Reasons why osteoarthritis predicts mortality: path analysis within a Cox proportional hazards model

Purpose:

There is increasing evidence for a relationship between osteoarthritis and premature mortality. The current and expected increase in prevalence of osteoarthritis indicates a need to understand the reasons for premature mortality and to guide approaches to clinical care and population health. Osteoarthritis is associated with comorbidity. It is possible that specific comorbidities enhance the mechanism by which osteoarthritis results in mortality. The purpose of this study was to identify potential mechanisms of the impact of osteoarthritis on mortality and examine the role of specific comorbidities (anxiety, depression, cognitive impairment, insomnia, obesity) and walking frequency. The study uses a novel approach to examine mediation using path analysis with Cox proportional hazard modelling (survival analysis).

Methods:

A population-based prospective cohort study was conducted using data from the North Staffordshire Osteoarthritis Project (NorStOP), in which primary care medical record data was linked to self-report information collected by questionnaire in adults aged 50 years and over (n=8066). Individuals were defined as having osteoarthritis if they had consulted general practice for osteoarthritis, identified by Read codes in the primary care medical record, and indicated moderate to severe pain interference in daily life in the Medical Outcomes Short Form 36 at baseline (2002). A Cox proportional hazards analysis was performed to determine the total effect (TE) of osteoarthritis on mortality, both with and without adjustment for confounding variables (age, gender, education level, and occupational status). Within the Cox model, path analysis was used to decompose the TE to assess the indirect (IE) and direct effects (DE) for each of six potential mediators (anxiety, cognitive impairment, depression, insomnia, obesity, walking frequency; all measured by questionnaire) with adjustment for confounders. Results are expressed as hazard ratios (HR); bootstrap resampling was used to generate 95% confidence intervals (95% CIs).

Results:

Mean age of participants was 65.2 (SD 9.8) years and 51.6% were female. 2396 (29.7%) had osteoarthritis. Participants were followed up over 10 years during which time 1188 (14.7%) died. Osteoarthritis was significantly associated with mortality in unadjusted (HR 1.39; 95% CI 1.24, 1.57) and adjusted analysis (1.14; 1.01, 1.28). The relationship between osteoarthritis and mortality was mediated by walking frequency and four of the five comorbidities (obesity did not mediate the relationship (IE HR 1.00; 0.98, 1.02)). The strongest mediator was walking frequency (TE 1.13; 1.01, 1.27: DE 1.01; 0.90, 1.14: IE 1.12; 1.09, 1.16), followed by depression (IE 1.10; 1.07, 1.15), cognitive impairment (IE 1.05; 1.02, 1.08)), insomnia (IE 1.04; 1.02, 1.07) and anxiety (IE 1.03; 1.00, 1.06).

Conclusions:

This is the first study to examine mediation and highlights the importance of a number of targets to reduce mortality in older adults with osteoarthritis. Encouraging people to maintain levels of physical activity and targeting a reduction in physical limitation in clinical practice to allow this, is important. The findings also confirm the need to consider the impact of comorbidity in older adults with osteoarthritis to reduce the increased risk of mortality.