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Review

Inter-relations between osteoarthritis and metabolic syndrome: A common link?

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ABSTRACT

Osteoarthritis (OA) is a degenerative disorder of the joint, principally occurring during aging, and characterized by a focal degradation of cartilage. It is the most prevalent rheumatic disease in industrialized countries and represents the second cause of disability in France. However, the etiology of OA remains unclear. There is only one cell type found in cartilage, chondrocyte, which is responsible for its repair and the synthesis of the elements of the extra-cellular matrix. A dysfunction of these cells results in an imbalance between repair and degradation in cartilage, leading to its destruction.

Recently, a link between OA and metabolic syndrome (MetS) has been suggested, introducing a notion of metabolic OA, and a new vision of the disease. MetS is characterized by a cluster of factors (insulin resistance, hypertension, dyslipidemia, visceral obesity), although there is still no clear definition of it. During the 20th century, MetS dramatically increased with changes in population lifestyle, becoming a major health issue in industrialized countries. MetS concerns 10–30% of the worldwide population, but is prevalent in 59% of OA patients. Patients with both OA and MetS have more severe symptoms, occurring sooner than in the general population. Indeed, OA is generally a disease concerning the population over 65 years old, but with an associated MetS the target population is around 50 years old.

In this review, we will focus on common factors in OA and MetS, such as hypertension, obesity, dyslipidemia, mitochondrial dysfunction and hyperglycemia, linking one disease to the other.

Contents

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Abbreviations list

ADAMTS	A Disintegrin And Metalloproteinase with ThromboSpondin motifs
AGE	Advanced glycation end-products
AHA/NHLBI	American Heart Association/National Heart, Lung, Blood Institute
ATP	Adenosine triphosphate
BMI	Body mass index
BMP	Bone morphogenetic protein
CEL	N-ε-(carboxyethyl)lysine
CML	N-ε-(carboxymethyl)lysine
COX-2	Cyclooxygenase 2
CVD	Cardiovascular disease
GLUT-1	Glucose transporter 1
HDL-C	High-density lipoprotein-cholesterol
IDF	International Diabetes Federation
IL-1	Interleukin-1
LDL-R	Low-density lipoprotein receptor
LOX-1	Lectin-like oxidized lipoprotein receptor-1
LXR	Liver X receptor
MCP-1	Monocyte chemoattractant protein-1
MetS	Metabolic syndrome
MG	Methylglyoxal
MMP	Matrix metalloproteinase
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NO	Nitric oxide
OA	Osteoarthritis
p38 MAPK	p38 mitogen-activated protein kinase
PPAR γ	Peroxisome proliferator-activated receptor γ
PGE2	Prostaglandin E2
RAGE	Receptor for advanced glycation end-products
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
sOb-R	Soluble leptin receptor
sRAGE	Soluble receptor for advanced glycation end-products
TGF-β	Transforming growth factor β
TNF-α	Tumor necrosis factor α
VEGF	Vascular endothelial growth factor
WHO	World Health Organization

1. Introduction

Osteoarthritis (OA) is the most common rheumatic disease in the world and represents the first cause of disability in the world after 40 years old [1,2]. It is generally associated with aging, and several risk factors include sex, body weight, articular injuries, metabolic disorders and genetic predispositions [3] but the etiology is still not well known.

OA is a degenerative joint disease characterized by cartilage degradation, inflammation of the synovial membrane and restructuration of subchondral bone. The disease results from the loss of balance between degradation and repair inside cartilage, in favor of degradation, with increased activity of catabolic enzymes such as matrix metalloproteinases (MMP-1, -3 and -13) and decreased production of type II collagen and aggrecan. Chondrocytes, the only cell type found in cartilage, are responsible for the repair and biosynthesis of elements of the extracellular matrix (type II collagen, proteoglycans etc.). Dysfunction of these cells results in an imbalance between repair and degradation in cartilage, which leads to its weakening and finally destruction [4]. During OA pathogenesis, quiescent chondrocytes become active, thus triggering their cellular proliferation and increased production of catabolic enzymes [4].

Type II collagen and aggrecan are the main components in articular cartilage: aggrecan monomers are linked to type II collagen fibrils, their association conferring the mechanical properties of cartilage (elasticity and resistance to compression). Aggrecan degradation seems to be an early event in OA; however, the loss of this protein can be reversed by *de novo* synthesis by chondrocytes. Unlike aggrecan, collagen degradation is irreversible, because collagen fibrils have a very long lifetime and therefore a low turnover under normal physiological conditions [5]. In OA disease, MMP-13 is the main expressed collagenase, but expression of MMP-1 and 3 can also be enhanced [6].

Recently, a possible link between OA and metabolic syndrome (MetS) has been revealed, for a notion of metabolic OA, and with it, a new view of both diseases. Metabolic OA could now be considered as a subtype of OA, the second most frequent after aging [7]. It targets a middle-aged population (between 45 and 65 years) [8] and patients show faster development and progression of the