Kidney Support

Noninvasive Measurement of Cardiac Output in Hemodialysis Patients by Task Force Monitor: A Comparison with the Transonic System

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Cardiovascular disease is the leading cause of morbidity and mortality in maintenance hemodialysis (MHD) patients. The Transonic (TRS; Transonic Systems, Ithaca, NY) device is frequently used for determination of cardiac output (CO) by an indicator dilution technique. The Task Force Monitor (TFM; CN Systems, Graz, Austria) has gained attention as noninvasive tool for continuous beat-to-beat assessment of cardiovascular variables, including CO by impedance cardiography. Despite its use in cardiology and intensive care settings, the TFM has yet not been validated in dialysis patients.

This study compares CO measurements in 12 MHD patients by TFM and TRS. Bland-Altman and regression analysis were used. CO was measured simultaneously by TRS and TFM. Average CO was 5.4 L/min by TRS and 5.0 L/min by TFM, respectively. Bland-Altman analysis revealed no significant systematic differences between the two methods (mean difference: 0.4 L/min; SD: 0.6; $p > 0.05$). Linear regression analysis showed significant correlation between both techniques ($r = 0.802$, $p = 0.002$). The SD of mean individual CO values was 1.1 L/min with TRS and 0.8 L/min with TFM, respectively.

CO measured by TFM and TRS does not differ significantly, thus making the TFM an attractive noninvasive tool for the continuous beat-to-beat assessment of CO in MHD patients. *ASAIO Journal* 2007; 53:561–565.

Cardiovascular disease is the leading cause of morbidity and mortality in maintenance hemodialysis (MHD) patients.[1–3] Evaluation of cardiac function by measurement of key cardiovascular variables such as heart rate, blood pressure, cardiac output (CO), and total peripheral resistance (TPR) is of particular interest in this patient cohort.

Since invasive techniques, such as dye-dilution or thermodilution, are not practical in outpatient settings, a pressing need exists for an easy, noninvasive and continuous (*i.e.*, throughout a whole dialysis treatment) assessment of cardiac function.[4]

The Transonic (TRS, Transonic Systems, Ithaca, NY, USA) device is a validated and widely used method for the assessment of CO in MHD patients. The TRS system uses an ultrasound indicator dilution technique,[5–7] requiring the injection of 0.9% sodium chloride solution. The method is noncontinuous, and typically one to two CO measurements per dialysis session are performed. Because of the need to inject an indicator (0.9% saline), the method is not entirely noninvasive.

Impedance cardiography (ICG) has been shown to be a useful tool for noninvasive continuous CO measurements.[8–10] Recently, the Task Force Monitor (TFM; CN Systems, Austria) has gained increased attention for the continuous beat-to-beat assessment of several cardiovascular variables, among them stroke volume and CO. Furthermore, the TFM measures beat-to-beat systolic, diastolic, and mean arterial blood pressure (BP) by the vascular unloading technique and has the capability to assess baroreceptor sensitivity and to perform spectral analysis of heart rate and blood pressure variability.[11] Although the TFM is frequently used in cardiology and intensive care settings, nothing has been reported about the feasibility of the technique in MHD patients so far.[12–14] This study compares CO measurements by TFM and TRS in MHD patients.

Methods

Patients on standard thrice-weekly MHD with arteriovenous fistula as vascular access and an access recirculation of <4% were enrolled after obtaining their written informed consent. The study was approved by the Institutional Review Board at the Beth Israel Medical Center, New York.

Cardiac output was measured simultaneously with both devices in supine patients after 1, 2, and 3 hours on dialysis. Each measurement took approximately 1 minute. This is the time needed by the TRS device to report the CO. The mean of the beat-to-beat COs provided by the TFM was recorded. On average, five CO measurements per patient were obtained (minimum 3, maximum 7; in total 61 measurements). The mean CO per dialysis session for each subject was used for further statistical analyses. By design, each patient was in the supine position for at least 60 minutes before the first measurement started.

Task Force Monitor Measurements

Impedance cardiography measures intrathoracic fluid shifts during a cardiac cycle. Task Force Monitor electrodes were

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attached to the patient as described elsewhere.[15] Stroke volume is calculated by the equation of Sramek *et al.*,

$$SV = V_{th} \times LVET \times \frac{(dZ/dt)_{max}}{Z_0} \quad (1)$$

with LVET being the left ventricular ejection time [sec.], Z_0 the base impedance [kΩ], and t the time [sec.]. V_{th}, the electrically participating thoracic volume is calculated as

$$V_{th} = (0.17\ H)^3/4.2 \quad (2)$$

where H is the body height.

Cardiac output is calculated as the product of SV and heart rate (HR)

$$CO = SV \times HR \quad (3)$$

The crucial element of CO measurements with ICG is to obtain a good estimate for V_{th}. Hence, Sramek *et al.* estimate V_{th} by modeling the thorax as a truncated cone or frustum, respectively.[15] Underweight people are expected to have a more cylindrical thorax shape, whereas the obese will have a more frustum-shaped thorax. In a new aspect of estimating V_{th}, the influence of body composition (by body mass index; BMI), as well as of the base impedance Z_0 is considered

$$V_{th} = C_1 \times H^3 \times \frac{BMI^n}{Z_0{}^m} \quad (4)$$

where the scaling factor C_1 and the powers *n* and *m* are subject to proprietary nondisclosure.[15]

Transonic System Measurements

Cardiac output measurement with TRS requires the injection of a 10-mL bolus of isotonic saline into the venous line as an indicator substance. After the passage through heart and lungs, the arterial line indicator concentration curve is recorded. Cardiac output, which is inversely proportional to the concentration of the indicator sampled downstream, is then automatically computed from the area of the concentration curve according to the following equation (Stewart-Hamilton equation):

$$CO = \frac{V_v}{\int C\ dt} \quad (5)$$

with V_V being the quantity of the indicator [mL], C the indicator concentration, and t the time.

Statistical Analyses

Continuous data are presented as mean ± standard deviation (SD) and range. Cardiac output measurements by TFM and TRS were compared by means of Bland-Altman and Pearson regression analysis. The mean difference between both methods for CO measurements was tested against the *a priori* defined value of 0 mL/min by the one-sample t test. A two-sided *p* value <0.05 was considered significant. All statistical analyses were performed with the SPSS version 11.5 (SPSS Inc., Chicago, IL).

Table 1. Baseline Characteristics of the Study Population

Age (years)	49.2 ± 10.5 (37 to 65)
Sex (F/M)	3/9 (25%/75%)
Race	
White	2 (16.7%)
Black	7 (58.3%)
Other	3 (25%)
Ethnicity	
Hispanic	2 (16.7%)
Non-Hispanic	10 (83.3%)
Patients with diabetes	4 (33.3%)
BMI (kg/m^2)	24.4 ± 3.5 (19.5 to 31.4)
Dialysis vintage (years)	8.6 ± 3.5 (4.8 to 14)
eKdrt/V*	1.4 ± 0.2 (0.9 to 1.8)
enPCR (g/kg bw/d)†	0.9 ± 0.2 (0.5 to 1.4)
Albumin (g/dL)	4.1 ± 0.4 (3.3 to 4.7)
Hemoglobin (g/dL)	12.1 ± 0.9 (10.4 to 13)
Phosphorus (g/dL)	5.2 ± 1.2 (3.9 to 8.9)
Calcium (g/dL)	9.7 ± 0.6 (8.4 to 10.9)

n = 12; values are mean ± SD/percent or range.

* The dose of dialysis is generally defined as the total urea removal provided during each treatment (dialyzer urea clearance /K/ × treatment time /t/) divided by the urea distribution volume (V) derived from urea kinetic modeling. eKt/V (e for equilibrated) reflects the dose calculated from the postdialysis blood urea nitrogen after rebound of nitrogen into the blood compartment has occurred; d indicates that urea clearance achieved with the individual dialysis treatment is taken into account, and r indicates that the individual residual renal function is taken into account.

† The equilibrated normalized protein catabolic rate is used to assess dietary protein intake in patients who are in steady state (in grams per kilogram body weight per day).

Results

The baseline characteristics of the study population are shown in **Table 1**. In the 12 patients studied, mean CO with TRS was 5.4 L/min (SD = 1.1 L/min) and 5.0 L/min with TFM (SD = 0.8 L/min).

Comparison Between TRS and TFM

Linear regression analysis showed good correlation between both techniques (**Figure 1**; r = 0.802, $R^2 = 0.64$, $p = 0.002$). Bland-Altman analysis (**Figure 2**) revealed no systematical difference for CO measurements between the two methods. The mean difference for the CO measurements between the two methods (0.4 L/min) was not significantly different from zero (95% CI: −0.01 to 0.8; SD: 0.6; $p > 0.05$).

Group Comparison

The study population was dichotomized by using the cohort's median of the average of CO measurements (5.2 L/min) for both techniques. For patients with CO below the cohort's median, the mean difference for CO measurements between the two methods (0.01 L/min) was not significantly different from zero (95% CI: −0.3 to 0.3; SD: 0.8; $p = 0.963$), whereas for patients above the cohorts median, the mean difference between the two techniques was significantly different from zero (95% CI: 0.4 to 1.1; SD: 1; $p < 0.001$).

Within-Patient Variability

The SD of the differences between single CO values and the respective subject's mean CO did not differ significantly be-

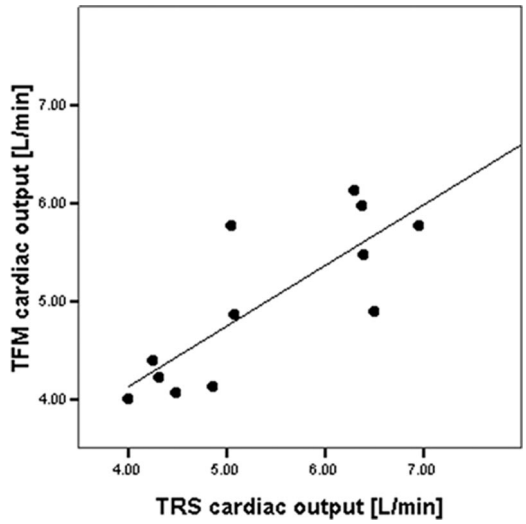

Figure 1. Correlation between TRS and TFM (n = 12) by means of linear regression analysis including the linear regression line ($CO_{TFM} = 1.66 + 0.62 \times CO_{TRS}$; $R^2 = 0.64$).

tween the two methods ($p > 0.05$) with 0.8 L/min (TRS) and 0.5 L/min (TFM), respectively (**Figure 3**, A and B).

Discussion

The main finding of this study is that absolute CO measurement and reproducibility by TFM and TRS do not differ significantly. CO assessment by the TRS system is well established in dialysis patients and is based on the well-explored theory of tracer dilution techniques (Stewart-Hamilton equation).[5–7] It can be easily performed by a nurse and has a low potential for side effects, although it cannot be considered as completely noninvasive. However, this method lacks the possibility of continuous (*i.e.,* throughout a whole dialysis session) monitoring of cardiovascular variables (*e.g.*, CO, CI, TPR, and BP). The strength of the TFM is the capability to assess CO (and other key cardiovascular variables) on a continuous, noninvasive beat-to-beat basis without the need of indicator injection or permanent nurse attendance. A shortcoming of the TFM is the fact that theoretical foundations of bioimpedance and ICG still need to be refined for further improvement of the results. Nevertheless, CO measurements with ICG have already been shown to be closely related with echocardiographic measurements in MHD patients and useful for estimation of individual hemodynamic changes during the dialysis procedure.[9,16] Furthermore, Wynne *et al.* demonstrated that ICG variables correlate significantly with the amount of fluid removed during a hemodialysis session.[17] This feature is of special interest, since an ultrafiltration rate >10 mL/h per kilogram body weight was found to be associated with higher odds of intradialytic hypotension and a higher risk of mortality in the Dialysis Outcome and Practice Patterns Study.[18]

Many underlying causes are known for the development of intradialytic blood pressure drops, such as autonomic neurop-

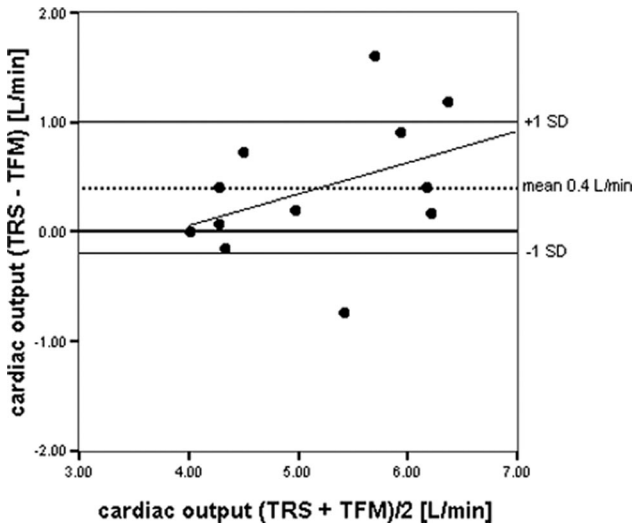

Figure 2. The Bland-Altman plot depicts the differences between TRS and TFM for CO measurements against the mean value of the measurements including the mean, the SD of the differences and the linear regression line ($CO_{(TRS\ -\ TFM)} = -1.09 + 0.29 \times CO_{(TRS\ +\ TFM)/2}$; $R^2 = 0.16$).

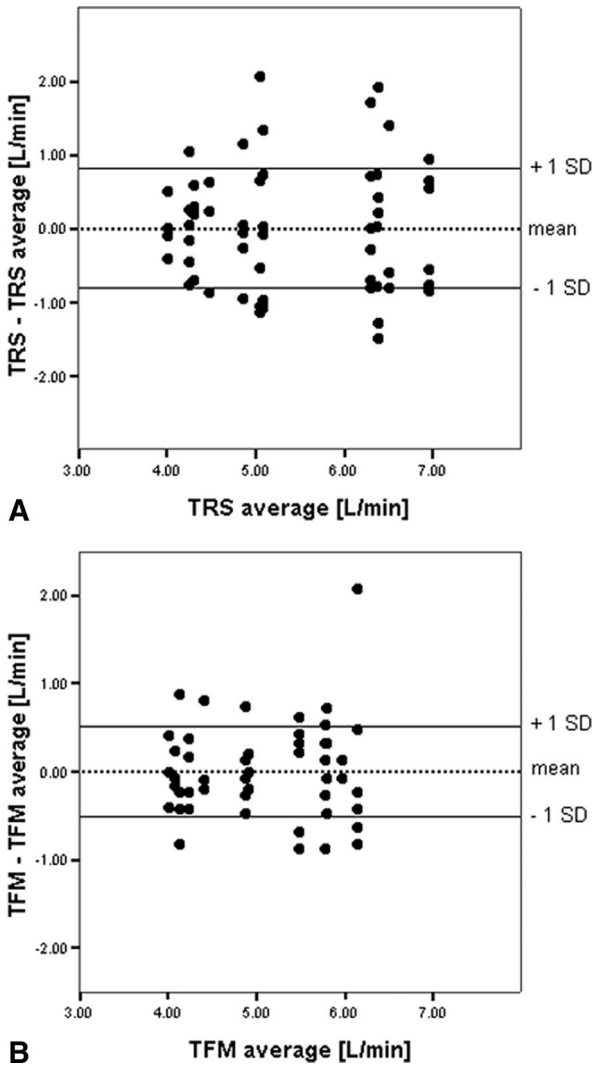

Figure 3. Bland-Altman plots of the differences between single CO values minus the subject average against the subject average for (A) TRS and (B) TFM.

athy (resulting in an inadequate increase of arteriolar tone during ultrafiltration), impaired baroreceptor sensitivity, cardiac systolic or diastolic dysfunction, or reduced stroke volume resulting from a mismatch between ultrafiltration rate and plasma refilling rate; yet the underlying pathophysiology behind is not completely understood.[19–24] Yoshii *et al.* suggested that a reduction in parasympathetic activity next to sympathetic nerve activation and a pronounced increase in TPR are responsible mechanisms for maintaining blood pressure in patients on MHD.[25] Due to its capability to measure SV, HR, CO, CI, BP, and TPR continuously, online monitoring of cardiovascular variables by TFM is a promising tool to further elucidate the pathophysiology of intradialytic hypotension.

Admittedly, there are shortcomings to our study. No differences between the two methods were discerned; however, this may be due to the small sample size of the study population (n = 12). This is especially true given the relatively large measurement error and poor resolution (0.5 L/min) for indicator dilution technique. Furthermore, it would be interesting to see how ICG accuracy varies as a function of CO. Although our study was not specifically designed to elucidate this issue, it is important to note that the difference between the two methods increases with higher CO. However, since none of the two methods can be considered the gold-standard, we cannot tell whether TRS overestimates or if TFM underestimates CO. The use of an invasive method for CO determination would be most useful to further explore that point, but potentially severe complications argue against such an approach.

Another method that allows good estimation of CO is echocardiography; however, it is a highly operator-dependent method and particularly difficult to reproduce during hemodialysis. Moreover, a simultaneous determination of CO by echocardiography and ICG is problematic, because of the bioimpedance electrodes in place.

In view of the fact that body composition influences the calculation of V_{th} (**Equation 4**), which is a vital information for SV calculation, a broad range of BMIs (from 19.5 to 31.4) has been included in the present study. Thus, the method seems to be established within the above range of BMIs but at present it cannot be recommended in patients outside the studied BMI range. More basic research in the field of ICG is needed, particularly the study of the hemodynamics in subjects with very low and high BMIs, given that MHD patients with a low BMI have a worse clinical outcome as compared with their more obese or more muscular fellow patients.[26–29] In addition, the formula by Sramek *et al.* assumes that in a large normal adult population, the averaged linear distance between the electrodes is 17% of total body height, in that way eliminating the need for length measurements.[10,15] Since this information is also used for the calculation of the electrical participating thoracic volume (V_{th}; **Equation 2**) needed for SV calculation, the assumption by Sramek *et al.* may be violated in patients at the extremes of body size, and further studies in these patient groups are needed.

Another important point to consider is the fact that key parameters needed to compute CO by impedance cardiography are based on data obtained in healthy subjects with normal hydration status. Hemodialysis patients are characteristically overhydrated and undergo rapid "correction" by ultrafiltration during dialysis. Our study was not designed to explore the effect of interdialytic weight gain and ultrafiltration rate on CO. Moreover, a study of the variation of CO measurements in a group of elderly, wasted, and ethnically diverse patients is also needed to further evaluate the bioimpedance-based TFM technology.

In conclusion, the TFM is a practical noninvasive device for the continuous beat-to-beat monitoring of cardiovascular variables in MHD patients. In addition, it might be a promising technique to shed light on the underlying pathophysiological mechanisms of intradialytic hemodynamic events.

References

1. Cheung AK, Sarnak MJ, Yan G, *et al*: Cardiac diseases in maintenance hemodialysis patients: results of the HEMO Study. *Kidney Int* 65: 2380–2389, 2004.
2. Covic A, Gusbeth-Tatomir P, Goldsmith DJ: The epidemics of cardiovascular disease in elderly patients with chronic kidney disease: two facets of the same problem. *Int Urol Nephrol* 38: 371–379, 2006.
3. Golebiowski T, Weyde W, Krajewska M, *et al*: Coronary heart disease in patients with end-stage renal disease on maintenance dialysis, II: prophylaxis and treatment. *Postepy Hig Med Dosw (Online)* 60: 290–294, 2006.
4. Fagard R, Conway J: Measurement of cardiac output: Fick principle using catheterization. *Eur Heart J* 11: 1–5, 1990.
5. Kisloukhine VV, Dean DA: Validation of a novel ultrasound dilution method to measure cardiac output during hemodialysis. *ASAIO J* 42: M906–M907, 1996.
6. Krivitski NM, Depner TA: Cardiac output and central blood volume during hemodialysis: methodology. *Adv Ren Replace Ther* 6: 225–232, 1999.
7. Nikiforov YV, Kisluchine VV, Chaus NI: Validation of a new method to measure cardiac output during extracorporeal detoxification. *ASAIO J* 42: M903–M905, 1996.
8. Denniston JC, Maher JT, Reeves JT, Cruz JC, Cymerman A, Grover RF: Measurement of cardiac output by electrical impedance at rest and during exercise. *J Appl Physiol* 40: 91–95, 1976.
9. Karakitsos DN, Patrianakos AP, Paraskevopoulos A, *et al*: Impedance cardiography derived cardiac output in hemodialysis patients: a study of reproducibility and comparison with echocardiography. *Int J Artif Organs* 29: 564–572, 2006.
10. Summers RL, Shoemaker WC, Peacock WF, Ander DS, Coleman TG: Bench to bedside: electrophysiologic and clinical principles of noninvasive hemodynamic monitoring using impedance cardiography. *Acad Emerg Med* 10: 669–680, 2003.
11. Gratze G, Fortin J, Holler A, *et al*: A software package for noninvasive, real-time beat-to-beat monitoring of stroke volume, blood pressure, total peripheral resistance and for assessment of autonomic function. *Comput Biol Med* 28: 121–142, 1998.
12. Braun MU, Schnabel A, Rauwolf T, Schulze M, Strasser RH: Impedance cardiography as a noninvasive technique for atrioventricular interval optimization in cardiac resynchronization therapy. *J Interv Card Electrophysiol* 13: 223–229, 2005.
13. Fortin J, Marte W, Grullenberger R, *et al*: Continuous noninvasive blood pressure monitoring using concentrically interlocking control loops. *Comput Biol Med* 36: 941–957, 2006.
14. Ramirez MF, Tibayan RT, Marinas CE, Yamamoto ME, Caguioa EV: Prognostic value of hemodynamic findings from impedance cardiography in hypertensive stroke. *Am J Hypertens* 18: 65S–72S, 2005.
15. Fortin J, Habenbacher W, Heller A, *et al*: Noninvasive beat-to-beat cardiac output monitoring by an improved method of transthoracic bioimpedance measurement. *Comput Biol Med* 36: 1185–1203, 2006.
16. Ristovska V, Masin G, Ivanovski N, *et al*: Bioelectric impedance in the estimation of hemodynamic and fluid status in dialysis patients. *Acta Med Croatica* 53: 67–71, 1999.
17. Wynne JL, Ovadje LO, Akridge CM, Sheppard SW, Vogel RL, Van de Water JM: Impedance cardiography: a potential monitor for hemodialysis. *J Surg Res* 133: 55–60, 2006.
18. Saran R, Bragg-Gresham JL, Levin NW, *et al*: Longer treatment time and slower ultrafiltration in hemodialysis: associations

with reduced mortality in the DOPPS. *Kidney Int* 69: 1222–1228, 2006.
19. Cases A, Coll E: Chronic hypotension in the dialysis patient. *J Nephrol* 15: 331–335, 2002.
20. Chang MH, Chou KJ: The role of autonomic neuropathy in the genesis of intradialytic hypotension. *Am J Nephrol* 21: 357–361, 2001.
21. Nette RW, van den Dorpel MA, Krepel HP, *et al*: Hypotension during hemodialysis results from an impairment of arteriolar tone and left ventricular function. *Clin Nephrol* 63: 276–283, 2005.
22. Straver B, Roggekamp MC, de Vries PM, ter Wee PM: Systemic vascular resistance in intradialytic hypotension determined by means of impedance cardiography. *Blood Purif* 16: 281–289, 1998.
23. Thayssen P, Andersen KH, Pindborg T: Noninvasive monitoring of cardiac function during haemodialysis. *Scand J Urol Nephrol* 15: 313–317, 1981.
24. van der Sande FM, Mulder AW, Hoorntje SJ, *et al*: The hemodynamic effect of different ultrafiltration rates in patients with cardiac failure and patients without cardiac failure: comparison between isolated ultrafiltration and ultrafiltration with dialysis. *Clin Nephrol* 50: 301–308, 1998.
25. Yoshii M, Minami J, Ishimitsu T, Yamakoshi K, Matsuoka H: Noninvasive monitoring of hemodynamic changes during hemodialysis by the use of a newly developed admittance cardiograph. *Ther Apher Dial* 9: 154–160, 2005.
26. Abbott KC, Glanton CW, Trespalacios FC, *et al*: Body mass index, dialysis modality, and survival: analysis of the United States Renal Data System Dialysis Morbidity and Mortality Wave II Study. *Kidney Int* 65: 597–605, 2004.
27. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, Kilpatrick RD and Horwich TB: Survival advantages of obesity in dialysis patients. *Am J Clin Nutr* 81: 543–554, 2005.
28. Kalantar-Zadeh K, Kopple JD: Obesity paradox in patients on maintenance dialysis. *Contrib Nephrol* 151: 57–69, 2006.
29. Kotanko P, Thijssen S, Kitzler T, *et al*: Size matters: body composition and outcomes in maintenance hemodialysis patients. *Blood Purif* 25: 27–30, 2007.