加强護理病人身體組成的研究: 總體水分測定方法的比較

Body composition studies in intensive care patients: comparison of methods of measuring total body water

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Changes in total body water (TBW) were monitored in 12 critically-ill intensive care patients using four independent methods. Over the 10-day study period TBW measured by tritium dilution changed from 51.3 ± 2.5 (SEM) kg to 43.6 ± 2.3 kg, an average loss of 7.7 ± 0.8 kg. A six-compartment model of the body incorporating measurements of protein by *in vivo* neutron activation analysis and fat and bone mineral by dual-energy X-ray absorptiometry was used to determine TBW by difference from body weight. The 10-day change in TBW measured by this approach was 8.4 ± 0.9 kg which correlated well with the tritium dilution changes (r=0.84, $P<0.01$, SEE=1.83 kg). The changes measured by single frequency and multi-frequency bio- electrical impedance analysis were not significantly different from the tritium results (9.7 ± 1.3 and 8.2 ± 0.8 kg, respectively) although the prediction errors were high for both methods (SEE=3.29 and 2.72 kg, respectively) with correlations that were statistically significant for the single frequency approach but not for the multi-frequency approach (r=0.71, $P<0.01$ and r=0.45, ns, respectively). The high prediction errors render these impedance techniques inappropriate, at the present time, for monitoring total water changes in individual intensive care patients.

Introduction

Critical illness is characterized by dramatic changes in body composition which include marked losses of body protein and expansion of body water. If these changes are large and prolonged they are associated with immunosuppression, compromised wound healing, loss of muscle function and finally, multiple-organ dysfunction or failure and in some cases, death. Reliable monitoring of the body composition of these patients offers a tool for testing the efficacy of new therapies designed to modify the metabolic disturbances suffered by these patients and thence to enhance their recovery. New developments in body composition technology have expanded the range of measurements that can be applied to such patients. For example, dual-energy X-ray absorptiometry (DEXA) allows both total and regional fat, lean tissue and bone mineral assessment[1] and estimation of total appendicular muscle mass[2]. Multiple frequency bioimpedance analysis (MFBIA) is under development to measure the total water compartment and its distribution across the intra- and extracellular spaces[3]. Both MFBIA and single frequency bioimpedance analysis (SFBIA) have yielded encouraging results when applied to healthy individuals[3–5]. In this report we have examined four independent methods of measuring total body water (TBW) in critically ill patients who have suffered either major trauma or serious sepsis. Our approach was to compare an established isotope dilution procedure for total water measurement with results given by SFBIA, MFBIA, and the combination of DEXA and in vivo neutron activation analysis (IVNAA).

Methods

Subjects

The study group comprised 12 patients (median age 25 years, range 16 to 53 years, 11 men, 1 woman) admitted to the Department of Critical Care Medicine, Auckland Hospital, suffering from major trauma (injury severity score > 16) or septic shock. Table 1 shows relevant clinical data. The study was approved by the Research Ethics Committee of the Auckland Hospital, and informed consent was obtained from the patients' next of kin.

Table 1. Clinical data for 12 intensive care patients.

Patient	Sex	Age (yrs)	Diagnosis
CT	M	17	Head injury. Right extradural haematoma requiring surgical drainage.
SA	M	20	Industrial trauma with ruptured spleen and left renal contusion. Splenectomy.
IS	F	19	Traumatic pancreatitis requiring distal pancreatectomy and splenectomy.
RF	M	26	Meningococcal meningitis leading to meningococcal septicemia.
DB	M	23	Head injury with multiple frontal lobe contusions. No surgery required.
DH	M	53	Head injury with facial fractures. Fractured ribs. Right lung contusion.
HJ	M	25	Intra-abdominal abscess.
MK	M	39	Basal skull fracture. Pneumothorax. Fractures of left humerus and ribs. Bilateral fracture of clavicles.
DP	M	32	Head injury. Right intracerebral haematoma.
GP	M	53	Urolithiasis causing septic shock.
KS	M	16	Trauma-frontal lobe haematoma. Fractures of left tibia, radius and ulna.
ST	M	25	Multiple abscesses. Laparotomy required.

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Body composition measurements

Tritium dilution. TBW was determined following the IV injection of a tracer dose of tritiated water (3.7 MBq) as described in detail elsewhere[6]. Blood samples were taken at 4, 5 and 6 hours after injection and tritium assayed in water extracted from the serum. TBW is assumed to be the tritiated water space as given by the mean of the 4-, 5- and 6-hour samples.

In vivo neutron activation analysis. The prompt gamma IVNAA technique as implemented in this Department for the measurement of critically-ill patients has been described in detail elsewhere[7]. The patient lies supine on a horizontal couch which is driven at a constant speed between two ^{238}Pu-Be neutron sources, one above and one beneath the couch. Collimated beams of fast neutrons from the sources irradiate the patient. Gamma rays emitted during the irradiation are counted by four 5 x 6 cm sodium iodide scintillation counters mounted two on each side of the patient. Net counting rates due to neutron capture gamma rays from nitrogen (10.8 Mev) are recorded. Total body protein (P) is calculated assuming nitrogen comprises 16% of the protein in the body.

Dual-energy X-ray absorptiometry. DEXA can be used to partition body mass into three components: total body fat (F), bone mineral content (B), and fat-free soft tissue (L)[1,8]. DEXA measurements were performed using a commercial scanner (model DPX+, Lunar Radiation Corpn, Madison, WI, USA) and the manufacturer's whole-body software (version 3.6y).

Single frequency bio-electrical impedance analysis. A four-terminal impedance analyser was used to measure resistance and reactance following the manufacturer's instructions (Model BIA-101, RJL Systems, Detroit, MI, USA). Gel electrodes were placed on the hand and foot of the dominant side and measurements were taken with arms and legs slightly spread. The measured values of resistance and reactance were entered into the computer program supplied by RJL Systems, along with the subject's weight, height, age, and sex, to provide estimates of TBW.

Multiple frequency bio-electrical impedance analysis. A Xitron-4000B impedance analyser (Xitron Technologies, Inc., San Diego, CA, USA) was used to measure resistance, reactance, impedance and phase angle at 48 frequencies between 5 and 500 kHz. A tetrapolar arrangement of gel electrodes was applied as for the single frequency measurement. The data collected by an online computer were fitted to modelling software provided by the manufacturers. The Cole-Cole electrical circuit model for muscle tissue is used to generate values for the resistivities of the extra- and intracellular fluid spaces and the volumes of these spaces are derived from equations developed by the manufacturers based on the volume theories of Hanai[9].

Calculations and statistical analysis. TBW was calculated from the IVNAA and DEXA results by a difference method which assumes a six-compartment model for the body, ie:

$$\text{TBW by difference} = \text{weight} - P - B - F - G - NB, \quad (1)$$

where the small non-bone minerals (NB) and glycogen (G) compartments are estimated from total protein and total minerals, respectively, based on the sizes of these compartments in reference man[10]. NB is calculated as 5.7% of total protein and G is estimated as 15% of total minerals (B+NB). Inclusion of these two components reduces the systematic error that would otherwise arise in extracting TBW by a difference approach.

Tritium dilution was compared with the other methods of

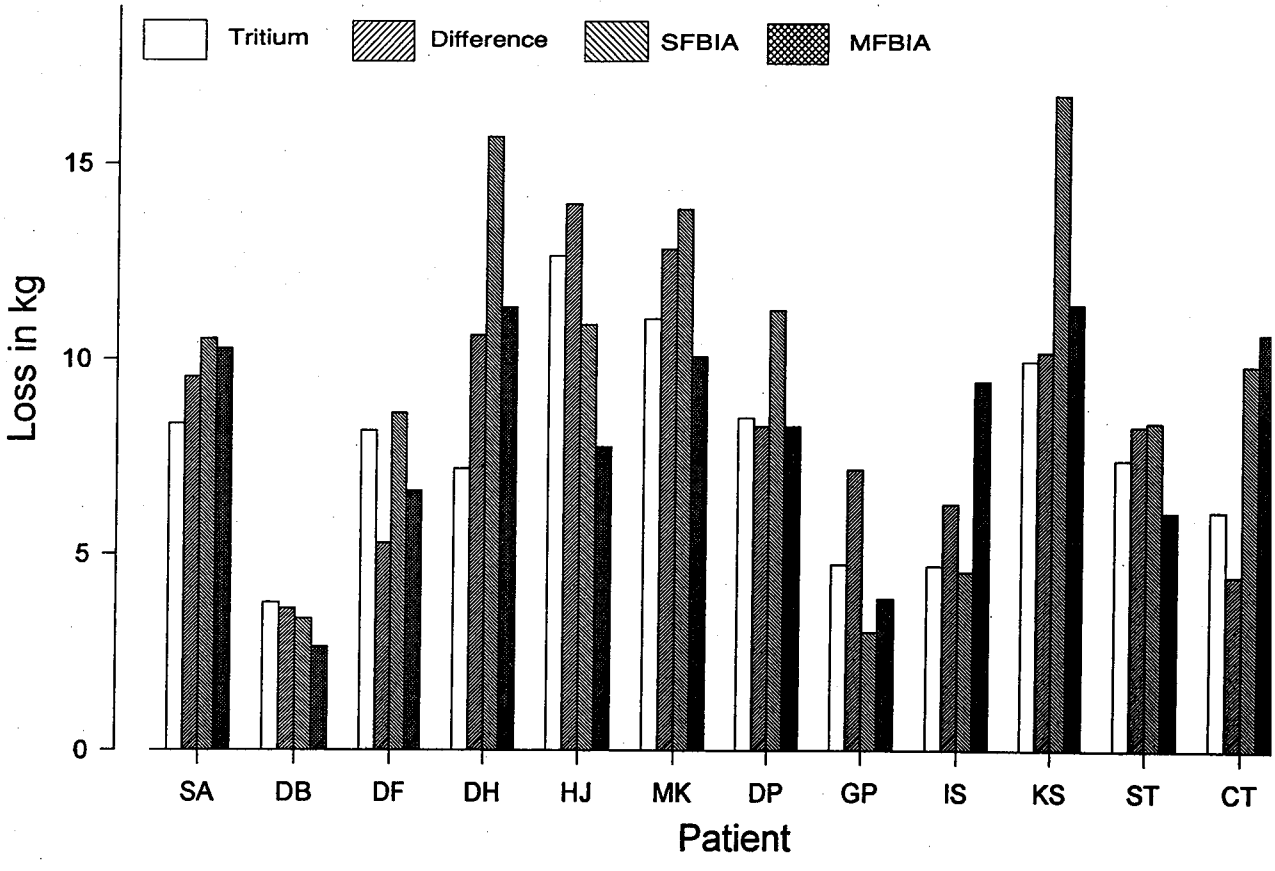

Figure 1 Ten day losses in total body water for each of 12 patients measured by tritium dilution, a compartmental modelling approach (difference method), single frequency (SFBIA) and multifrequency (MFBIA) bioimpedance analysis.

Table 2. Body composition changes over 10 days in 12 intensive care patients.

Patient	Components of body composition (kg). Weight		Protein		Fat		Bone mineral	
	Day 0	Day10	Day 0	Day 10	Day 0	Day 10	Day 0	Day 10
SA	85.3	74.2	12.44	12.36	6.89	5.66	4.14	3.99
DB	63.2	58.2	8.42	8.04	10.06	9.16	2.75	2.70
DF	76.4	67.9	11.73	10.18	8.23	6.86	3.01	2.88
DH	90.3	76.8	13.40	10.30	10.47	10.45	4.01	3.86
HJ	75.7	58.4	9.07	7.73	11.55	9.99	2.93	2.75
MK	90.7	75.1	12.56	10.19	17.10	16.95	3.00	3.04
DP	74.9	64.7	10.08	8.77	8.94	8.64	2.95	2.81
GP	90.5	84.2	10.58	9.44	23.14	21.68	3.01	3.08
IS	57.8	51.1	7.43	6.65	13.83	14.56	2.65	2.41
KS	80.9	67.0	11.74	8.97	8.19	7.61	3.29	3.31
ST	95.3	87.7	12.76	12.66	13.79	14.39	3.53	3.81
CT	74.2	67.6	10.40	9.08	8.80	8.31	4.05	3.86
Differences								
Mean	−10.2		−1.35		−0.56		−0.07	
SEM	1.2		0.28		0.22		0.04	
P^*	<0.0001		0.0006		0.029		ns	

* t-test for 10 day difference; ns, not significant.

TBW estimation by using repeated measures analysis of variance and regression analyses as indicated. All statistical analyses were carried out using SAS (Statistical Analysis System)[11]. Limits of agreement (mean difference ± 2SD of the differences) between TBW by tritium dilution and the other methods were calculated using the method of Bland and Altman[12]. A significance level of 5% was used.

Protocol

Patients were transported to the body composition laboratory of the Department of Surgery as soon as they were haemodynamically stable. An electrically operated hoist incorporating a load cell for weighing the patient was used to transfer the patient to the scanning couches for body composition assessment. The measurements were repeated on each patient 10 days following the initial assessment. Supine height of each patient was used to determine scanning time for IVNAA. Standing height was measured following recovery.

Results

The changes in body weight and in body composition assessed by DEXA and IVNAA for the 12 patients over 10 days are shown in Table 2. A dramatic fall in body weight was observed (mean loss 10.2 kg, $P<0.0001$) and all patients lost protein (mean loss 1.4 kg, $P<0.001$). The individual 10 day changes in TBW as measured by four independent methods are presented in Figure 1. Table 3 shows the mean changes in TBW over the 10 days measured by tritium dilution compared with measurements using the bioimpedance and difference techniques. The 10 day losses were statistically significant for all four methods (paired t-tests, $P<0.0001$). Repeated measures ANOVA indicated no significant difference between tritium dilution and TBW measured by any of the other three methods for either day of measurement or for the 10 day changes. When measurements for both days are combined the correlations between tritium TBW and the other TBW methods were all highly significant ($P<0.0001$) (Table 4). The linear regressions of each of these three other methods on tritium TBW were not significantly different from the line of identity although the SEE for the difference method was approximately half those found for the bioimpedance methods. When the 10 day *changes* in TBW by tritium dilution were correlated with the changes measured by the difference, SFBIA and MFBIA techniques the respective correlation coefficients were 0.84 ($P<0.001$), 0.71 ($P<0.01$), and 0.45 (ns) (Table 5). For all the measurements taken the difference technique measures on average 1.09 ± 0.35 (SEM) kg more than tritium dilution with limits of agreement ranging between −4.5 and 2.4 kg (Table 6). Although the bias is not significant for the SFBIA method (mean difference 0.93 ± 0.69 kg) the limits of agreement range between −7.7 and 5.8 kg. The MFBIA method underestimates the water space given by tritium dilution with similarly wide limits of agreement ranging from −4.4 to 9.2 kg.

Table 3. Total body water measurements (kg) in 12 patients over 10 days by four methods (mean ± SEM).

	Day 0	Day 10	10 day loss	P value*
Tritium	51.3±2.5	43.6±2.3	7.7±0.8	<0.0001
Difference	52.8±2.5	44.4±2.2	8.4±0.9	<0.0001
SFBIA	53.3±2.9	43.5±2.4	9.7±1.3	<0.0001
MFBIA	49.2±2.6	41.0±2.6	8.2±0.8	<0.0001
ANOVA†	ns	ns	ns	

* t-test for 10-day loss.
† Repeated measures ANOVA comparing the four methods of measurements; ns, not significant.

Table 4. Correlations (r) between TBW measured by tritium dilution and three other methods for measurements on 12 patients on two occasions.

Method	Slope*	Intercept*	SEE(kg)	CV(%)	r	P
Difference	1.00	1.32	1.76	3.6	0.98	<0.0001
SFBIA	1.09	−3.13	3.37	7.0	0.95	<0.0001
MFBIA	1.02	−3.36	3.46	7.7	0.94	<0.0001

*Slope and intercept for the regression on TBW by tritium dilution

Table 5. Correlations (r) between 10 day changes in TBW measured by tritium dilution and three other methods for 12 patients.

Method	Slope*	Intercept*	SEE(kg)	r	P
Difference	1.02	0.51	1.83	0.84	0.0006
SFBIA	1.21	−0.42	3.29	0.71	0.009
MFBIA	0.49	−4.45	2.72	0.45	ns

*Slope and intercept for the regression on TBW by tritium dilution.

Table 6. Mean differences (±SEM) and limits of agreement for comparison of TBW measured by tritium dilution with three other methods for measurements on 12 patients on two occasions.

Method	Mean difference (kg)*	SEM (kg)	Limits of agreement (kg)
Difference	–1.09	0.35	–4.53 – 2.35
SFBIA	–0.93	0.69	–7.68 – 5.84
MFBIA	2.40	0.69	–4.38 – 9.18

*TBW by tritium dilution minus other method.

Discussion

Tracer dilution methods, using deuterated or tritiated water, are well established as a means of determining the size of the total body water compartment in human subjects. These methods necessitate, however, time-consuming analyses of blood samples and, in the case of tritium, a radiation dose to the subject. A rapid, safe, noninvasive and straightforward technique for measuring this, the largest compartment of the body, would prove to be of considerable benefit both to the clinician and to the body composition researcher. BIA is such a technique which has proved reliable for assessment of TBW in healthy subjects[3–5]. Its reliability in pathological conditions, however, is controversial[13,14]. In the present study we have compared TBW measurements from two BIA instruments and a compartmental modelling approach with tritium dilution as an established reference technique for body water estimation. We have demonstrated that in a group of patients undergoing large changes in hydration status BIA can reliably monitor these fluid changes. The residual variances about the regressions on TBW by dilution and the wide limits of agreement between the dilution and the BIA techniques suggest that the BIA methods are inappropriate at the present time for measuring changes in total water in the individual intensive care patient. The compartmental modelling approach agrees well with the results of tritium dilution and confirms, at least for the measurement of changes in TBW, the accuracy of the latter. For the measurement of absolute size of the water compartment both approaches are subject to small systematic errors which, in the case of tritium dilution, derive from the extent of exchange with non-aqueous hydrogen[15], and in the case of the difference approach, derive largely from fluctuations in the glycogen compartment.

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