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Assessment of body composition in ESRF

To the Editor: We read with interest the recent article of Cooper et al, in which they proposed hand-to-feet bioelectrical impedance analysis (BIA) as an accurate and very useful surrogate marker for total body water (TBW) in patients with end-stage renal failure (ESRF) [1]. Despite this assertion, the authors also acknowledged that a great variation existed between TBW assessed by BIA compared to the gold standard (deuterium oxide) technique (−10.9 to 8.4 L). This wide variation is in agreement with our very recent findings (unpublished data), in which we also found a significant discrepancy between TBW assessed by multifrequency BIA and deuterium oxide (−3.4 to 20.3 l) in 18 patients with hemodialysis, and that BIA tended to underestimate TBW.

This discrepancy between TBW and isotope dilution techniques found by various authors is in contradiction with the agreement between TBW assessed by BIA and isotope dilution techniques found in healthy controls and, as recently published by our group, in patients who have had renal transplants [2].

Interestingly, in hemodialysis patients, we found a significant correlation between a marker of the hydration state of the body (TBW/body weight) and the discrepancy between TBW as assessed by BIA and deuterium oxide ($r = 0.74$). As already suggested by Zhu, Schneditz, and Levin, at least part of this discrepancy is due to the fact that TBW in the trunk is almost never measured by standard hand-to-feet BIA measurements [3]. The water in the trunk of an overhydrated patient is unlikely to be adequately predicted by a method that only takes the resistance of the extremities into account. The use of the sum of segmental resistances, which includes a separate measurement of the trunk, might present a solution to this dilemma. However, this technique still must be validated against gold standard techniques with regard to the assessment of absolute values of TBW in renal patients.

We propose that BIA measurements that do not take into account the resistance of the trunk with a separate measurement are unlikely to predict absolute values of TBW accurately in patients with large abnormalities in fluid status and should not be used as a surrogate marker for TBW in patients with ESRF.

Jeroen P. Kooman, Petronella L.M. Cox-Reijven, Frank M. van der Sande, Eugenie C. van den Ham, and Karel M.L. Leunissen
Maastricht, The Netherlands

Correspondence to J.P. Kooman, M.D., Ph.D., Department of Internal Medicine, PO Box 5800, 6202 AZ Maastricht, The Netherlands. E-mail: JKOO@SINT.AZM.NL

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Reply from the authors

In response to the letter by Kooman et al with regard to our recently published article on the assessment of body composition in end-stage renal failure (ESRF), we agree that measurement of total body water (TBW) using bioelectrical impedance analysis (BIA) in patients with renal disease is associated with high limits of agreement and is subject to greater variability than the same method performed in normal healthy subjects. This is stated clearly in our article [1]. It is, however, indisputable that our BIA results were more accurate than TBW derived by other commonly used methods. Kooman et al have suggested that segmental BIA assessment of TBW may be a more accurate method. The paper they cited to support their argument [2] compared standard whole body BIA (as used in our study) with segmental BIA in patients undergoing hemodialysis. Equilibration between fluid compartments was not considered in their experiments. Measurements were performed in both the sitting and supine positions. In this dynamic setting segmental BIA produced a more accurate mean estimate of TBW. However, the limits of agreement were similar to those of the whole body technique. The inaccuracies of whole body BIA in measuring TBW in situations in which fluid shifts are occurring have previously been reported [3–6]. What is not clear is whether the segmental BIA technique is superior to whole body BIA in patients with ESRF with inherent differences in TBW. A confirmed gain in accuracy produced by this technique must be established to offset the increased complexity and time required performing and analyzing the results. There-

fore, further validation of TBW by segmental BIA against a gold standard is required.

Bruce Cooper and Carol A. Pollock
Sydney, New South Wales, Australia

Correspondence to Professor Carol Pollock, Department of Medicine, Wallace Freeborn Building, Royal North Shore Hospital, St. Leonards, NSW 2065, Australia
E-mail: carpol@medicine.usyd.edu.au

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Accuracy of methods used to quantify cell hyperplasia

To the Editor: We are interested in the recent article in *Kidney International* by Hebert et al discussing an association between patients with proteinuria and proximal tubular epithelial cell hyperplasia [1]. We are concerned with the method used to quantify cell hyperplasia. The method used produced data related to structure in the two-dimensional tissue sections, but it did not generate data allowing deductions regarding the true number of tubule cells.

The authors, by counting numbers of nuclei on tissue sections, report an increase in number of nuclei per proximal tubule cross-section in patients with increased proteinuria. The authors, in fact, counted the number of nuclear profiles per proximal tubule cross-section. The number of particle profiles per tissue area is not directly related to the number of particles per tissue volume. If the volume of the particle is increased or the volume of the tissue decreased (definite possibilities in these patients), an increase in profile number per area would be expected without any necessary increase in absolute cell number. Therefore, this method cannot determine if true tubular cell number is increased.

During the past 20 years, new techniques have been developed for obtaining precise and unbiased information about three-dimensional structures from two-dimensional images. Nyengaard has written an excellent review of these modern morphometric techniques as they relate to the kidney [2].

Recently, there have been journal editorials calling for the use of these unbiased and efficient techniques [3, 4] and we agree with this approach. We suggest that the editors of *Kidney International* adopt policies assuring that manuscripts published in the journal contain accurate structural data that are derived using the principles described in Nyengaard's review.

John M. Basgen and Michael Mauer
Minneapolis, Minnesota, USA

Correspondence to Michael Mauer, M.D., Pediatric Nephrology, University of Minnesota, Box 491, 420 Delaware Street S.E., Minneapolis, Minnesota 55455, USA.

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Reply from the authors

We did not use the stereologic method described by Nyengaard to assess hyperplasia because one of our coauthors, Dr. Mahan, who trained under Dr. Mauer in morphometric techniques, determined that we did not have sufficient renal biopsy tissue. The stereologic technique requires multiple sections for analysis, and such material often is not available from needle kidney biopsies obtained for clinical purposes.

With respect to the conclusion of our study, that is, that heavy proteinuria is associated with proximal tubular hyperplasia, we emphasize that this conclusion was based not only on the morphometric studies, but also on the qualitative findings on renal biopsy. As shown in Figure 1 of our article, the degree of tubular hyperplasia in some patients was extraordinary, with proximal tubular epithelial cells piling up on one another and encroaching on the tubular lumen. These findings cannot be attributed to a change in nuclear volume or tubular volume, which are the concerns of Mr. Basgen and Dr. Mauer.

The severity of proximal (and perhaps distal) tubular hyperplasia seen in some patients with heavy proteinuria is remarkable. Indeed, it is amazing that this phenomenon has not previously been reported, given the scrutiny often applied to analysis of human renal biopsy material. It seems likely that tubular hyperplasia contributes to