BODY WATER SPACES AND CELLULAR HYDRATION DURING HEALTHY AGING

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ABSTRACT

Age-related changes in the proportions of intracellular or extracellular water to total body water, and in the ratio of total body water to fat-free mass are debatable. These are important issues both for medical reasons (dehydration is a threat in the diseased elderly), and for methodological reasons (most techniques for assessing of body composition assume constant hydration of the fat-free mass). This study compared hydration in young and elderly (> 60 yrs) people. In the first part of the study, we analyzed the literature, and computed the ratio of total body water over fat-free mass, Hf. Eligible studies involved independent measurements of fat-free mass and total body water. Hf does not appear to change with age. The second part of this study computed Hf in 103 individuals studied in our own laboratory. The mean values were not different in young (73.2±2.4%) and in elderly people (73.4±2.4%). At all ages, the proportion of intracellular or extracellular water (as measured by bromide dilution) to total body water (as measured by oxygen 18 dilution) was similar. The same finding holds for the proportion of intracellular water to fat-free mass.

We conclude that hydration of fat-free mass and cellular hydration are not affected in healthy aging.

Key-words : extracellular water, total body water, oxygen 18, bromide, fat-free mass.

INTRODUCTION

Natural aging is associated with well-known changes in body composition, as has been established from both cross-sectional (1) and longitudinal studies (2). Briefly, with age fat-free mass (FFM), i.e. the sum of muscle mass, bone mass, and organs decreases. At the same time fat mass increases, both in absolute values and relative to weight.

Fat-free mass is mainly composed of water, probably around 73% per weight. Therefore, it is expected that total body water (TBW) decreases with natural aging. However, at the whole-body level, TBW can be separated in intracellular water (ICW) and extracellular (ECW) water. Whether the relative proportions of ICW and ECW are altered by age is still debated (3). The hydration of FFM, that can be considered as an indicator of cellular hydration, is defined as the ratio of TBW over FFM. Whether hydration of fat-free mass changes with age is uncertain. On the one hand, Visser et al (4) studying many individuals showed that the mean value was the same for adults and healthy elderly people. On the other hand, if there was a change in either ICW, or ECW, or both, independent of the changes in FFM, cellular hydration would be altered, as is the case in many diseases (5). This point is not only an academic discussion. Firstly, diseased elderly people are prone to dehydration, the consequences of which on mortality and morbidity are well recognized (6). It could be hypothized that a chronic state of minor cellular dehydration would predispose the elderly to dehydration. Secondly, the hydration of fat-free mass is a key factor in most techniques for assessing body composition. Siri's (7) equations that are used to calculate % fat from body density (either measured by underwater weighing or estimated from skinfold thicknesses) rely on a 72% hydration of fat-free mass. Furthermore, any calculation of FFM from measured TBW is directly related to the hydration of fat-free mass. The influence of this hydration factor (Hf) in measurements acquired with dual-x-ray-absorptiometry is still problematic. Only the state-of-the-art five-compartment model is not affected by Hf (8). However, this approach is not available in routine practice.

Therefore, the aim of the present study was to assess whether hydration of FFM and cellular hydration are affected by natural aging.

METHODS

1 - <u>Evaluation of the hydration of FFM in published studies</u>

Siri's 3-compartment model (C3, 7) can be used to calculate % fat from body density (Db), total body water, and weight (equation 1 : where w is the water fraction of body mass : TBW/weight) :

$\%fat_{d,w}=100\ (2.1176/D_b-0.78w-1.351)$ (Eq 1).

Siri's four-compartment (C4) model is a partition of body mass as fat, water, minerals, and solids. It requires an estimate of the mineral fraction of body mass (m), and uses equation 2 :

$\%fat_{d,w,m}=100\ (2.747/D_b - 0.714\ w + 1.146\ m - 2.0503)$ (Eq2).

Db in equation 1 and 2 was either measured by underwater weighing or estimated from skinfold thicknesses (9). These models make no assumption about the hydration of fat-free mass. Therefore, FFM (body weight minus fat mass) is first calculated, and then the ratio TBW/FFM (hence Hf).The literature was searched. Only articles providing data on healthy non obese adults or elderly volunteers and with independent measurements of FFM and TBW were considered (17 articles). Five more papers had FFM data acquired with dual x-ray absorptiometry (DXA see below). Data on total body water were considered only if the measurements were made using the dilution principle. The tracers were D_2O, ^3H_2O, or $H_2{}^{18}O$. FFM values were taken from the article where available or were recalculated with C3 and C4 models.

Another model uses DXA measurements of bone, fat-free mass, and fat-mass. It qualifies for an estimate of Hf since body composition measurements appear to be independent of hydration (10, 11). Furthermore, as DXA becomes a "routine" means for measuring body composition, we felt appropriate to use it in computations.

The five-compartment model (C5) was described in details by Wang et al (8) where measurements are taken by in vitro neutron activation analysis (IVNAA). Although this equipment is rarely available, it is the most comprehensive means for measuring body composition in combination with TBW measurements.

2 – Hydration of FFM and water compartments in the study participants

2.1 : Participants. Data from the 103 people whom we studied were computed. All participants were healthy non-obese volunteers ; measurements of both TBW and skinfold thicknesses were taken for adjusting the parameters of energy or protein metabolism. Where studies involved an intervention (such as diet, exercise) the baseline data only were considered. All studies were approved by the local medical school's ethical committee. The participants were separated in 68 healthy elderly people and 35 adults. Table 1 gives their physical characteristics.

2.2 : Body composition measurements. Body weight was measured to the nearest 0.1 kg on a SECA 709 scale (SECA, Les Mureaux France). TBW was measured with the $H_2{}^{18}O$ dilution technique (12). ECW was determined with the bromide technique (12, 13). Skinfold thicknesses were measured by the same investigator with a Harpenden calliper at the 4 classical sites following Durnin and Womersley (9). D_b was calculated using equations derived by Durnin and Womersley (9). Siri's C3 model (7) was used to calculate %fat with equation 1 (cf above).

3 – Statistical methods

The results are expressed as means and SDs. People were separated according to their sex and their age : young meant individual ages < 60y ; elderly meant ages > 60y. The same criteria were applied to data obtained from the literature ; young and elderly refer to the mean age for the group. For values taken or calculated from data in the literature, "grand mean" values were computed by weighing the means for the group by the number of participants. For data acquired in this laboratory mean values for the different categories were compared using analysis of variance. Statistical significance was accepted at the 5 % level. Statistical calculations were performed with Statview 4 package (Abacus Concept Inc, Ca). Since TBW differed between age groups, a straightforward comparison of ECW or ICW in absolute values (kg) between them does not convey enough information. Therefore, it was necessary to compare ECW or ICW in relative terms to TBW, or to FFM. Such a comparison was made by analysis of covariance (14). Firstly the slopes of the regression lines for each group were compared. Then, for those that were not different, the elevations or adjusted means for each group were compared.

RESULTS

1.Results from the literature survey : Table 2 displays the Hf values that were either collected from the articles or calculated from data in them. The mean values ranged from 68.7 to 73.6% with Siri's C3 model ; from 72.3 to 73.7% with Siri's C4 model ; from 70.5 to 75.1% with the DXA model ; and from 71.1 to 73.9% with the IVNAA C5 model. The "grand mean" values calculated with Siri’s C3 model appear to be similar in young (72.7%, n=292) and elderly people (72.5%, n=360), but may be slightly lower in men than in women (Table 2). The values obtained with Siri’s C3 and C4 models were very close to each other and to those obtained with the C5 model (Table 3). Mazagieros et al (15) gave values obtained with the C5 and C3 models from the same participants that are in good agreement (Table 2). The DXA model "grand mean" values for Hf were consistently higher than values obtained with any other model. Excluding the data obtained with DXA model (n=823, Hf = 74.0%) the "grand mean" value obtained by combining the other models was 72.5% (n=919).

2. Results obtained on the study subjects : The mean Hf for the 103 individuals was 73.4±2.4%, ranging from 67.0 to 79.5%. This value was not statistically different from the classical 73.2% published by Sheng and Huggins (16). Further, the Hf value was not different between young (73.2±2.4) and elderly people (73.4±2.4, P=0.9).

Expressed in absolute values (kg) TBW, ECW, and ICW were higher in the young than in the elderly (Table 1). Figure 1 displays the ECW (panel A) and ICW (panel B) in values relative to TBW. It shows that : i) both ECW and ICW are correlated with TBW, ii) the slopes of the regression lines do not differ between groups both for ECW and ICW, and iii) the adjusted means do not differ significantly. Figure 2 displays ICW in values relative to FFM, and shows that the two were correlated in both age groups. Neither the slope nor the adjusted mean were significantly different between young and elderly persons.

DISCUSSION

The present study suggests that both the hydration of fat-free mass and the relative proportions of the water compartments are not affected in healthy aging. The main result concerns the hydration of FFM, directly measured by ICW. Direct measurement was necessary because of the known age-related changes in body composition. Since it is established that FFM, mainly in the form of muscle tissues, declines with age it was expected that both TBW and ICW also will decrease. The question is whether the proportion of TBW or ICW to FFM remains the same throughout the aging process. A relative increase in ECW in elderly subjects has been described (3). Therefore, we might consider that opposing changes in ICW and ECW would cancel each other out. Hence, TBW in the ratio TBW over FFM is subject to complex influences and may not reflect cellular hydration. The results reported on the healthy elderly people studied here show that TBW, ICW, and ECW decreased with age. However, we established that the proportion of ICW or ECW relative to TBW was similar in young and elderly people by analyzing covariance which is the most sensitive technique for comparing proportion when TBW differs between age groups (17). Having demonstrated that relative to TBW, ICW is similar between age groups, it remained to be shown that this also is the case relative to FFM. We chose the Siri’s 3-compartment assessment of fat mass because it makes no assumption about hydration. Body density was estimated from skinfold thicknesses (9). This technique, which relates subcutaneous fat thickness to body density, has been validated for the age range of 18-72 yrs. Therefore, the present study strongly suggests that the ratio of ICW over FFM, i.e., the cellular hydration within FFM is not affected by age. This finding is associated with a demonstrated constancy of the TBW over FFM ratio. Analysis of published values confirm this result. We believe that these data are valid because great care was taken to calculate FFM with models making no assumptions about the hydration of FFM : Siri's 3 and 4-compartment models, and in vivo neutron activation analysis. Table 2 shows that with those techniques, Hf is very similar between age groups, with a ″grand mean″ close to the 73.2% (classical figure by Sheng and Huggins, 16) and to the 73.4% figure that we found.

In conclusion, our analysis resolves the debate about whether with age Hf is unchanged (18-20) or increased (1, 15, 21-25). Chemical analysis on six non-edematous adults (25 to 63 years of age) showed no trend for Hf with age (23). Therefore, assessment of body composition for a group of healthy elderly people can assume a constant cellular hydration and hydration of FFM.

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Table 1 : Physical characteristics of the participants

	Young adults n = 35	Healthy elderly subjects n=68
Age (yr)	38.1±4.3[1]	66.1±0.6
Weight (kg)	70.3±1.5	69.1±1.3
BMI ($kg.m^{-2}$)	23.1±0.4[1]	26.0±0.4
FFM (kg)	56.4±1.0[1]	46.1±1.1
TBW (kg)	41.3±0.7[1]	33.9±0.8
ECW (kg)	18.3±0.5[1]	15.1±0.4
ICW (kg)	23.1±0.7[1]	18.8±0.5

1 $p < 0.001$ between age-groups (one-way ANOVA)

Table 2. Hydration factor (HF) of FFM taken from the literature or calculated therein

Method	Reference	Age	Sex	n	HF (%)	Mean
Siri C3	21	young	women	20	72.1	
	15	young	women	19	73.3	
	26	young	women	38	72.5	
	27	young	women	27	73.2	
	28	young	women	15	73.1	72.8
Siri C3	29	young	men	37	73.3	
	26	young	men	55	72.1	
	27	young	men	29	73.2	
	30	young	men	24	70.5	
	28	young	men	16	72.8	
	31	young	men	14	73.4	72.6
Siri C3	21	old	women	18	73.5	
	15	old	women	19	72.7	
	32	old	women	10	72.4	
	33	old	women	30	72.6	
	26	old	women	21	69.7	
	30	old	women	20	72.5	
	27	old	women	71	73	
	34	old	women	16	73.4	
	35	old	women	4	73.6	72.6
Siri C3	33	old	men	30	71	
	26	old	men	19	68.7	
	27	old	men	32	73.1	
	30	old	men	20	69	
	34	old	men	19	71.6	
	36	old	men	23	72.9	
	35	old	men	8	71.6	71.4
Siri C4	31	young	men	14	72.6	
	21	young	women	20	72.3	
	21	old	women	18	73.7	
	28	young	men/women	38	72.8	72.8
DXA C4	4	young	women	78	73.3	
	4	young	women	96	73.8	
	37	young	women	12	74.5	73.6
DXA C4	4	young	men	88	74.2	
	4	young	men	54	73.8	
	36	young	men	16	73.3	73.9
DXA C4	25	old	women	188	74.8	
	4	old	women	96	73.8	
	38	old	women	15	73	74.4
DXA C4	25	old	men	127	73.9	
	36	old	men	12	75.1	
	4	old	men	62	73.5	
	38	old	men	12	70.5	73.7
IVNAA	13	old	women	19	72.5	
	13	young	women	19	73.5	
	39	old/young	women	15	72.2	
	24	old/young	women	12	72.7	
	40	old/young	women	35	72.6	
	39	old/young	men	16	72.5	
	24	old/young	men	13	72.9	
	40	old/young	men	33	71.1	
	41	old/young	women/men	36	72.2	72.3

Table 3. Summary of HF values

Methodology	n	HF
Siri C3	654	72.3
Siri C4	90	72.8
IVNAA	198	72.3
This study	103	73.4
DXA	828	74.0

IVNAA : in vivo neutron activation analysis

DXA : dual x-ray absorptiometry

Legends for the figures

Figure 1 Panel A Linear relationship between ECW and TBW in elderly people and adults. The slope and the adjusted means are not different. Panel B Linear relationship between ICW and TBW in elderly individuals and adults. The slope and the adjusted means are not different.

Figure 2. Linear relationship between ICW and FFM in elderly people and adults. The slope and the adjusted means are not different.