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Contents

Bimonthly Volume 6 Number 3 May 6, 2017

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Study

World Journal of Nephrology
Volume 6 Number 3 May 6, 2017

Contents

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ORIGINAL ARTICLE

Retrospective Study

Advanced wasting in peritoneal dialysis patients

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Author contributions: Xu Z composed the first draft of this report; Murata GH made the statistical analysis and critical changes in the report; Glew RH made critical changes in the report; Sun Y assisted in the collection of data and made critical changes in the report; Vigil D assisted in the collection of data and made critical changes in the report; Servilla KS assisted in the collection of data and made critical changes in the report; Tzamaloukas AH designed the study and assisted in the collection of the data and the writing of the report.

Institutional review board statement: This study was reviewed and approved by the Human Research Committee of the Raymond G. Murphy VA Medical Center.

Informed consent statement: Patients were not required to give informed consent to the study because the study used anonymous clinical data that were obtained to evaluate nutrition and adequacy of dialytic treatment to which each patient had agreed.

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Abstract

AIM

To identify patients with end-stage renal disease treated by peritoneal dialysis (PD) who had zero body fat (BF) as determined by analysis of body composition using anthropometric formulas estimating body water (V) and to compare nutritional parameters between these patients and PD patients whose BF was above zero.

METHODS

Body weight (W) consists of fat-free mass (FFM) and

BF. Anthropometric formulas for calculating V allow the calculation of FFM as V/0.73, where 0.73 is the water fraction of FFM at normal hydration. Wasting from loss of BF has adverse survival outcomes in PD. Advanced wasting was defined as zero BF when V/0.73 is equal to or exceeds W. This study, which analyzed 439 PD patients at their first clearance study, used the Watson formulas estimating V to identify patients with $V_{Watson}/0.73 \geqslant W$ and compared their nutritional indices with those of PD patients with $V_{Watson}/0.73 < W$.

RESULTS

The study identified at the first clearance study two male patients with $V_{Watson}/0.73 \geqslant W$ among 439 patients on PD. Compared to 260 other male patients on PD, the two subjects with advanced wasting had exceptionally low body mass index and serum albumin concentration. The first of the two subjects also had very low values for serum creatinine concentration and total (in urine and spent peritoneal dialysate) creatinine excretion rate while the second subject had an elevated serum creatinine concentration and high creatinine excretion rate due, most probably, to non-compliance with the PD prescription.

CONCLUSION

Advanced wasting (zero BF) in PD patients, identified by the anthropometric formulas that estimate V, while rare, is associated with indices of poor somatic and visceral nutrition.

Key words: Weight deficit; Fat-free mass; Nutrition; Body water; Anthropometry; Peritoneal dialysis; Watson formulas; Wasting

Core tip: This retrospective study of patients with end-stage renal disease treated by peritoneal dialysis (PD) analyzed the relationship between advanced wasting and other indicators of nutritional status, including body weight and serum albumin concentration. Advanced wasting was defined as zero body fat based on estimates of body water obtained from formulas based on gender, age, height and weight. Only two male patients, both young, were identified as having advanced wasting among the 439 patients (262 men and 177 women) on PD we studied. Both of these patients with advanced wasting had poor nutrition as evidenced by their remarkably low body weights and serum albumin levels. We conclude that advanced wasting, as defined in this study, is rare in patients on PD, but when present is strongly indicative of an exceedingly poor overall state of nutrition.

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INTRODUCTION

The overall prognosis and survival of patients with chronic diseases, including those whose end-stage renal disease is treated by dialysis, is strongly linked to their nutritional status. The nutritional status of patients on chronic peritoneal dialysis (PD) has been assessed by anthropometry[1-3], biochemical parameters including serum albumin[4,5] and pre-albumin[5,6], and evaluation of body composition by bioelectrical impedance[7-9], dual energy X-ray absorptiometry[10,11], and measurement of total body potassium by stable isotopic methods[10].

In addition to the aforementioned direct analytical methods, indices estimated from the excretion of nitrogenous products in urine and in spent dialysate have also been applied to evaluate nutrition in patients receiving PD. These nutritional indices include the protein nitrogen appearance (PNA), which is derived from the excretion of urea nitrogen and provides an estimate of dietary protein intake[12], and lean body mass (LBM) which is estimated from the excretion of creatinine and provides an estimate of muscle mass[13]. A composite nutritional index derived by combining findings from history, physical examination and clinical laboratory analyses has been applied in PD patients[14,15].

This report addresses the identification and overall nutritional status of an advanced degree of weight deficit in PD patients. Weight deficit is encountered in approximately 7.5% of the patients on PD[2] and may result from muscle loss (sarcopenia) or from grossly diminished body fat (BF)[16]. Under several circumstances sarcopenia is associated with obesity rather than weight loss. In contrast, loss of BF is always associated with weight deficit. Low BF is defined as BF < 20% of body weight in women and < 12% of body weight in men[17]. BF can be assessed by anthropometry (skin-fold thickness), dual energy absorptiometry, bioelectrical impedance, and other methods usually restricted to research studies. Measurement of body water (V) by radioisotope dilution is one of the standard research methods for assessing BF and has been applied in PD studies[10]. In PD patients, V, which is needed for the calculation of fractional urea clearance (Kt/V urea) for assessing the adequacy of PD, is routinely estimated by anthropometric formulas. Estimates of V from anthropometric formulas can also be used to estimate BF[18,19].

Wasting in PD patients has been associated with adverse outcomes. This study had two aims: The first aim was to provide a definition of advanced wasting in PD patients by estimating BF calculated from V obtained from anthropometric formulas; the second was to identify PD patients with advanced wasting and to evaluate the association of advanced wasting with other traditional indices of nutritional status.

MATERIALS AND METHODS

Definition of advanced wasting

Table 1 defines the abbreviations used in this report.

Table 1 Abbreviations used in this report

Abbreviation	Interpretation
V	Body water, L; V_{Watson} = body water estimated by the Watson formula
W	Body weight, kg
IW	Ideal body weight, kg
BF	Body fat, kg
FFM	Fat-free mass, kg
BMI	Body mass index, kg/m^2
PNA	Protein nitrogen appearance, g; nPNA/W = PNA normalized to W, g/kg; nPNA/IW = PNA/IW = PNA normalized to IW, g/kg
Cr Ex	Creatinine excretion rate, mg/24-h; (MCr Ex)/W = measured Cr Ex normalized to W, (mg/kg)/24-h; (MCr Ex)/IW = Measured Cr Ex normalized to IW, (mg/kg)/24-h
M/P Cr Ex	Measured/Predicted creatinine excretion rate
LBM	Lean body mass estimated from Cr Ex, kg; LBM/W = LBM normalized to W; LBM/IW = LBM normalized to IW

Advanced wasting has been defined as zero BF calculated using an anthropometric formula to estimate V[18]. This calculation is based on the assumption that body weight (W) consists of fat-free body mass (FFM) and BF. When hydration abnormalities are absent, the water content of FFM, which essentially represents all the water in the body because fat contains miniscule amounts of water, is constant at 73% (FFM = V/0.73)[20]. The fraction of body weight represented by water (V/W) is low in obese subjects in whom BF is a large component of W and, conversely, high in patients with weight deficit in whom BF is a small fraction of W. Thus, the V/W ratio increases progressively as body weight decreases due to loss of BF. Accordingly, this increase in the ratio V/W becomes evident when V is calculated by means of anthropometric formulas[21]. The value V/0.73 approaches W with progressive weight loss and becomes equal to W at a specific weight and larger than W below this weight[18]. Subjects with FFM calculated as V/0.73 equal to or larger than W have zero BF. Therefore, it is reasonable to define advanced wasting as V/0.73 $\geqslant$ W.

Patients and nutrition indices

Using the Watson formulas[22] to calculate V (V_{Watson}), we computed FFM as V_{Watson}/0.73 and compared it to W in 439 patients (262 men and 177 women) on PD. This comparison was performed at the time of the first determination of urea and creatinine clearances for assessment of the adequacy of PD. We compared nutrition indices between PD patients with V_{Watson}/0.73 $\geqslant$ W and those with V_{Watson}/0.73 < W.

Ideal weight (IW) was calculated by the method of Hamwi[23,24]. PNA was calculated by the method of Bergstrom[12] and normalized to both actual weight (nPNA/W) and ideal weight (nPNA/IW)[25]. LBM estimated from creatinine kinetics was computed according to the method of Keshaviah[13] and normalized to both actual weight (LBM/W) and ideal weight (LBM/IW). Measured creatinine excretion in dialysate plus urine was normalized to actual weight [(MCr Ex)/W], ideal weight [(MCr Ex)/IW], and predicted creatinine excretion (M/P Cr Ex). Predicted creatinine excretion was calculated using the formula: Cr Ex, mg/24-h = 302.150 - 4.380 × Age, years + 171.234 × Gender (women: 0; men: 1) - 39.041 × Diabetes (no: 0; yes: 1) + 11.730 × Weight, kg[26]. Measured and computed nutrition indices were compared between patients with V_{Watson}/0.73 ≥ W and their respective 95%CIs in patients with V_{Watson}/0.73 < W (the control group). Statistical analysis was performed using SYSTAT version 13.1.

RESULTS

Table 2 summarizes the clinical characteristics of the only two patients (Patient 1, Patient 2) with V_{Watson}/0.73 $\geqslant$ W we identified among the 439 PD subjects analyzed. The frequency of advanced wasting was 0.5% in the population studied. Both subjects with advanced wasting were young (23 years or less), had renal failure due to primary glomerular diseases from childhood, were short and had a low body weight at the first clearance study. In both patients, body weight had changed by < 1 kg between initiation of PD and the first clearance study. Both Kt/V urea and creatinine clearance were inadequate in Patient 1 but adequate in Patient 2. Peritoneal transport characterized by a peritoneal equilibration test[27] was high in Patient 1 and low-average in Patient 2.

Table 3 compares the nutrition indices for Patients 1 and 2 with those of the control group of the remaining 260 male patients. Body mass index (BMI), the ratio of body weight to ideal weight (W/IW) and the serum albumin concentration were below the lower 95% confidence limit of the control group in both Patient 1 and Patient 2. In Patient 1, the serum urea nitrogen and creatinine levels were below the corresponding lower 95% confidence limits of the control group. In Patient 2 the serum urea nitrogen level was within the 95% confidence interval of the control group, while the serum creatinine level was above the upper 95% confidence limit of the control group.

In both Patient 1 and Patient 2 the nPNA/W and nPNA/IW values were within the 95% confidence interval of the control group. Normalized creatinine excretion values (MCr Ex)/W), (MCr Ex/IW) and the various indices derived from creatinine excretion (M/P Cr Ex, LBM/W, LBM/IW) were below the corresponding lower 95% confidence limits of the control group in Patient 1 and above the corresponding upper 95% confidence limits of

Table 2 Clinical characteristics of peritoneal dialysis patients with advanced wasting

Clinical characteristic	Patient 1	Patient 2
Sex	Male	Male
Cause of ESRD	Glomerulonephritis	Glomerulonephritis
Age, yr	21	23
Height, cm	149	155
Weight, kg	36.7	40.0
Kt/V urea[1], weekly	1.34	2.92
Creatinine clearance[1], L/1.73 m^2 weekly	49	218
Peritoneal transport (4-h D/P creatinine)[2]	High (0.84)	Low-average (0.54)

[1]Total (renal plus peritoneal) clearance; [2]Characterized by the value of the 4-h dialysate/plasma (D/P) creatinine concentration ratio in a peritoneal equilibration test (PET)[27]. ESRD: End-stage renal disease.

Table 3 Nutrition indices in two males with advanced wasting (Patient 1, Patient 2) and a control group

Nutrition index	Patient 1	Patent 2	Control group[1]
V_{Watson}/0.73	1.036	1.030	0.744 (0.521-0.932)
BMI, kg/m^2	16.5	16.6	25.5 (18.9-32.8)
W/IW	0.778	0.816	1.151 (0.935-1.367)
Serum albumin, g/dL	2.60	2.80	3.60 (3.15-4.05)
Serum urea nitrogen, mg/dL	41.0	58.0	56.8 (43.2-70.4)
Serum creatinine, mg/dL	2.02	13.55	7.38 (5.25-9.51)
nPNA/W, g/kg per 24 h	0.94	1.21	0.86 (0.70-1.02)
nPNA/IW, g/kg per 24-h	0.81	1.07	0.99 (0.75-1.13)
(MCr Ex)/W, mg/kg per 24-h	13.0	35.9	18.7 (13.9-23.5)
(MCr Ex)/IW, mg/kg per 24-h	11.4	27.9	21.5 (17.5-25.5)
M/P Cr Ex	0.51	1.680	0.97 (0.55-1.39)
LBM/W	0.64	1.420	0.66 (0.55-0.77)
LBM/IW	0.52	1.100	0.76 (0.66-0.86)

[1]The control group consisted of 260 men on PD analyzed in their first clearance study. The values in the control group column indicate mean (95%CI). BMI: Body mass index; PNA: Protein nitrogen appearance; LBM: Lean body mass; IW: Ideal body weight; PD: Peritoneal dialysis.

the control group in Patient 2 (Table 3).

DISCUSSION

This report has two main findings: First, the incidence of advanced wasting defined as zero BF as determined using the Watson formula estimating V was very low in patients on PD at the time of their first formal clearance study. Second, the two PD patients with advanced wasting defined by the use of the Watson formulas had very low body weight and serum albumin levels. However, several indices of nutritional status derived from urea nitrogen and creatinine excretion in these patients appeared to be normal or even elevated.

Weight excess and deficit are routinely evaluated in most populations by BMI, whereas deviation from ideal weight is used less frequently. The cut-off value for weight deficit is commonly set at a BMI of 18.5 kg/m^2 in guidelines for the general population[28] or at a W/IW ratio of < 0.9 in PD patients[1,2]. The BMI values that correspond to a W/IW of 0.9 are 18.8 kg/m^2 in women and 21.2 kg/m^2 in men when ideal weight is estimated from the Hamwi formulas[29]. There is, in general, good agreement between BMI, W/IW and BF expressed as a fraction of body weight. However, there is substantial disagreement between BMI and W/IW estimates in the classification of individuals on PD as obese, normal weight or underweight[30]. In addition, there is substantial disagreement between BMI and lean body mass, and consequently between BMI and BF when estimated by DXA in PD patients[29].

In addition to the discrepancies between BMI and W/IW listed above, weight status classification on the basis of BMI or W/IW is subject to error because it does not take into account sarcopenia when it is associated with obesity or changing body composition as people age. Classification of weight deficit by BF content is subject to fewer errors[16], but may require expensive, sophisticated technology that is usually available only for research studies. Identification of patients with BF deficit is important because numerous studies support the assertion that low BF is associated with a poor outcome for PD patients.

The effect of weight deficit or obesity on the outcomes of chronic dialysis was first evaluated in hemodialysis patients in whom weight deficit was identified as a predictor of poor survival, while obesity was found to offer a survival advantage[31,32]. The effect of obesity on the outcome of patients receiving PD is less clear. A large retrospective study of United States Medicare PD patients found that obesity does offer a survival advantage[33]. Subsequent studies in the United States reported that the survival advantage of obesity was much weaker for PD patients compared to hemodialysis patients[34,35] and that obesity is a risk factor for peritonitis[36]. Kutner and Zhang[37] reported that the relationship between obesity and survival of PD patients is modified by race and gender, with obese white women on PD having a high risk of mortality. The influence of race on the outcomes of obesity in PD was confirmed by similar studies conducted in Asia[38] and in Australia and New Zealand[39]. Other studies reported either adverse effects[40,41] or no effect[42,43] of obesity on the survival of PD patients.

The focus of the present report is advanced weight deficit, not obesity. Unlike obesity where there is disagreement about its effect on the survival of patients treated by PD, the adverse effects of weight deficit on the outcomes of PD have been uniformly concordant[33,39-43]. Weight loss in the first year of PD is associated with an increased risk of death[44]. Finally, a recent meta-analysis confirmed the risk of mortality from low body weight of PD patients[45].

In the present report, we analyzed the nutritional status of PD patients identified as having advanced wasting based on the use of anthropometric formulas to estimate V. In the two PD patients identified as having advanced wasting using this method, the finding of very low BMI and serum albumin levels confirmed a poor nutritional status, whereas nutrition indices based on

creatinine excretion provided conflicting findings. The potential pitfalls of creatinine excretion as a nutritional index in PD patients should be recognized.

An elevated serum creatinine value at the onset of PD[3], together with a high rate of creatinine excretion[46] is predictive of relatively long survival of PD patients. Creatinine production and excretion are directly related to muscle mass. High rates of creatinine excretion are indicative of preserved muscle mass and, therefore, good somatic nutrition[46]. However, high creatinine excretion rates are also encountered in clinical states causing muscle destruction, including certain disease states and drugs, and in unsteady states following rapid increases in creatinine clearance in patients with azotemia. Examples of clinical states causing rapid rise in creatinine clearance include elimination of the cause of urinary retention, correction of prerenal azotemia due to hypovolemia, hemodialysis sessions and resumption of the prescribed dose of PD by patients with previous poor compliance with the PD prescription. In this last case, calculating the M/P Cr in the unsteady state immediately following resumption of the prescribed PD dose has been proposed as an indicator of poor compliance with the prescribed dose of PD[47]. Creatinine excretion rates producing LBM/W values $\geqslant$ 0.9 x W are strong indicators of non-compliance[48]. LBM/W computed from creatinine excretion data is, on average, about 10% lower than fat-free mass (FFM) calculated as $V_{Watson}/0.73$[49]. The higher value of LBM/W compared to $V_{Watson}/0.73$ in Patient 2 (Table 3), who had no catabolic neuromuscular disease and was on no medications causing rhabdomyolysis, suggests that non-compliance was the reason for his very high creatinine excretion rate. Strong clinical evidence of non-compliance supports this conclusion.

The main limitations of the present report are the small number of patients categorized as having advanced wasting and especially the lack of information about survival, morbidity and overall quality of life in the two patients with advanced wasting and the control group. Further studies will be needed to evaluate the relationship between various nutrition indices in PD patients classified by anthropometric estimates of V as having advanced wasting and the outcomes of these patients. Another limitation is that anthropometric formulas may not provide accurate estimates of V at very low body weights, particularly in patients with sarcopenia and weight deficit. To test whether there are differences between various anthropometric formulas, we repeated the calculations using all formulas that estimate V[18] (data not shown). For all these calculations, both Patient 1 and Patient 2 exhibited a V/0.73 value that exceeded W. Thus, the characterization of advanced wasting in Patients 1 and 2 was consistent regardless of the anthropometric formula we used to estimate V. A third limitation of this report is that anthropometric V values systematically underestimate V in patients with edema[50]. Edema is common in PD populations[51-53]. Values V/0.73 greater than W when V is estimated by anthropometric formulas may result in some cases from combined loss of BF and severe sarcopenia or from wasting with water excess. In this second instance the degree of wasting is even greater than the degree suggested by V/0.73. We suggest that a patient's hydration status should be evaluated in patients when V/0.73 > W.

In conclusion, anthropometric formulas calculating V can accurately identify PD patients with advanced wasting. PD patients with advanced wasting identified by this method have poor nutrition indices. Special diagnostic and therapeutic efforts addressing the nutrition of these patients are required.

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COMMENTS

Background

Weight deficit caused by loss of body fat (BF) has adverse effects on the state of health and survival of patients with end-stage renal disease. BF is estimated as the difference between body weight and fat-free body mass. At normal hydration, fat-free body mass can be calculated as the fraction body water (V) over 0.73 fat-free body mass. Thus fat-free body mass and BF can be computed from V. In this study, the authors computed BF using anthropometric V estimates obtained at the first clearance study to evaluate adequacy of peritoneal dialysis (PD) and compared nutrition indices between the small number of patients with advanced body wasting (zero BF) and a large control group of patients with BF greater than zero.

Research frontiers

Because of the recognized effect of preservation of BF and fat-free body mass in patients on chronic dialysis, evaluation of body composition in these subjects has been an important focus of research. Various research methods have been applied in the study of body composition. These research methods require both costs for equipment and expertise. These requirements apply even to bioelectrical impedance analysis, which is the simplest method for evaluating body composition.

Innovations and breakthroughs

In contrast to research methods for evaluating body composition, the method proposed in this report utilizes only information and measurements necessary for evaluating the adequacy of PD and does not require any additional instruments or expertise. The method has no added cost.

Applications

Computation of BF using anthropometric V estimates could allow simple and free of any costs monitoring of body composition in PD patients. Body composition estimates from this method could be compared to both indices of nutrition and results of research methods evaluating body composition. These comparisons will establish the place of the method presented in this report in the clinical monitoring of PD patients.

Terminology

The following symbols are essential for comprehending this method. W: Body weight; FFM: Fat-free mass; BF: Body fat; V: Body water. The following equations express the method: W = FFM + BF; FFM = V/0.73; BF = W - V/0.73.

Peer-review

This manuscript is clinically interesting.

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