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Muscle mass versus body mass index as predictor of adverse outcome

Sarcopenia is a progressive skeletal muscle disorder, which is characterized by low muscle mass and strength and associated with increased risk of adverse outcomes, including premature death.[1] Despite improved awareness of the importance of sarcopenia by health care professionals, fundamental findings from research lack translation to clinical practice—a gap that must be bridged given the major personal, social, and economic burdens ensued by its presence.[1] We report on a renal transplant recipient who experienced substantial muscle wasting during 27.5 years of follow-up. Height-indexed 24 h creatinine excretion rate (CER index) was used as accurate marker of muscle mass.[2]

A 22-year-old Black male was diagnosed with terminal renal insufficiency in May 1981. Chronic intermittent haemodialysis was initiated and maintained until successful renal transplantation in March 1982 (*Figure* 1A and 1B). At that time, body mass index (BMI) was 19.8 kg/m^2 (*Figure* 1B). Serum creatinine had remained steady until *de novo* membranous glomerulopathy ensued in March 1985 and eventually graft failure in May 1986. Deteriorating renal function manifested as a gradual rise in serum creatinine (*Figure* 1A) and, interestingly, a concomitant decrease in CER index, indicating muscle wasting from chronic kidney disease (*Figure* 1B). Six years of haemodialysis followed until a second transplantation in June 1992. Importantly, CER index was considerably lower shortly after the second compared with the first transplantation (*Figure* 1B), whereas BMI had actually increased to 21.7 kg/m^2 (*Figure* 1B). Eighteen months later, serum creatinine abruptly rose because of interstitial rejection and membranous glomerulopathy (*Figure* 1A), whereafter haemodialysis was resumed in January 1994. During the years 1995–2003, complaints of generalized arthropathy from haemodialysis-associated β-2 microglobulin

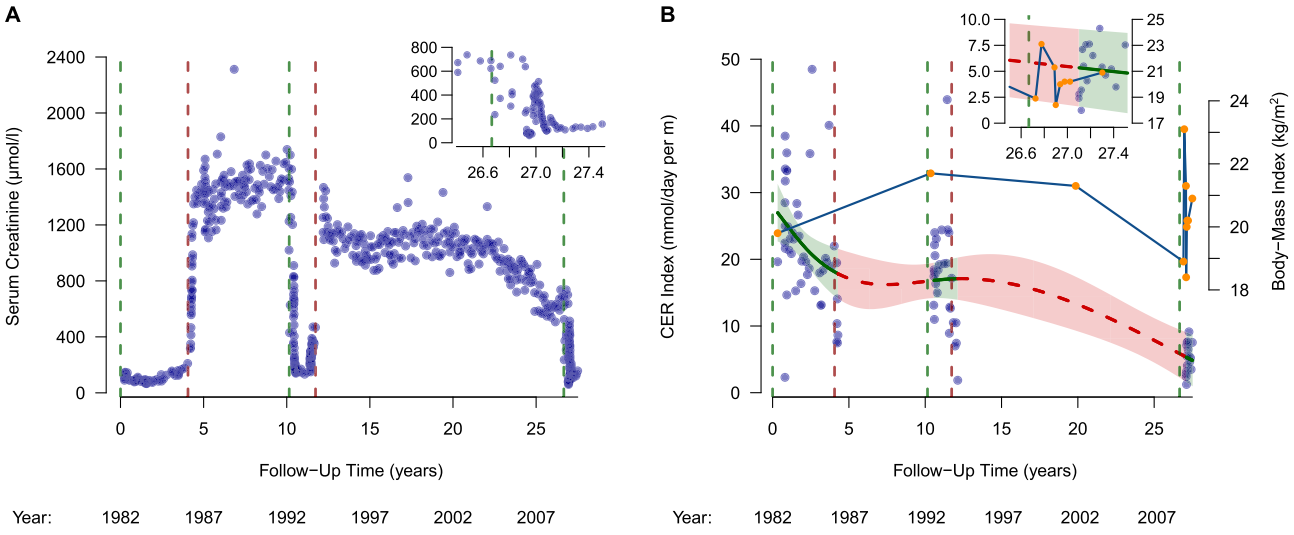

Figure 1 Serum creatinine, body mass index, and height-indexed 24 h creatinine excretion rate over the course of the patient's follow-up. Evolutions in serum creatinine (*A*), CER index, and BMI (*B*) are shown over the course of follow-up. Moments of renal transplantation are represented by the vertical dashed dark green lines, whereas moments of graft failure are represented by the vertical dashed red lines. The non-linear line represents the estimated CER index, and the shaded area about the line the associated 95% pointwise confidence interval. The line is solid and coloured dark green at follow-up times where CER index was actually observed, whereas the line is dashed and coloured dark red at periods of haemodialysis (interpolation). Non-linearity was modelled using natural cubic splines with two knots imposed at 2.1 and 11.7 years of follow-up. Boundary knots were set to the 5th and 95th percentiles of follow-up. The orange points through which the dark blue line is drawn represent observed BMIs. To facilitate appraisal of serum concentrations of creatinine, CER indices, and BMIs around the third renal transplantation (i.e. the rightmost vertical dashed dark green line), the range of the *x* and *y* axes of the original figure were cropped, and the resulting enlarged images are given in the upper border of the plots. BMI, body mass index; CER index, height-indexed 24 h creatinine excretion rate.

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amyloidosis gradually developed, which caused progressive decreases in mobility and, consequently, muscle mass and manifested as concomitant decreases in serum creatinine and CER index (*Figure* 1A and 1B). In December 2008, a third transplantation was performed because of progressive amyloid arthropathy. We observed an increase in BMI from 18.9 kg/m^2 (first day after transplantation) to 23.1 kg/m^2 (19 days later at discharge), and improved well-being was reported shortly after. Remarkably, CER index had massively dropped to a quarter of that in June 1992, indicating substantial muscle wasting. Despite increases in BMI in absence of oedema (beginning of February 2009: 18.4 kg/m^2; end of February 2009: 20.0 kg/m^2; March 2009: 20.2 kg/m^2; June 2009: 20.9 kg/m^2), CER index steadily waned in the remaining months until the patient's death in August 2009 (*Figure* 1B).

Body mass index—defined as weight divided by height in metres squared—is considered the 'gold standard' measure of weight and hence abundantly used in clinical decision making and research. In 1985, however, Andres and colleagues called this concept into question by demonstrating that the association between height-adjusted weight and mortality follows a U-shaped curve. Moreover, the nadir of that curve (i.e. the weight at which mortality rates were lowest) was highly dependent on age.[3] These findings gave rise to a concept referred to as the 'obesity paradox', which still receives much attention.[4] We built on this concept with the patient's gradual, yet inexorable, wasting of muscle mass as harbinger of deteriorating clinical condition and, eventually, death—all in absence of declining BMI. This fuels the notion that muscle mass is superior to BMI in mirroring clinical condition. Indeed, the phenomenon of changing body composition with steady (or even gained) weight can be explained by disproportionate losses of lean mass and concurrent deposition of intramuscular adipose tissue.[5] Additionally, the inexorable nature of the observed muscle wasting indicates the difficulty of rebuilding muscle after serious events. We urge that surrogates of muscle mass, like CER index, as potentially superior prognosticators of adverse outcome to BMI, be considered in study design and more frequently used to inform clinical decision making in settings of low muscle mass or muscle wasting.

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Dion Groothof
Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, Groningen, 9700RB, The Netherlands
d.groothof@umcg.nl

Adrian Post
Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, Groningen, 9700RB, The Netherlands

Harmke A. Polinder-Bos
Department of Internal Medicine, Erasmus Medical Center, Erasmus University Rotterdam, Rotterdam, The Netherlands

Bouke P.C. Hazenberg
Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Reinold O.B. Gans
Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, Groningen, 9700RB, The Netherlands

Stephan J.L. Bakker
Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, Groningen, 9700RB, The Netherlands

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