552 (28.8)	<0.0001
Yearly income ($<$ \$50,000)	719 (37.3)	504 (31.0)	<0.0001
PASE score (points)	158.4 (80.7)	170.0 (84.0)	<0.0001
Medical conditions			
Diabetes, n (%)	167 (8.8)	78 (4.9)	<0.0001
COPD, n (%)	38 (2.0)	34 (2.1)	0.81
Cardiovascular diseases, n (%)	131 (7.0)	88 (5.5)	0.08
Cancer, n (%)	101 (5.2)	72 (4.4)	0.27
Charlson comorbidity score (points)	0.4 (0.9)	0.3 (0.8)	0.01
NSAIDs, n (%)	362 (22.3)	483 (25.1)	0.06
CES-D (points)	6.4 (6.7)	6.5 (6.5)	0.93
Systolic blood pressure (mmHg)	119.4 (10.8)	117.1 (11.3)	<0.0001
Diastolic blood pressure (mmHg)	73.4 (8.1)	72.7 (8.6)	0.02

Numbers are mean values (and standard deviations) or number (and percentages), as appropriate.

*Unless otherwise specified, p -values are calculated with an independent Student's t -test for continuous and with a chi-square test for categorical variables, respectively.

BMI, body mass index; CES-D, Center for Epidemiologic Studies-Depression; COPD, chronic obstructive pulmonary disease; NSAIDs, nonsteroidal anti-inflammatory drugs; PASE, physical activity scale for the elderly.

FIG. 2. Risk of hypertension by presence of knee osteoarthritis at baseline.

Baseline analyses

The 3558 participants (1439 males/2119 females) had a mean age of 60.4 ± 9.0 years (range: 45–79). At baseline, 1930 people with knee OA were compared with 1628 people without knee OA.

The baseline characteristics of knee OA and non-OA participants (*i.e.*, participants at higher risk of knee OA) are reported in Table 1. The OA participants were more frequently older (61.8 ± 9.1 vs. 58.9 ± 8.8 years) than those without OA ($p < 0.0001$), whereas no significant differences emerged in terms of gender and race. Individuals with knee OA had significantly higher BMI values, had a higher educational level and income, and they were less active than the non-OA individuals (Table 1). Regarding medical conditions, participants with OA more frequently reported diabetes and had a higher CCI (Table 1). Finally, participants with knee OA showed significantly higher systolic blood pressure (119.4 ± 10.8 vs. 117.1 ± 11.3 mmHg, $p < 0.0001$) and diastolic blood pressure (73.4 ± 8.1 vs. 72.7 ± 8.6 mmHg, $p = 0.02$) values at baseline than participants without OA. No significant differences

emerged in terms of the use of NSAIDs between individuals with knee OA and the controls ($p = 0.06$).

Follow-up analyses

After a 96-month follow-up, 1428 individuals (40.2% of the baseline population) developed hypertension, with an incidence of 57 cases (95% CI: 23–85) per 1000 person-years. The incidence of newly diagnosed hypertension was significantly higher in people with knee OA at baseline (60 per 1000 person-years; 95% CI: 37–85) than those without (55 per 1000 person-years; 95% CI: 23–89) ($p < 0.0001$) as shown in Figure 2.

Figure 3 shows the means of systolic (left panel) and diastolic (right panel) blood pressure by presence of knee OA at baseline during the follow-up period. The presence of knee OA at baseline was associated with higher blood pressure mean values for systolic ($p = 0.04$), but not for diastolic blood pressure ($p = 0.97$).

On multivariate analysis, significant predictors of incident hypertension were knee OA that increased the chances of incident hypertension by 13% (HR = 1.13; 95% CI: 1.01–1.26; $p = 0.03$), age (for each year, HR = 1.02; 95% CI: 1.001–1.02; $p < 0.01$), female gender (HR = 1.15; 95% CI: 1.03–1.28; $p = 0.02$), non-white ethnicity (HR = 1.53; 95% CI: 1.34–1.75; $p < 0.01$), BMI (1 point corresponded to an increase in incident hypertension of 2% HR = 1.02; 95% CI: 1.01–1.03; $p = 0.002$), and systolic blood pressure at baseline (each mmHg increases the risk of hypertension at follow-up of 4%; HR = 1.04; 95% CI: 1.03–1.05; $p < 0.01$). Using a propensity score, the association between knee OA at baseline and incident hypertension remained evident (HR = 1.11; 95% CI: 1.01–1.24; $p = 0.048$).

Discussion

In this large prospective study, our data suggest that the presence of knee OA is associated with a small but significant increased chance of developing hypertension over an 8-year follow-up. Specifically, after adjusting for potential confounders (including baseline blood pressure values at

FIG. 3. Mean systolic (left) and diastolic (right) blood pressure values by the presence of knee osteoarthritis at the baseline. Lighter gray line represents people without knee osteoarthritis; darker line represents those with knee osteoarthritis.

baseline), knee OA was associated with a 13% greater chance of developing hypertension.

Knee OA was a significant predictor for developing hypertension at follow-up. Several mechanisms have been suggested to explain this possible association.³³ First, people with knee OA without hypertension at baseline may already have pathological modifications of ECM, leading to reduced elasticity of blood vessels and consequently to hypertension. These hypotheses are partially confirmed by our finding because the higher incidence of hypertension observed in people with knee OA at baseline seems to be attributable to higher systolic blood pressure values than diastolic blood pressure values, wherein it is known that systolic blood pressure is more dependent on ECM changes than diastolic blood pressure.³⁴ Second, molecules such as disintegrin and metalloproteinase involved in ECM remodeling appear to have a role in the development of hypertension.³⁵ Interestingly, as shown by our survival curves, people with knee OA at baseline developed hypertension mostly at the end of the follow-up. Even if we do not exactly know the reasons, we can assume that the pathways mentioned before need time for altering the ECM and so leading to hypertension. However, other studies are needed in this sense. Third, although OA is not considered an inflammatory arthritis, people with OA frequently present with a low-chronic inflammation grade^{35,36} that could have a role in the development of CVD and hypertension.³⁷ Finally, although adjusted for potential confounders, the conditions common between OA and hypertension (such as age, obesity, diabetes, and reduced physical activity) may be additional explanatory factors. Of particular note is that people with OA usually report lower levels of physical activity and are more sedentary than those without OA³⁸ and these factors probably play a relevant role in the development of hypertension.³⁹ However, using the propensity score and the analyses adjusted for these potential confounders, our findings did not significantly change, indicating that the role of these baseline confounders is probably marginal.

Previous studies investigating the role of OA as potential CVD risk factor reported that people with OA had a significant higher prevalence of hypertension.^{4,8–10} However, the nature of these studies did not allow the directionality of this association. We attempted to address this limitation in the literature in this study. The data propose that people with OA had a higher risk of developing hypertension at follow-up, indicating that blood pressure should be strictly monitored in these subjects. Of note, almost half of the people with knee OA at baseline assessment developed hypertension, suggesting the importance of this condition. Improved surveillance and management of this condition can have a significant impact on long-term health and prevention of diseases such as stroke and CVD.

Our findings should be considered within the limitations of our study. The measurement of blood pressure was made on one occasion with insufficient data to determine whether some individuals had blood pressure controlled through medications. The findings of this study, therefore, related to new-onset hypertension or uncontrolled hypertension with or without drug treatment. Second, the diagnosis of comorbidities was self-reported and not verified through a review of the participant's

medical notes. Third, we do not have sufficient information regarding the use of blood pressure-lowering medications, which could introduce bias in our findings. It is in fact possible that people having normal blood pressure at baseline is because of the use of medications and vice versa. Finally, we did not assess any inflammatory or ECM marker, although inflammation could be associated with higher CVD risk.⁴⁰ Nonetheless, allowing for these caveats, our study involves a large population over a long follow-up period. Moreover, we adjusted our analyses for multiple important confounders.

In conclusion, our study demonstrated that people with knee OA have a greater risk of developing hypertension over an 8-year period. Since some interventions aiming to improve OA symptoms (*e.g.*, increasing physical activity and weight loss reduction) seem to be effective from a cardiac perspective, further studies are needed to better understand whether treatment of OA can decrease hypertensive risk in these individuals.

Acknowledgments

The OAI is a public-private partnership comprising five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; and N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI was managed by the Foundation for the National Institutes of Health.

Disclaimer

This article was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners. The funding sources did not have any role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Author Disclosure Statement

No competing financial interests exist.

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013;380:2163–2196.
2. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: Estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73:1323–1330.
3. Hilgsmann M, Cooper C, Arden N, Boers M, Branco JC, Luisa Brandi M, et al. Health economics in the field of osteoarthritis: An expert's consensus paper from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Semin Arthritis Rheum* 2013;43:303–313.

4. Hall AJ, Stubbs B, Mamas MA, Myint PK, Smith TO. Association between osteoarthritis and cardiovascular disease: Systematic review and meta-analysis. *Eur J Prev Cardiol* 2016;23:938–946.
5. Stubbs B, Hurley M, Smith T. What are the factors that influence physical activity participation in adults with knee and hip osteoarthritis? A systematic review of physical activity correlates. *Clin Rehabil* 2015;29:80–94.
6. Stubbs B, Aluko Y, Myint PK, Smith TO. Prevalence of depressive symptoms and anxiety in osteoarthritis: A systematic review and meta-analysis. *Age Ageing* 2016;45:228–235.
7. Louati K, Vidal C, Berenbaum F, Sellam J. Association between diabetes mellitus and osteoarthritis: Systematic literature review and meta-analysis. *RMD Open* 2015;1:e000077.
8. Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: Population based cohort study. *BMJ* 2011;342:d1165.
9. Veronese N, Trevisan C, De Rui M, Bolzetta F, Maggi S, Zambon S, et al. Association of osteoarthritis with increased risk of cardiovascular diseases in the elderly: Findings from the Progetto Veneto Anziano Study Cohort. *Arthritis Rheumatol* 2016;68:1136–1144.
10. Rahman MM, Kopec JA, Cibere J, Goldsmith CH, Anis AH. The relationship between osteoarthritis and cardiovascular disease in a population health survey: A cross-sectional study. *BMJ Open* 2013;3:10.
11. Naghavi M, Wang H, Lozano R, Davis A, Liang X, Zhou M, et al. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;385:117–171.
12. Veronese N, Cereda E, Maggi S, Luchini C, Solmi M, Smith T, et al. Osteoarthritis and mortality: A prospective cohort study and systematic review with meta-analysis. *Semin Arthritis Rheum* 2016;46:160–167.
13. Bonnet CS, Walsh DA. Osteoarthritis, angiogenesis and inflammation. *Rheumatology* 2005;44:7–16.
14. Hardingham T. Extracellular matrix and pathogenic mechanisms in osteoarthritis. *Curr Rheumatol Rep* 2008;10:30–36.
15. Velagaleti RS, Gona P, Sundström J, Larson MG, Siwik D, Colucci WS, et al. Relations of biomarkers of extracellular matrix remodeling to incident cardiovascular events and mortality. *Arterioscler Thromb Vasc Biol* 2010;30:2283–2288.
16. Stubbs B, Binnekade TT, Soundy A, Schofield P, Huijnen IPJ, Eggermont LHP. Are older adults with chronic musculoskeletal pain less active than older adults without pain? A systematic review and meta-analysis. *Pain Med* 2013;14:1316–1331.
17. Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Association of knee osteoarthritis with the accumulation of metabolic risk factors such as overweight, hypertension, dyslipidemia, and impaired glucose tolerance in Japanese men and women: The ROAD study. *J Rheumatol* 2011;38:921–930.
18. Sohn M-W, Manheim LM, Chang RW, Greenland P, Hochberg MC, Nevitt MC, et al. Sedentary behavior and blood pressure control among osteoarthritis initiative participants. *Osteoarthritis Cartilage* 2014;22:1234–1240.
19. Nielen MMJ, van Sijl AM, Peters MJL, Verheij RA, Schellevis FG, Nurmohamed MT. Cardiovascular disease prevalence in patients with inflammatory arthritis, diabetes mellitus and osteoarthritis: A cross-sectional study in primary care. *BMC Musculoskelet Disord* 2012;13:150.
20. Morovic-Vergles J, Salamon L, Marasovic-Krstulovic D, Kehler T, Sakic D, Badovinac O, et al. Is the prevalence of arterial hypertension in rheumatoid arthritis and osteoarthritis associated with disease? *Rheumatol Int* 2013;33:1185–1192.
21. Miksch A, Hermann K, Rolz A, Joos S, Szecsenyi J, Ose D, Rosemann T. Additional impact of concomitant hypertension and osteoarthritis on quality of life among patients with type 2 diabetes in primary care in Germany—A cross-sectional survey. *Health Qual Life Outcomes* 2009;7:19.
22. Liu Y, Zhang H, Liang N, Fan W, Li J, Huang Z, et al. Prevalence and associated factors of knee osteoarthritis in a rural Chinese adult population: An epidemiological survey. *BMC Public Health* 2016;16:94.
23. Hochberg MC. New paradigms in the management of osteoarthritis patients with hypertension. *Osteoarthritis Cartilage* 2010;18:S1–S2.
24. Bae Y-H, Shin J-S, Lee J, Kim M, Park KB, Cho J-H, Ha I-H. Association between hypertension and the prevalence of low back pain and osteoarthritis in Koreans: A cross-sectional study. *PLoS One* 2015;10:e0138790.
25. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension. *Ann Intern Med* 2003;139:761–776.
26. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cartilage* 2016;15:A1–A56.
27. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;15:1833–1840.
28. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: A statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association. *Hypertension* 2005;45:142–161.
29. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care* 1996;34:73–84.
30. Washburn RA, McAuley E, Katula J, Mihalko SL, Boileau RA. The physical activity scale for the elderly (PASE): Evidence for validity. *J Clin Epidemiol* 1999;52:643–651.
31. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
32. Yanovitzky I, Zanutto E, Hornik R. Estimating causal effects of public health education campaigns using propensity score methodology. *Eval Program Plann* 2005;28:209–220.

33. Fernandes GS, Valdes AM. Cardiovascular disease and osteoarthritis: Common pathways and patient outcomes. *Eur J Clin Invest* 2015;45:405–414.
34. Xu J, Shi G-P. Vascular wall extracellular matrix proteins and vascular diseases. *Biochim Biophys Acta* 2014;1842: 2106–2119.
35. Berenbaum F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis Cartilage* 2013;21:16–21.
36. Berenbaum F, Eymard F, Houard X. Osteoarthritis, inflammation and obesity. *Curr Opin Rheumatol* 2013;25: 114–118.
37. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, et al. Low grade inflammation and coronary heart disease: Prospective study and updated meta-analyses. *BMJ* 2000;321:199–204.
38. Wallis JA, Webster KE, Levinger P, Taylor NF. What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. *Osteoarthritis Cartilage* 2013;21:1648–1659.
39. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol* 2012;2: 1143–1211.
40. Libby P. Inflammation and cardiovascular disease mechanisms. *Am J Clin Nutr* 2006;83:456S–460S.

Address correspondence to:
Nicola Veronese
National Research Council
Neuroscience Institute
Aging Branch
Via Giustiniani
Padova 2-35128
Italy

E-mail: ilmannato@gmail.com

Received: January 3, 2017

Accepted: June 23, 2017