self-reported arthritis and those without arthritis reporting chronic or sporadic joint symptoms compared to those who have no arthritis and no joint symptoms.
Methods: Data from the 2008 Canadian Community Health Survey (15+; n = 66,013) were used for analyses. Respondents were asked about arthritis as a long-term chronic health condition diagnosed by a health professional. Participants not-reporting arthritis were asked about joint symptoms excluding back and neck over the past 12 months. Analyses were conducted for the following mutually exclusive groups: arthritis, chronic joint symptoms (symptoms present on most days in the past month), sporadic joint symptoms (other joint symptoms in the past 12 months (SJS)), and no arthritis and no joint symptoms (NJS). Log-Poisson regression was used to determine risk factors for each of these groups. Similar regressions, adjusting for socio-demographic, lifestyle factors, and comorbidities were used to estimate the risks of reporting physical inactivity, health outcomes (poor/fair overall health, poor/fair mental health, activity limitation), and five measures of healthcare use.
Results: 16.0% of the population reported arthritis, 10.1% reported CJS and 11.6% reported SJS. Individuals with arthritis were older than those with CJS or SJS. Women reported arthritis and CJS more often while men reported SJS. Other than age, the profile of risk factors for arthritis and CJS was similar, notably obesity and overweight. After adjusting for age, sex, SES, lifestyle factors and comorbidities, prevalence ratios showed similar risks for physical inactivity, health outcomes and health care use for the arthritis and CJS group, and these were higher than those for SJS group.
Conclusions: CJS was reported by one-in-ten of the adult population. The similarities in risk factors, other than younger age, for CJS and arthritis suggest that the CJS group represent people in early stages of arthritis (based on population frequency most likely osteoarthritis) who have not yet being diagnosed. The impact that CJS has on health outcomes and increased healthcare use was similar to that of arthritis, suggesting that arthritis education and management interventions are likely beneficial for this group with possible unrecognized OA.

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THE mtDNA HAPLOGROUP J MODULATES THE NITRIC OXIDE (NO) PRODUCTION AND TELOMERE LENGTH. ROLE IN OSTEOARTHRITIS (OA)

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Purpose: (1) To measure the telomere length of chondrocytes and peripheral blood leukocytes (PBLs) in OA patients and healthy controls, and (2) To analyze the incidence of the mtDNA haplogroup J in both the telomere length and the Nitric Oxide (NO) production, as indirect approaches of oxidative stress.
Methods: The telomere length was analyzed by means of a validated qPCR method. For the comparison of the telomere length between OA patients and healthy controls, the DNA was obtained from both uncultured chondrocytes and blood of the same individual in a cohort of 39 OA patients and 20 healthy controls from Hospital Universitario A Coruña. A second larger cohort of 166 healthy controls and 79 OA patients was used to compare the telomere length of PBLs between haplogroup J (n = 155) and non-J carriers (n = 90), as well as between OA patients and healthy controls. The NO production was assessed in 7 carriers of the haplogroup J and 21 non-J carriers by means of the Griess reagent in the supernatants of cultured chondrocytes. Inducible nitric oxide synthase (iNOS) mRNA from these samples was analyzed by qPCR. Appropriated statistical approaches were carried out using SPSS v1.17.
Results: The telomere length in chondrocytes was assessed as the ratio "*telomere length of chondrocytes: telomere length of PBLs of the same individual*", and was significantly shorter in OA patients than in healthy controls (1.72±0.41 vs 2.12±0.64; mean±sd; p = 0.028). No statistical differences were detected between OA patients and healthy controls when analyzed the telomere length of PBLs in the larger cohort set; however, carriers of the haplogroup J showed a significantly longer telomere length of PBLs than non-J carriers, regardless of age, gender and diagnosis (p = 0.025). The NO production for chondrocytes carrying this haplogroup was also significantly lower (p = 0.05), and a strong positive correlation between NO production and iNOS expression was also observed (correlation coefficient = 0.791, p < 0.001).
Conclusions: The decreased telomere length in chondrocytes from OA affected joints may imply a local advanced senescence that could contribute to the pathogenesis or progression of OA. The relation of the mtDNA haplogroup J with both lower NO production and longer telomere length of PBLs indicates a lower oxidative stress in carriers of the mtDNA haplogroup J, which could explain the protective effect of this haplogroup in the OA disease.

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LOSS OF METHYLATION IN CPG SITES IN THE NUCLEAR FACTOR KAPPA B (NF-κB) ENHANCER ELEMENTS OF INDUCIBLE NITRIC OXIDE SYNTHASE (INOS) IS RESPONSIBLE OF GENE INDUCTION IN HUMAN ARTICULAR CHONDROCYTES

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Osteoarthritis (OA) is a complex disease of the joint, associated with cartilage degradation by matrix proteases (aggrecanases and collagenases). Nitric oxide (NO), the product of inducible nitric oxide synthase (iNOS), not only suppresses the synthesis of cartilage matrix, but also increases expression of proteases in OA; however, normal chondrocytes do not produce NO. Although iNOS is readily inducible in almost all rodent cell types in culture, in contrast, normal human cells are recalcitrant to induction with cytokines due to epigenetic silencing by DNA methylation. Unlike the murine iNOS promoter, the first 1.0 kb of the human iNOS gene 5′ flanking region is not sufficient for iNOS induction. Instead, inducible NF-kB elements upstream −4.7 kb are required for cytokine activation of the promoter. However, it is not known whether the activation of iNOS in OA chondrocytes can be attributed to epigenetic "unsilencing" with implications for therapeutic intervention in OA.
Objective: To examine and correlate mRNA expression of iNOS with the DNA methylation status of specific CpG sites in the iNOS promoter and NF-kB enhancer elements regions, and to examine if the increased expression of iNOS in OA chondrocytes is attributable to loss of DNA methylation.
Methods: Control chondrocytes were obtained from fracture neck of femur (#NOF) patients; these patients typically suffer from osteoporosis, which does not affect the cartilage. #NOF patients are widely used as a suitable non-OA control. OA chondrocytes were isolated from the femoral heads of patients undergoing hip replacement surgery due to OA. Genomic DNA and total RNA were extracted simultaneously. Expression of iNOS was quantified by qRT-PCR and the DNA methylation status of the iNOS promoter and enhancer regions was determined by bisulfite modification, followed either by cloning and sequencing or pyrosequencer analysis to quantify percentage methylation. CpG methylation on activities of both iNOS enhancer and promoter was determined using reporter assay with CpG-free luciferase vector and a CpG methyltransferase (M.SssI). On the other hand, co-transfections with NF-kB subunits (p50, p65 and p50/p65) were carried out to analyse the effect of this transcription factor on iNOS activity.
Results: OA samples showed a 13-fold increase in iNOS expression compared to #NOF samples (n = 14, P < 0.05). The iNOS promoter has only 7 CpG sites in over 1000bp, 6 of which were highly methylated in both controls and OA and the CpG site at −289 was un-methylated in both groups; the sites in the coding region (+13, +33 and +38), were largely unmethylated in #NOF and OA patients. Three NF-kB enhancer elements regions were analyzed by pyrosequencing, the enhancer regions at −5.2 kb and −5.4 kb were found to be totally unmethylated in all samples (<10%); however, the enhancer region at −5.8 was significantly de-methylated in OA samples (n = 12, P < 0.05) compared with #NOF samples, with an approximate 10% loss of methylation. Transcriptional activation of iNOS was possible after co-transfection of the −5.8 kb enhancer element with p65 (45-fold increase, n = 5, P < 0.05) or p50/p65 NF-kB subunits (15-fold increase, n = 5, P < 0.05). Critically, methylation treatment of the enhancer element was associated with a 25-fold decrease in iNOS activity in reporter assay.