

Obesity and kidney disease: Hidden consequences of the epidemic

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on behalf of the World Kidney Day Steering Committee*

Obesity is a growing worldwide epidemic. It is one of the strongest risk factors for new-onset chronic kidney disease, and also for kidney stones and kidney cancer. This article is an accompaniment to World Kidney Day on 9 March 2017 to promote education on the harmful consequences of obesity and its association with kidney disease, advocating healthy lifestyle and health policy measures that make preventative behaviours an affordable option.

In 2014, over 600 million adults worldwide were obese. Obesity increases the risk of developing major risk factors for chronic kidney disease (CKD), such as diabetes and hypertension, and it has a direct impact on the development of CKD and end-stage renal disease (ESRD). The good news is that obesity 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 World Kidney Day on 9 March 2017.

Epidemiology of obesity

Over the last three decades, the worldwide prevalence of excess weight and obesity (BMI ≥ 25 kg/m²) has increased substantially (GBD 2013 Risk Factors Collaborators, 2015), and it is projected to grow by 40% in the next decade. This increasing prevalence has implications for CKD, as obesity is one of the strongest risk factors for new-onset CKD (Elsayed et al, 2008; Tsujimoto et al, 2014).

Definitions of obesity are typically based on BMI. 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

intra-abdominal (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 levels include a waist circumference 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 (Elsayed et al, 2008).

Association of obesity with CKD and other renal complications

Numerous studies have shown an association between measures of obesity and both the development and the progression of CKD. In general, the associations between obesity and worse renal outcomes persist even after adjustments for possible mediators of obesity's cardiovascular and metabolic effects, such as high blood pressure and type 2 diabetes, suggesting that obesity may affect kidney function through mechanisms in part unrelated to these complications. The deleterious effect of obesity on the kidneys extends to other complications, including kidney stones (Curhan et al, 1998; Taylor et al, 2005; Scales et al, 2012) and kidney malignancies (Renehan et al, 2008; Bhaskaran et al, 2014; Arnold et al, 2015).

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About this article

This article has been submitted by the World Kidney Day Steering Committee simultaneously to a wide range of medical and paediatric journals. It aims to provide a summary and rationale for World Kidney Day 2017, the focus of which is on the relationship between obesity and chronic kidney disease.

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Page points

1. Obesity is associated with both the development and the progression of chronic kidney disease (CKD).
2. However, a nuanced approach is needed, as obesity has also been associated with reduced mortality rates in people with advanced CKD and end-stage renal disease (ESRD).
3. Strategies to control obesity-related CKD can include both population-level interventions to reduce obesity rates and individual-level treatments to slow the progression of CKD.

Mechanisms of action underlying the renal effects of obesity

The exact mechanisms whereby obesity may worsen or cause CKD remain unclear. Some of the deleterious renal consequences of obesity may be mediated by comorbid obesity-related conditions such as type 2 diabetes or hypertension, but the adipose tissue itself can also impact the kidneys directly (Figure 1). These various effects result in specific pathological changes in the kidneys (Kambham et al, 2001).

Obesity in people with advanced CKD: The need for a nuanced approach

In a seemingly counterintuitive manner, obesity has been consistently associated with lower mortality rates in people with advanced CKD (Kovesdy et al, 2007; Lu et al, 2014) and ESRD (Beddhu et al, 2003; Kalantar-Zadeh et al, 2006). It is possible that the seemingly protective effect of a high BMI is simply the result of the imperfection of BMI as a measure of obesity. However, there is evidence to suggest that higher adiposity, especially subcutaneous (non-visceral) fat, may also be

associated with better outcomes in people with ESRD (Kalantar-Zadeh et al, 2006). Such benefits may be present in patients who have very low short-term life expectancy, such as most of those with ESRD (Dekker et al, 2008), including benefits from better nutritional status and higher muscle mass.

Potential interventions for management of obesity

Strategies for controlling the obesity-related CKD epidemic at the population level and for countering the evolution of CKD toward kidney failure in obese patients represent the most tantalising task that today’s health planners, health managers and nephrologists face.

Countering CKD at the population level

Calls for public health interventions in the community to prevent and treat CKD at an early stage have been made by major renal associations. In the US, Healthy People 2020, a programme that sets 10-year targets for health promotion and prevention goals, focuses both on CKD and obesity. A successful surveillance system for CKD has already

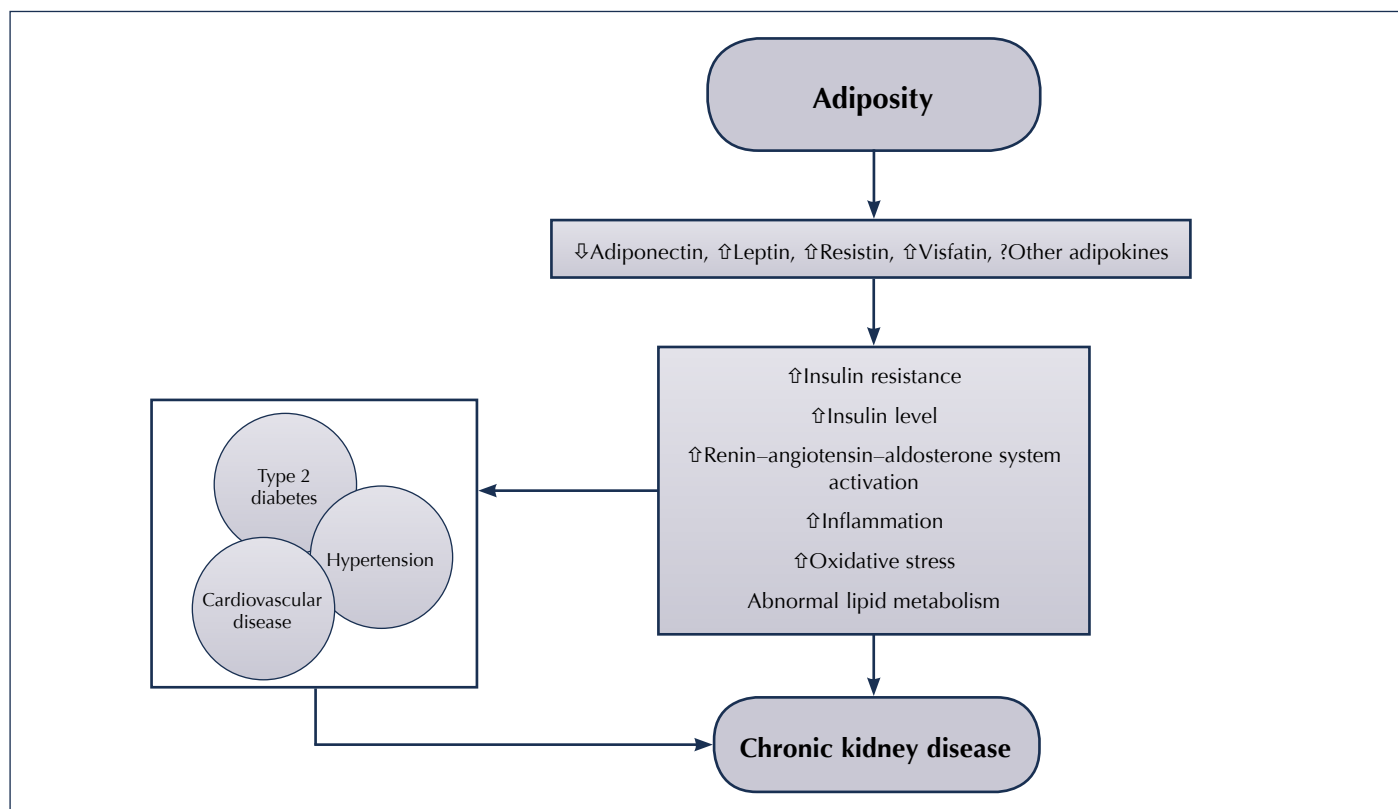


Figure 1. Putative mechanisms of action whereby obesity causes chronic kidney disease.

been implemented in some places, such as the UK (O'Donoghue and Stevens, 2012), and this may serve as a platform to improve the prevention of obesity-related CKD. Campaigns aiming at reducing the obesity burden are now centre-stage worldwide and are strongly recommended by the World Health Organization, and it is expected that these campaigns will reduce the incidence of obesity-related complications, including CKD.

Prevention of CKD progression in obese people with CKD

Obesity-related goals in obese patients with CKD remain vaguely formulated, largely because of the paucity of high-level evidence from intervention studies to modify obesity in people with CKD (Bolignano and Zoccali, 2013). In overweight or obese people with type 2 diabetes, a lifestyle intervention, including caloric restriction and increased physical activity, reduced the risk of incident CKD by 30% compared with standard follow-up (Look AHEAD Research Group, 2013). In a recent meta-analysis collating experimental studies in obese patients with CKD, interventions aimed at reducing body weight showed coherent reductions in blood pressure, glomerular hyperfiltration and proteinuria (Bolignano and Zoccali, 2013). A *post hoc* analysis of the REIN (Ramipril Efficacy In Nephropathy) study showed that the renoprotective effect of angiotensin-converting enzyme (ACE) inhibition in proteinuric CKD patients was maximal in those who were obese, but minimal in those with normal or low BMI (Mallamaci et al, 2011). Bariatric surgical interventions have been suggested for selected patients with CKD and ESRD (Jamal et al, 2015; Chang et al, 2016; Friedman and Wolfe, 2016).

Globally, these experimental findings provide a proof of concept for the usefulness of weight reduction and ACE inhibition interventions in the treatment of CKD in obese people. Studies showing a survival benefit of increased BMI in people with CKD, however, remain to be explained (Ahmadi et al, 2015). These findings limit our ability to make strong recommendations about the usefulness and safety of weight reduction among individuals with more advanced stages of CKD. However, lifestyle recommendations to reduce body weight in obese people at risk of CKD and in those with early CKD

appear justified, particularly recommendations for the control of diabetes and hypertension.

Conclusions

The worldwide epidemic of obesity affects the Earth's population in many ways. Diseases of the kidneys, including CKD, kidney stones and kidney cancers, are among the more insidious effects of obesity, but which nonetheless have wide-ranging deleterious consequences, ultimately leading to significant excess morbidity and mortality and excess costs to individuals and society. Population-wide interventions to control obesity could have beneficial effects in preventing the development or delaying the progression of CKD. It is incumbent upon the entire healthcare community to devise long-ranging strategies toward improving the understanding of the links between obesity and kidney diseases, and to determine optimal strategies to stem the tide. The 2017 World Kidney Day is an important opportunity to increase education and awareness to that end. ■

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Page points

1. In overweight or obese people with type 2 diabetes, diet- and lifestyle-based intervention has been associated with a 30% reduction in the incidence of CKD.
2. Angiotensin-converting enzyme inhibition has also been shown to be renoprotective in obese people with CKD, but not in those with normal or low BMI.
3. Bariatric surgery has also been suggested for selected patients with CKD and ESRD.

“Population-wide interventions to control obesity could have beneficial effects in preventing the development or delaying the progression of chronic kidney disease.”

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About World Kidney Day

World Kidney Day is a global awareness campaign aimed at raising awareness of the importance of our kidneys. Celebrated every year on the second Thursday of March, World Kidney Day has grown dramatically to become the biggest event focused on kidney health around the world and the most successful effort to raise awareness with the general public, medical professionals and government health officials about the dangers of kidney disease.

Our mission

World Kidney Day aims to raise awareness of the importance of our kidneys to our overall health and to reduce the frequency and impact of kidney disease and its associated health problems worldwide.

Our objectives

- Raise awareness about our “amazing kidneys”. Highlight that diabetes and high blood pressure are key risk factors for chronic kidney disease (CKD).
- Encourage systematic screening of all people with diabetes and hypertension for CKD.
- Encourage preventative behaviours.
- Educate all medical professionals about their key role in detecting and reducing the risk of CKD, particularly in high-risk populations.
- Stress the important role of local and national health authorities in controlling the CKD epidemic. On World Kidney Day, all governments are encouraged to take action and invest in further kidney screening.
- Encourage transplantation as a best-outcome option for kidney failure, and the act of organ donation as a life-saving initiative.

For the 2017 World Kidney Day campaign, the International Society of Nephrology (ISN) and the International Federation of Kidney Foundations (IFKF) have again teamed up, with one focus: **Kidney Disease and Obesity: Healthy Lifestyle for Healthy Kidneys.**

World Kidney Day helps fight CKD in three ways:

- We actively encourage education and prevention schemes, through grass-roots movements spreading the message about the disease and some of the simple steps that can be taken to reduce its impact, and help to set up early screening programmes worldwide to help people get diagnosed and start treatment earlier.
- Through effective communication and social media, we help the various players inside and outside the medical field to spread the word about CKD. We stimulate these communities in their year-long effort, which culminates in the major global event that is World Kidney Day, on the second Thursday of March each year.
- ISN and IFKF encourage their membership base to stimulate and assist advocacy efforts, both nationally and internationally, as a top-down approach to tackling the disease. Through this effort, we aim to convince both national governments and international bodies such as the World Health Organization to dedicate further efforts to combat CKD around the world, and to give CKD an increased level of recognition as an important threat to the world population, and a major health priority worldwide.

World Kidney Day Steering Committee

Members of the World Kidney Day Steering Committee are Philip Kam Tao Li, Guillermo Garcia-Garcia, Mohammed Benghanem-Gharbi, Rik Bollaert, Sophie Dupuis, Timur Erk, Kamyar Kalantar-Zadeh, Csaba Kovesdy, Charlotte Osafo, Miguel C Riella and Elena Zakharova

World Kidney Day is a joint



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