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Obesity and kidney disease: Hidden consequences of the epidemic[☆]

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ABSTRACT

Obesity has become a worldwide epidemic, and its prevalence has been projected to grow by 40% in the next decade. This increasing prevalence has implications for the risk of diabetes, cardiovascular disease and also for Chronic Kidney Disease. A high body mass index is one of the strongest risk factors for new-onset Chronic Kidney Disease. In individuals affected by obesity, a compensatory hyperfiltration occurs to meet the heightened metabolic demands of the increased body weight. The increase in intraglomerular pressure can damage the kidneys and raise the risk of developing Chronic Kidney Disease in the long-term. The incidence of obesity-related glomerulopathy has increased tenfold in recent years. Obesity has also been shown to be a risk factor for nephrolithiasis, and for a number of malignancies including kidney cancer. This year the World Kidney Day promotes education on the harmful consequences of obesity and its association with kidney disease, advocating healthy lifestyle and health policy measures that makes preventive behaviors an affordable option.

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Obesidad y enfermedad renal: consecuencias ocultas de la epidemia

RESUMEN

La obesidad se ha convertido en una epidemia mundial y se estima que su prevalencia crecerá en un 40% durante la próxima década. Este incremento de prevalencia tiene implicaciones de riesgo para el desarrollo de diabetes, enfermedad cardiovascular y enfermedad renal crónica. Un índice elevado de masa corporal es uno de los factores de riesgo más importantes para el inicio de la enfermedad renal crónica. En los individuos afectados por obesidad se produce una hiperfiltración compensatoria para cubrir el exceso de demanda metabólica que impone el incremento del peso corporal. El aumento de la presión intraglomerular puede dañar el riñón y aumentar el riesgo de desarrollar enfermedad renal crónica en el largo plazo. La incidencia de la glomerulopatía relacionada con la obesidad ha aumentado 10 veces en años recientes. La obesidad también constituye un factor de riesgo para la nefrolitiasis y para un número de enfermedades malignas, incluyendo al cáncer de riñón. Este año el Día Mundial del Riñón promueve la educación sobre las consecuencias

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perjudiciales de la obesidad y su asociación con la enfermedad renal, a la vez que aboga por la adopción estilos de vida saludables y las políticas de salud que permitan convertir a la prevención en una opción asequible de prevención.

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Introduction

In 2014, over 600 million adults worldwide, 18 years and older, were obese. Obesity is a potent risk factor for the development of kidney disease. It increases the risk of developing major risk factors for Chronic Kidney Disease (CKD), like diabetes and hypertension, and it has a direct impact on the development of CKD and end-stage renal disease (ESRD). In individuals affected by obesity, a (likely) compensatory mechanism of hyperfiltration occurs to meet the heightened metabolic demands of the increased body weight. The increase in intraglomerular pressure can damage the kidney structure and raise the risk of developing CKD in the long-term.

The good news is that obesity, as well as the related CKD, is largely preventable. Education and awareness of the risks of obesity and a healthy lifestyle, including proper nutrition and exercise, can dramatically help in preventing obesity and kidney disease. This article reviews the association of obesity with kidney disease on the occasion of the 2017 World Kidney Day.

Epidemiology of obesity in adults and children

Over the last 3 decades, the prevalence of overweight and obese adults ($BMI \geq 25 \text{ kg/m}^2$) worldwide has increased substantially [1]. In the US, the age-adjusted prevalence of obesity in 2013–2014 was 35% among men and 40.4% among women [2]. The problem of obesity also affects children. In the US in 2011–2014, the prevalence of obesity was 17% and extreme obesity 5.8% among youth 2–19 years of age. The rise in obesity prevalence is also a worldwide concern [3,4], as it is projected to grow by 40% across the globe in the next decade. Low- and middle-income countries are now showing evidence of transitioning from normal weight to overweight and obesity as parts of Europe and the United States did decades ago [5]. This increasing prevalence of obesity has implications for cardiovascular disease (CVD) and also for CKD. A high body mass index (BMI) is one of the strongest risk factors for new-onset CKD [6,7].

Definitions of obesity are most often based on BMI (i.e. weight [kilograms] divided by the square of his or her height [meters]). A BMI between 18.5 and 25 kg/m^2 is considered by the World Health Organization (WHO) to be normal weight, a BMI between 25 and 30 kg/m^2 as overweight, and a BMI of $>30 \text{ kg/m}^2$ as obese. Although BMI is easy to calculate, it is a poor estimate of fat mass distribution, as muscular individuals or those with more subcutaneous fat may have a BMI as high as individuals with larger intraabdominal (visceral) fat. The latter type of high BMI is associated with substantially higher risk of

metabolic and cardiovascular disease. Alternative parameters to more accurately capture visceral fat include waist circumference (WC) and a waist-hip ratio (WHR) of $>102 \text{ cm}$ and 0.9, respectively, for men and $>88 \text{ cm}$ and >0.8 , respectively, for women. WHR has been shown to be superior to BMI for the correct classification of obesity in CKD.

Association of obesity with CKD and other renal complications

Numerous population based studies have shown an association between measures of obesity and both the development and the progression of CKD (Table 1). Higher BMI is associated with the presence [8] and development [9–11] of proteinuria in individuals without kidney disease. Furthermore, in numerous large population-based studies, higher BMI appears associated with the presence [8,12] and development of low estimated GFR [9,10,13], with more rapid loss of estimated GFR over time [14] and with the incidence of ESRD [15–18]. Elevated BMI levels, class II obesity and above, have been associated with more rapid progression of CKD in patients with pre-existing CKD [19]. A few studies examining the association of abdominal obesity using WHR or WC with CKD, describe an association between higher girth and albuminuria [20], decreased GFR [8] or incident ESRD [21] independent of BMI level.

Higher visceral adipose tissue measured by computed tomography has been associated with a higher prevalence of albuminuria in men [22]. The observation of a BMI-independent association between abdominal obesity and poorer renal outcomes is also described in relationship with mortality in patients with ESRD [23] and kidney transplant [24], and suggests a direct role of visceral adiposity. In general, the associations between obesity and poorer renal outcomes persist even after adjustments for possible mediators of obesity's cardiovascular and metabolic effects, such as high blood pressure and diabetes mellitus, suggesting that obesity may affect kidney function through mechanisms in part unrelated to these complications (vide infra).

The deleterious effect of obesity on the kidneys extends to other complications such as nephrolithiasis and kidney malignancies. Higher BMI is associated with an increased prevalence [25] and incidence [26,27] of nephrolithiasis. Furthermore, weight gain over time, and higher baseline WC were also associated with higher incidence of nephrolithiasis [27]. Obesity is associated with various types of malignancies, particularly cancers of the kidneys. In a population-based study of 5.24 million individuals from the UK, a 5 kg/m^2 higher BMI was associated with a 25% higher risk of kidney cancers, with 10% of all kidney cancers attributable to excess weight

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