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Chronic kidney disease in older people with intellectual disability: Results of the HA-ID study

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ABSTRACT

With increasing longevity and cardiovascular events, chronic kidney disease may also become a significant problem in older people with intellectual disability (ID). We studied prevalence and associations of chronic kidney disease as part of the Healthy Ageing and Intellectual Disability (HA-ID) study, a large Dutch cross-sectional study among people with ID aged 50 years and over, using creatinine and cystatin-C measurement in plasma. Glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. Equations based on creatinine (as the MDRD equation) may underestimate kidney dysfunction in people with sarcopenia, because low muscle mass leads to a low creatinine production. Therefore, also prevalence of chronic kidney disease was studied in the sarcopenic group, using different GFR equations. Prevalence of chronic kidney disease, among 635 participants, was 15.3%, which equals prevalence in the general Dutch population. In the group of participants with sarcopenia ($n = 82$), the CKD-EPI equation based on creatinine and cystatin-C gave a higher prevalence of chronic kidney disease than did the MDRD equation, but confidence intervals were very wide. Chronic kidney disease was associated with higher age, Down syndrome, obesity, hypercholesterolemia and hypothyroid disease.

GFR should be measured in all older people with ID and polypharmacy, and in older people with ID and Down syndrome as part of the regular health checks. Moreover, if sarcopenia is present and information on GFR is required, this should not be measured based on creatinine only, but additional measures, such as cystatin-C, should be taken into account.

1. Introduction

Chronic kidney disease is a major health problem, especially in older people and in people with cardiovascular disease, diabetes or hypertension. It can proceed into kidney failure and also contributes to increased morbidity and mortality from cardiovascular disease. As people with intellectual disability (ID) tend to get older, chronic diseases and polypharmacy become increasingly prevalent in this group. Eighty percent of people with ID aged 50 years and over have two or more chronic diseases (Hermans & Evenhuis, 2013), whereas 52% use four or more types of medication (Zaal, van der Kaaij, Evenhuis, & van den Bemt, 2013). In these conditions renal functioning should be taken into account.

There are several reasons to suspect that people with ID are at risk of renal dysfunction. Some genetic syndromes are associated with renal dysfunction. In a study among 66 children with Down syndrome, eight percent had congenital kidney

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disease or glomerulopathy. Of these children, 4.5% had renal failure (Malaga, Pardo, Malaga, Orejas, & Fernandez-Toral, 2005). In another study among 103 persons with Down syndrome aged 1–57 years, a significantly lower excretion of creatinine in urine was found as compared to non-ID controls. The authors suggest that this might be due to oxidative stress, which also leads to premature ageing in Down syndrome (Campos, Guzman, Lopez-Fernandez, & Casado, 2011; Guzman, Campos, Lopez-Fernandez, & Casado, 2011). Some more rare genetic syndromes are associated with congenital kidney diseases. Renal anomalies are present in 46% of people with Bardet–Biedl syndrome, mostly hyperechoic kidneys and cystic dysplasia. Many people with this syndrome (70%) develop chronic renal failure and 10–30% require kidney replacement therapy. People with Lowe syndrome have a specific tubulopathy. In Joubert syndrome people have, depending on the genetic mutation, nephronophtisis (chronic tubule-interstitial nephritis) (Schurman & Scheinman, 2009). In Williams syndrome, renal anomalies may occur, such as hypoplastic kidneys and renal artery stenosis (Morris, 1993).

In a large Taiwanese study among adolescents with ID by heterogeneous causes a significantly increased prevalence of renal dysfunction was found (Lin, Lin, Hsieh, & Lin, 2010). Information about patient characteristics was limited, which reduces insight into possible selection bias or other underlying mechanisms for an increased risk on renal dysfunction. Although the authors did not mention sarcopenia (low muscle mass), which results in underestimation of renal dysfunction with the used diagnostic methods, the significantly lower prevalence in the subgroup with underweight points in this direction, and suggests that the prevalence published in this study was an underestimation of the actual amount of renal dysfunction in this group.

Risk factors for renal damage are (as they are in the general population) the presence of diabetes, hypertension, smoking and use of lithium. These risk factors were studied in the Healthy Ageing and Intellectual Disability (HA-ID) study, a large Dutch cross-sectional study into health of people with ID aged 50 years and over. There is an increased risk on the development of diabetes, whereas hypertension and smoking occur as frequently as in the general population (de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2012). Peripheral arterial disease (atherosclerosis distal from the aortic bifurcation) indicates atherosclerosis and thus is a risk for microvascular renal damage. The increased risk on diabetes is probably due to metabolic changes based on muscular inactivity in people with an impaired mobility and in the large group with a sedentary lifestyle (Hilgenkamp, Reis, van Wijck, & Evenhuis, 2011), and to the widespread use of antipsychotic drugs (de Kuijper et al., 2010). We have recently shown that also the risk on peripheral arterial disease is increased as compared to the general population (de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2013). Moreover renal functioning is directly influenced by thyroid hormones, as these induce glomerular filtration (Gopinath, Harris, Wall, Kifley, & Mitchell, 2013). Hypothyroid disease is also a significant problem in people with ID (Visser, de Rijke, van Toor, & Visser, 2011). These are reasons to expect that renal dysfunction can be a relevant problem in older people with ID.

Sarcopenia (loss of muscle mass) is highly prevalent (14%) in older people with ID (Bastiaanse, Hilgenkamp, Echteld, & Evenhuis, 2012). It is unknown if sarcopenia occurs more often than in the general population, but the presence of motor disabilities from early age on in addition to the age-related motor problems support this hypothesis (Bastiaanse et al., 2012). The, inherent to sarcopenia, low creatinine production can lead to underestimation of renal dysfunction. This means that creatinine measurement, although it is the most widely used technique, may not be the most reliable indicator of renal damage. Cystatin-C is a protease inhibitor produced by nearly all cells in the body. This protein is, after filtration by the glomerulus, metabolised in the proximal tubular epithelial cells. It may be a good indicator for renal dysfunction in older people, as it is not influenced by the muscle metabolism (Shlipak et al., 2005). Both creatinine and cystatin-C can be used to calculate the estimated glomerular filtration rate (eGFR), the measure for kidney functioning. Most widely used in clinical practice is the Modification of Diet in Renal Disease (MDRD) study equation for calculating the eGFR (Levey et al., 2006). However, this equation is not reliable for the normal range of GFR and tends to over-estimate kidney disease, which is why a new equation to predict GFR, based on serum creatinine, was developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI creatinine equation) (Levey et al., 2009). This equation more accurately classified people into GFR categories than did the MDRD (Stevens et al., 2011). Because of the better performance in people with low muscle mass, GFR estimating formulas have also been designed based on cystatin-C (CKD-EPI cystatin C equation), but the most reliable estimation is based on both creatinine and cystatin-C (CKD-EPI creatinine-cystatin-C equation) (Inker et al., 2012).

To our knowledge, there has been no research into renal dysfunction in older people with ID. Therefore, the aims of the present study were:

1. To determine the prevalence of chronic kidney disease in older people with ID.
2. To determine the prevalence of chronic kidney disease in the sarcopenic group based on different GFR equations (MDRD and CKD-EPI using creatinine and cystatin-C measurement).
3. To identify correlates of renal dysfunction in older people with ID (gender, age, level of ID, mobility, Down syndrome, diabetes, hypertension, obesity, hypercholesterolemia, smoking, peripheral arterial disease, use of antipsychotic drugs, sarcopenia, hypothyroid disease).

2. Methods

2.1. Design

This study is part of the large cross-sectional HA-ID study (Hilgenkamp et al., 2011a). Three care-providing organisations in the Netherlands participated in the study. These organisations offer low to high level specialised support and care to