Review of soluble biomarkers of osteoarthritis: lessons from animal models

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PURPOSE

Osteoarthritis (OA) is one of the leading causes of disability within the adult population. Currently, its diagnosis is mainly based on clinical examination and standard radiography. To date, there is no way to detect the disease at a molecular level, before the appearance of structural changes and symptoms. So an attractive alternative for monitoring OA is the measurement of biochemical markers in blood, urine or synovial fluid, which could reflect metabolic changes in joint tissue and therefore disease onset and progression. Animal models are relevant to investigate the early stage of OA and metabolic changes occurring in joint tissues. The goal of this review is to summarize the scientific data available in the literature on soluble biomarkers in animal models of OA.

METHODS

A literature search was conducted using the Pubmed/Medline and Scopus databases between February 1995 and December 2014. All original papers, systematic and narrative reviews published in French or in English were considered. The author selected the papers on the basis of the title and abstract and, then assessed whether the study met the inclusion criteria. Then the full article was retrieved. The flow diagram for selection of studies is presented in **Fig.1**.

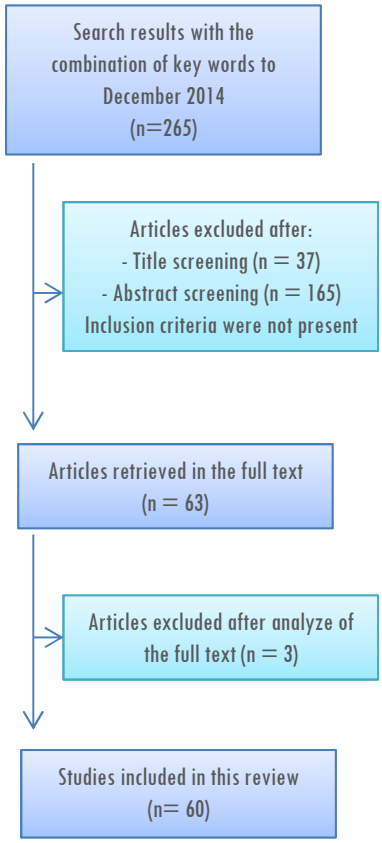

Fig.1

RESULTS

We summarized the data of 59 studies and proposed a classification scheme for OA biomarkers in animal studies, largely inspired of the BIPED classification. The most investigated biomarkers in terms of burden of disease assessment are those derived from type II collagen metabolism. Most particularly, ColI2-1 is particularly precocious. In serum of guinea pig, ColI2-1 increase is coincident with the early disruption of the collagen fibril visible by birefringence before the appearance of structural changes observable by conventional microscopy.

Many interventions have been tested in rat, dog, horse and guinea pig models using biomarkers derived from type II collagen and aggrecan. Among diagnostic biomarkers, in guinea-pigs, only the ratio C2C/CPII were demonstrated to discriminate OA-prone Hartley and strain 13 animals. Moreover, in mice, serum levels of MDA, CTX-II and CPII were elevated in obese and hyperlipidemic STR/ORT (STR) mice compared to control CBA mice. Finally, to our knowledge there is no biomarker that can be classified as prognostic biomarkers.

CONCLUSION

This systematic review indicates that some markers could be valuable to evaluate the burden of OA disease and to assess the therapeutic response in animal models. The most investigated biomarker in terms of burden of disease assessment are those derived from type II collagen metabolism. Since OA represents a process of matrix damage, turnover, and attempted repair, the use of multiple biomarkers, both anabolic and catabolic, could likely be most accurate in characterizing OA disease. Finally, soluble biomarkers can be as useful "drug development tools" that should be early integrated in the research program of new drugs.

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