Annals of Physical and Rehabilitation Medicine 59 (2016) 157–160

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Review

Osteoarthritis, obesity and type 2 diabetes: The weight of waist circumference

Martine Duclos [a,b,c,*]

[a] Department of Sport Medicine and Functional Explorations, University-Hospital (CHU), G.-Montpied Hospital, 63003 Clermont-Ferrand, France
[b] INRA, UMR 1019, UNH, CRNH Auvergne, 63000 Clermont-Ferrand, France
[c] Clermont University, University of Auvergne, Unité de Nutrition Humaine, BP 10448, 63000 Clermont-Ferrand, France

ARTICLE INFO

Article history:
Received 9 December 2015
Accepted 13 April 2016

Keywords:
Obesity
Type 2 diabetes
Abdominal obesity
Osteo-arthrosis
Adipokines
Physical activity

ABSTRACT

Background: Obesity and type 2 diabetes (T2D) significantly increase the risk of developing an arthritic condition.
Methods: We performed a review of literature on the pathophysiological mechanisms that underpin the relationships between obesity, T2D and osteoarthritis (OA).
Results: The pathophysiology of the link between obesity and OA is related to both the direct effect of excess mechanical loads being placed on the cartilage and to an adipose tissue effect. Adipocytes produce and release adipokines (e.g. leptin). They are also the seat of a local inflammatory reaction when the adipose tissue is ectopic (visceral vs. subcutaneous adipose tissue), and then systemic effects that add even more to a micro-inflammatory mechanism. In diabetics, insulin resistance can add to these mechanisms, which can damage cartilage, bone and synovial tissue. These all act together to reduce mobility in obese subjects and contribute to a vicious cycle centered on OA, especially when the obesity is predominantly abdominal and/or associated with T2D.
Discussion: Prevention of obesity-related OA must be the focus in high-risk subjects, such as those who are obese with metabolic syndrome > "metabolically healthy" obese, have T2D, and normal weight subjects with abdominal obesity (defined as waist circumference > 102 cm for men and 88 cm for women). The primary component of this prevention effort is weight loss combined with a balanced diet and regular physical activity.

In France, the prevalence of obesity in adults has increased 70% since 1997 (from 8.5% to 15%, but remained stable in children at about 6%), while the percentage of overweight adults has remained stable at 32.3%. This increase has impacted women more than men, and has increased by 35% over 3 years in the 18–25 year age group [1]. The medical and economic consequences of obesity make this a true public health problem.

Although two obese or overweight subjects may have the same body mass index (BMI), one may have a metabolic or cardiovascular disorder while the other may only have joint complications. As a consequence, a high BMI is not always sufficient to discriminate between obese or overweight persons who have an elevated risk of health problems. In 1947, Jean Vague introduced the waist circumference measurement to differentiate between abdominal (or central) obesity (visceral, ectopic adipose tissue) and peripheral obesity (subcutaneous, which is the typical location for adipose tissue). The location of excess fat mass varies between subjects. Imaging (CT and MRI) has revealed differences between subjects in the proportion of adipose tissue lodged in the abdominal cavity: certain obese individuals have little visceral adipose tissue, while others with the same total fat mass, have a greater amount of visceral adipose tissue. This visceral adipose tissue is associated with a higher risk of metabolic and cardiovascular diseases and certain cancers, not to mention the risk of non-alcoholic steatohepatitis (NASH). This visceral adipose tissue induces local and then systemic micro-inflammation, and is accompanied by an accumulation of pericardial and intramuscular fat; this prevents the organs in questions—and the entire body—from functioning normally. This leads to the above-described diseases after several years. A recent study on more than 650,000 adults showed that no matter the BMI (normal, overweight, obese; BMI ranging from 20 to 50 kg/m^2), an increase in waist circumference leads to a significant and identical increase in the mortality risk, independent

* Department of Sport Medicine and Functional Explorations, University-Hospital (CHU), G.-Montpied Hospital, 63003 Clermont-Ferrand, France.
E-mail address: mduclos@chu-clermontferrand.fr.

http://dx.doi.org/10.1016/j.rehab.2016.04.002
1877-0657/

of BMI. Relative to a waist circumference of < 90 cm for men and < 70 cm for women, a 5 cm increase in circumference increases mortality by 7% in men and 9% in women [2]. However, recent studies show that an increased waist circumference, no matter the BMI, is also a risk factor for osteoarthritis (OA).

People with type 2 diabetes (T2D) also have an increased risk of developing arthritic complications. Data from the ObEpi cohort provides a profile of type 2 diabetics in 2014: 5.5% of the adult population, average age of 65.9 years, 55% male, BMI 29.9 kg/m^2. The first problem – elevated prevalence of obesity, which affects 43% of T2D (39.9% of men and 47.1% of women) versus 10% in the general population; the combination of obesity and being overweight affects 80% of T2D. Second important point – there is a high prevalence of treated comorbidities: 60% dyslipidemia, 60% high blood pressure, myocardial infarction/heart failure (10%), sleep apnea (8.3%) and OA (10.7%), keeping in mind that this is treated OA, so the prevalence is likely much higher [1].

The primary objective of this review was to explore the links between obesity, T2D and OA, with a focus on the effect of ectopic (intra-abdominal) localization of the fat mass. The second objective was to define the functional consequences of OA in this population, which often has other comorbidities, and how to treat and prevent it.

1. Prevalence of OA in overweight/obese subjects and/or T2D

Obesity and T2D significantly increase the risk of developing OA. This relationship has been strongly demonstrated for obesity and is emerging for T2D. The risk of knee OA increases 15% for each 1 unit increase in BMI [3]. In those who are overweight (25 < BMI < 30 kg/m^2), the relative risk of undergoing joint arthroplasty is increased by 2.76 [95% CI: 2.05–3.70] in men and by 1.80 [95% CI: 1.75–185] in women. In those who are obese, it is increased by 4.20 [95% CI: 2.76–6.41] in men and 1.96 [95% CI: 1.88–2.04] in women based on a meta-analysis of three prospective cohort studies [4].

A recent meta-analysis has shown that OA prevalence is higher in diabetics than in non-diabetics (29.5 ± 1.2% in 5788 diabetic subjects) with an odds ratio (OR) of 1.46 (95% CI: 1.08–1.96; $P = 0.01$). In addition, the prevalence of diabetes is higher in those with OA than those without (14.4 ± 0.1% in 645,089 persons with OA; OR = 1.41, 95% CI: 1.21–1.65; $P < 0.00001$) [5]. However, only 12 studies in this meta-analysis reported an OR adjusted for BMI. Among these studies, five found no relationship between diabetes and OA, and seven identified diabetes as an independent risk factor. Although this meta-analysis had methodological limitations (selected studies were very heterogeneous; presence of confounding factors such as age and obesity that can impact the results), this was the first meta-analysis to show a link between OA and diabetes.

2. Pathophysiology of association between obesity, T2D and OA

2.1. Role of obesity

2.1.1. Direct effect of mechanical loads on cartilage

Excessive weight increases the mechanical loads on the hip and knee joint during physical activity, which is the most likely mechanism through which obesity contributes to OA. In fact, each additional kilogram of body weight adds 6 kg of load to each of the two knees [6]. This excess weight can induce cartilage degeneration because of greater mechanical stress on weight-bearing joints.

2.1.2. Role of adipose tissue independent of location: subcutaneous or ectopic (intra-abdominal)

In combination with these biomechanical factors, cytokines produced by the adipose tissue (adipokines, with leptin being the most well-known and studied, but also resistin and adiponectin) can also be incriminated. The existence of an association between obesity and OA in non-weight-bearing joints, particularly in the hands and fingers, support this hypothesis.

Leptin is a cytokine produced by adipocytes in white adipose tissue (hence its name "adipokine"), which is released into systemic circulation where it can reach the joints through the subchondral vascular network [7]. Chondrocytes are known to have leptin receptors. These adipokines play an important role in cartilage and bone homoeostasis; but at overly high concentrations, they contribute to the appearance and progression of OA (destruction of cartilage) (see [8] for review). A higher leptin concentration has been found in the synovial fluid of arthritic joints than that of non-arthritic joints [9].

2.1.3. Role of micro-inflammation: ectopic adipose tissue with and without obesity

Micro-inflammation depends more on the location of the adipose tissue that the total amount of adipose tissue. Ectopic adipose tissue induces a local inflammatory reaction and subsequently a systemic one (low-level inflammation or micro-inflammation). For this reason, OA is predominantly found in people with abdominal obesity, including those with normal BMI who have abdominal obesity.

There is abundant published scientific data suggesting that inflammatory mediators of adipose origin play a major role in the initiation and perpetuation of the OA process. These inflammatory mediators are released from adipose tissue (TNFα, IL-6, etc.) into systemic circulation and reach the joint through the subchondral vascular network [7]. These mediators have deleterious effects on cartilage, bone and synovial tissue.

In all, adipokines play an important role on the homeostasis of cartilage and bone. They are currently recognized as important mediators linking obesity, adipose tissue, micro-inflammation and OA [9]. Insulin resistance and dyslipidemia (increased LDL levels and decreased HDL levels) associated with visceral obesity, or even more highly to T2D, could further add to the micro-inflammation.

2.1.4. Additional mechanism in type 2 diabetics: insulin resistance?

The pathophysiology of this association between T2D and OA has not been determined. High blood glucose could trigger inflammation and cartilage degradation through the means of oxidative stress and an accumulation of inflammatory mediators and advanced glycation end-products (AGEs). In addition, beyond a chronic excess of glucose, T2D is characterized by increased insulin resistance, which can be implicated in the development of osteophytes and subchondral sclerosis. Prospective studies are needed to determine if diabetes is a risk factor independent of ectopic obesity for the development of OA or its severity.

3. Functional consequences of obesity and T2D

Obesity is associated with a functional decline and functional incapacity in cross-sectional and longitudinal studies, accelerating the disability and need to resort to arthroplasty in subjects with knee OA [10]. However, beyond BMI, the distribution of fat mass is an important element to consider. It has been well-proven that a predominantly abdominal distribution of the fat mass is involved in OA pathophysiology.

Cross-sectional studies have found a relationship between a large amount of intra-abdominal fat mass (visceral obesity) and functional incapacity in people with normal BMI [11]. Longitudinal studies are of even greater value and have confirmed these findings; for example, the longitudinal, multicenter, observational study called the "Osteoarthritis Initiative" with 2210 subjects with an average age of 68 years (range 67.1–69). The goal was to identify