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Editorial

Obesity and kidney disease: Hidden consequences of the epidemic

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1. 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, are 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.

2. Epidemiology of obesity in adults and children

Over the last 3 decades, the prevalence of overweight and obese adults (Body Mass Index [BMI] ≥ 25 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 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 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 cm and 0.9, respectively, for men and >88 cm and >0.8, respectively, for women. WHR has been shown to be superior to BMI for the correct classification of obesity in CKD.

3. 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

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Table 1
Studies examining the association of obesity with various measures of CKD.

Study	Patients	Exposure	Outcomes	Results	Comments
Prevention of renal and vascular end-stage disease (PREVEND) study [8]	7676 Dutch individuals without diabetes	Elevated BMI (overweight and obese[a]), and central fat distribution (waist-hip ratio)	Presence of urine albumin 30-300 mg/24 h Elevated and diminished GFR	Obese + central fat: Higher risk of albuminuria Obese ± central fat: Higher risk of elevated GFR Central fat ± obesity associated with diminished filtration	Cross-sectional analysis
Multinational study of hypertensive outpatients [20]	20,828 patients from 26 countries	BMI and waist circumference	Prevalence of albuminuria by dip stick	Higher waist circumference associated with albuminuria independent of BMI	Cross-sectional analysis
Framingham multi-detector computed yomography (MDCT) cohort [22]	3099 individuals	Visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT)	Prevalence of UACR > 25 mg/g in women and > 17 mg/g in men	VAT associated with albuminuria in men, but not in women	Cross-sectional analysis
Coronary artery risk development in young adults (CARDIA) study [11]	2354 community-dwelling individuals with normal kidney function aged 28–40 years	Obesity (BMI > 30 kg/m^2) Diet and lifestyle-related factors	Incident microalbuminuria	Obesity (OR: 1.9) and unhealthy diet (OR: 2.0) associated with incident albuminuria	Low number of events
Hypertension detection and follow-up program [10]	5897 hypertensive adults	Overweight and obese BMI[a] vs. normal BMI	Incident CKD (1+ or greater proteinuria on urinalysis and/or an eGFR < 60 mL/min/1.73 m^2)	Both overweight (OR: 1.21) and obesity (OR: 1.40) associated with incident CKD	Results unchanged after excluding diabetics
Framingham offspring study [9]	2676 individuals free of CKD stage 3	High vs. normal BMI[a]	Incident CKD stage 3 Incident proteinuria	Higher BMI not associated with CKD3 after adjustments Higher BMI associated with increased odds of incident proteinuria	Predominantly white, limited geography
Physicians' health study [13]	11,104 initially healthy men in US	BMI quintiles Increase in BMI over time (vs. stable BMI)	Incident eGFR < 60 mL/min/ 1.73 m^2	Higher baseline BMI and increase in BMI over time both associated with higher risk of incident CKD	Exclusively men
Nation-wide US veterans administration cohort [14]	3,376,187 US veterans with baseline eGFR ≥ 60 mL/min/ 1.73 m^2	BMI categories from < 20 to > 50 kg/m^2	Rapid decline in kidney function (negative eGFR slope of > 5 mL/ min/1.73 m^2)	BMI > 30 kg/m^2 associated with rapid loss of kidney function	Associations more accentuated in older individuals
Nation-wide population-based study from Sweden [12]	926 Swedes with moderate/ advanced CKD compared to 998 controls	BMI ≥ 25 vs. < 25 kg/m^2	CKD vs. no CKD	Higher BMI associated with 3× higher risk of CKD	Risk strongest in diabetics, but also significantly higher in non-diabetics Cross-sectional analysis
Nation-wide population-based study in Israel [17]	1,194,704 adolescent males and females examined for military service	Elevated BMI (overweight and obesity) vs. normal BMI[a]	Incident ESRD	Overweight (HR: 3.0) and obesity (HR: 6.89) associated with higher risk of ESRD	Associations strongest for diabetic ESRD, but also significantly higher for non-diabetic ESRD
The Nord-Trøndelag health study (HUNT-1) [15]	74,986 Norwegian adults	BMI categories[a]	Incidence of ESRD or renal death	BMI > 30 kg/m^2 associated with worse outcomes	Associations not present in individuals with BL < 120/80 mmHg
Community-based screening in Okinawa, Japan [16]	100,753 individuals > 20 years old	BMI quartiles	Incidence of ESRD	Higher BMI associated with increased risk of ESRD in men, but not in women	Average BMI lower in Japan compared to Western countries
Nation-wide US veterans administration cohort [19]	453,946 US veterans with baseline eGFR < 60 mL/min/1.73 m^2	BMI categories from < 20 to > 50 kg/m^2	Incidence of ESRD Doubling of serum creatinine Slopes of eGFR	Moderate and severe obesity associated with worse renal outcomes	Associations present but weaker in patients with more advanced CKD
Kaiser permanente Northern California [18]	320,252 adults with and without baseline CKD	Overweight, class I, II and extreme obesity; vs. normal BMI[a]	Incidence of ESRD	Linearly higher risk of ESRD with higher BMI categories	Associations remained present after adjustment for DM, hypertension and baseline CKD

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