To the editor,

Schalkwijk et al. [1] show interesting data on a negative correlation between renal function and plasma adiponectin levels in type 1 diabetes. A relationship between adiponectin and renal function has previously been observed in diabetic and non-diabetic nephropathy.

Adiponectin is elevated in patients on dialysis. There is a substantial decrease in plasma adiponectin after kidney transplantation. However, there is no correlation between changes in renal function and changes in adiponectin concentrations [2]. Mechanisms underlying the association between adiponectin and renal function are still poorly understood. In our opinion, close scrutiny in the methods used to estimate renal function should be applied to better understand the association between adiponectin and renal function.

Like most previous authors, Schalkwijk et al. estimate renal function by the Cockcroft-Gault formula. This equation estimates creatinine clearance from serum creatinine by an algorithm that includes gender, age, and body weight as determinants of muscle mass and thus creatinine supply.

Adiponectin is an adipocyte-specific plasma protein and its plasma concentration is strongly negatively associated with total body fat and body mass index, i.e. factors closely related to body weight. Moreover, adiponectin levels are higher in women. Therefore, two important determinants of adiponectin other than renal function are included in the Cockcroft-Gault formula. So, use of this formula is prone to induction of a systematic error in studies on the association between renal function and adiponectin.

Becker et al. [3] studied non-diabetic subjects with renal dysfunction (median GFR 63 ml/min, interquartile range 38-96), using the gold standard—iothalamate clearance technique—for assessment of renal function. In their study, adiponectin correlated with age, but not with renal function. It would be of interest to know whether the discrepancy with Schalkwijk’s data might relate to the use of the Cockcroft-Gault formula.

Normalization of renal function for body surface area is also relevant to consider. Schalkwijk et al. show creatinine clearance as ml/min/1.73 m2, which complies with the usual practice to express renal function per 1.73 m2. However, body surface area is usually estimated from the combination of height and body weight. Therefore, this may also induce bias in analyses on obesity-associated parameters. To circumvent this from happening, it has been recommended to use height-corrected renal function in such analyses [4].

As adiponectin predicts cardiovascular events in renal patients [3], better understanding of the relation between adiponectin and renal function is important. Studies addressing this issue should take the above-mentioned pitfalls into account in assessing and analyzing renal function.
References

Reply Schalkwijk

To the editor,
We appreciate the interest in our article on adiponectin and renal function in type 1 diabetic patients [1] and the opportunity to respond to the concerns raised by Lely and colleagues [2]. We demonstrated that adiponectin is inversely associated with renal function in type 1 diabetic patients.

We used the Cockcroft-Gault formula \( \frac{(140-\text{age (years)}) \times \text{weight (kg)} \times F}{\text{plasma creatinine (µmol/L) \times 72}} \) in mL/min with F=1 if male and 0.85 if female) as an estimate of glomerular filtration rate (GFR). As two important determinants of adiponectin (weight and gender) are included in the Cockcroft-Gault formula, it is indeed important to be certain whether this influences the association of GFR and adiponectin that we observed. We have studied this in detail and below present the additional analyses.

Adiponectin was associated with GFR in crude analysis (st.beta -0.415, P < 0.0001) and after adjustment for age, gender, HbA1c, duration of diabetes and systolic blood pressure (model 1, st.beta -0.330, P < 0.0001) as shown in Table 4 of the article. Additional adjustment of model 1 for weight or height did not materially change the significance of the association or materially alter the standardised beta coefficient (st.beta -0.324, P < 0.001 and st.beta -0.265, P < 0.001, respectively). This suggests that the association between adiponectin and GFR is independent of weight and height.

In addition, we stratified the association of adiponectin with GFR for gender and quartiles of weight and height. The association between GFR and adiponectin did not differ between males and females, or by quartiles of weight and height. Another point of concern is the use of body surface area as estimated from the combination of height and body weight. We addressed this by expressing GFR in ml/min instead of ml/min/1.73m² and then adjusted for height, as suggested by Lely and colleagues (2). The association of adiponectin with GFR expressed in ml/min was negative with similar st.betas as...
with GFR when expressed in ml/min /1.73m2 (st.beta -0.345, P < 0.001). Adjustment for height did not change the association (st.beta -0.322, P < 0.001).

Taken together, this demonstrates that the association between adiponectin and renal function as estimated by GFR in type 1 diabetic patients is independent of weight, height, gender and body surface area.

References


List of publications


Lely AT, Bakker SJL, Navis GJ. Adiponectin and renal function: pitfalls of renal function estimates and correction for BSA. J Clin Endocrinol Metab. 2006 April 5; electronic letter.


