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Thyroid function is more strongly associated with body impedance than anthropometry in healthy subjects

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ABSTRACT. Since fat-free tissues are responsible for 95% of basal energy expenditure, fat-free mass is expected to be a better determinant of thyroid size and function than anthropometry. We tested the hypothesis that fat-free tissues as qualitatively determined by body resistance (R) at 50 kHz are more strongly associated with TSH than anthropometric indicators in healthy subjects. A number of 78 euthyroid adults of both sexes were consecutively studied. R was the best single predictor of TSH (R^2_{adj}=0.65, *p*<0.0001). It explained 36% more variance than bw (R^2_{adj}=0.29, *p*<0.0001), the most accurate anthropometric predictor. Sex had no effect on the relationship between TSH, bioelectrical impedance analysis and anthropometry. After the contribution of R to TSH was taken into account, anthropometric indicators were not able to explain any additional part of TSH variance. We conclude that in healthy subjects, bioelectrical resistance is a better indicator of thyroid function than anthropometry, probably because of its more direct relationship with fat-free tissues. Further studies are needed to test whether this relationship holds in under- and over-weight subjects.
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INTRODUCTION

It is well-established that the thyroid gland exerts a substantial control over the metabolic activity of tissues and organs. Body weight (bw) is a proxy indicator of tissue and organ mass and body height (bh) is the second most important body dimension after bw so that thyroid size is directly associated with them (1). Since fat-free tissues are responsible for 95% of basal energy expenditure (2), fat-free mass (FFM) is expected to be a better determinant of thyroid size and function than bw (3). However, the measurement of FFM involves the use of techniques not readily available in clinical practice (4).
Bioelectrical impedance analysis (BIA) allows the estimation of FFM from the resistance index (RI), *i.e.* the ratio between squared bh and body resistance (R) (5). Very frequently, BIA algorithms include bw among predictors so that the relative contribution of BIA and bw to the estimate cannot be established (6). A well-known limit of predictive algorithms is their population-specificity. In particular, algorithms developed on healthy subjects may give spurious results when applied to ill subjects because of changes in the underlying body composition (6). Despite the evidence that body composition changes substantially during thyroid disease (7-9), most BIA studies of disthyroid patients have employed algorithms developed on healthy subjects and their conclusions must therefore be taken with caution (10, 11). On the other hand, BIA studies of euthyroid subjects have frequently employed formulae that had not been cross-validated in the samples of interest (3).
However, BIA is not limited to quantitative estimates of body compartments. R is by itself an index of fat-free tissues because it is inversely proportional to total body water (TBW), which is the major constituent of FFM (12). Using BIA as an exploratory tool, we tested the hypothesis that fat-free tissues as qualitatively determined by R are more strongly associated with TSH than anthropometric indicators in healthy subjects. We studied TSH instead of thyroid size because TSH is the index of thyroid activity employed in practice and the correlation between thyroid size and TSH in healthy subjects is low (1).

Key-words: Bioelectrical impedance, anthropometry, thyroid.

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MATERIALS AND METHODS

Subjects

A number of 78 healthy subjects were consecutively enrolled as outpatients after giving informed consent. Inclusion criteria were: 1) age ≥18 and ≤65 yr, *i.e.* adult subjects; 2) BMI ≥18.5 and ≤24.9 kg/m^2, *i.e.* normal-weight subjects; 3) absence of disease as determined by clinical history, physical examination and selected blood and urine chemistries, *i.e.* healthy subjects; 4) normal levels of TSH, FT_3 and FT_4, *i.e.* euthyroid subjects.

Measurements

Bw and bh were measured following the Anthropometric Standardization Reference Manual (13). BMI was calculated as bw (kg)/bh (m)^2 (14). R was measured at a frequency of 50 kHz using a tetrapolar impedance plethysmograph (BIA 101/S, RJL Systems, U.S.A.) according to standardized procedures (5). RI was calculated as height^2 (cm^2)/R (Ω) (5). TSH, FT_3 and FT_4 were measured between 08:00 h and 08:30 h after an overnight fasting using an electroluminescent immuno-assay (ECLIA, Roche Diagnostics, Germany).

Statistical analysis

Statistical analysis was performed on a MacOS computer using the Statview 5.0.1 and SuperANOVA 1.1 software packages (SAS Institute, Cary, U.S.A.). All measured and calculated variables were normally distributed (including regression residuals) and between-group variances were homogeneous. The main study hypothesis was tested using a general linear model (GLM) employing TSH as the dependent variable and R as regressor, with sex and an interaction term between R and sex (R*sex) as covariates to control for the effect of sex. Assuming a SD of 50 Ω for R and a correlation of 0.5 between TSH and R, 80 subjects were needed to achieve a 99% power to detect a difference of 0.5 units in the slope of the regression line at a significance level of 0.01. The values of the adjusted determination coefficient (R^2_{adj}) and the percent root mean square error (RMSE%= RMSE/measured value of Y) were used to determine the accuracy of R in predicting TSH. The same approach was used for anthropometric variables. Statistical significance was set to a value of $p<0.05$ for all tests.

Table 1 - *Measurements of the subjects. Data are mean±SD.*

	All	Females	Males
No.	78	51	27
Age (yr)	46±9	48±9*	42±6
bw (kg)	60.8±7.8	56.9±5.2°	68.1±6.5
bh (m)	1.67±0.08	1.63±0.05°	1.75±0.07
BMI (kg/m^2)	21.7±1.4	21.3±1.4**	22.3±1.2
TSH (mU/l)	2.0±0.6	1.8±0.5°	2.4±0.5
FT_3 (pmol/l)	5.6±0.9	5.5±0.9	5.8±1.0
FT_4 (pmol/l)	14.9±1.8	14.7±2.0	15.1±1.3
R (Ω)	584±52	611±40°	531±26

*p=0.01, **p=0.0005 and °p<0.0001 *vs* males. FT_3: free T_3; FT_4: free T_4; bh: height; R: body resistance at 50 kHz; bw: weight.

Table 2 - *Variance of TSH explained by anthropometry and body resistance in the pooled sample.*

Predictor (X)	R^2_{adj}	RMSE%
R	0.65**	17
RI	0.42**	22
bw	0.29**	24
BMI	0.24**	25
bh	0.13*	27

*p=0.006 and **p<0.0001. bh: height; R: body resistance at 50 kHz; RI: resistance index; R^2_{adj}: adjusted coefficient of determination; RMSE%: percent root mean square error; bw: weight.

RESULTS

The measurements of the study subjects are given in Table 1. Females were on average 6 yr older than males (p=0.01) and had lower values of bw (p<0.0001), bh (p<0.0001) and BMI (p=0.00005). TSH was lower in females than males (p<0.0001) but FT_3 and FT_4 were similar (p=NS). R was higher in females than males (p<0.0001).

The variance of TSH separately contributed by bw, bh, BMI, R and RI is given in Table 2. Age did not contribute any variance at all (p=NS). The sex and X*sex covariates were not significant for any relationship (p=NS) so that analyses were performed on the pooled sample. R was the best single predictor of TSH (R^2_{adj}=0.65, p<0.0001). It explained 23% and 36% more variance of TSH than RI (R^2_{adj} =0.42, p<0.0001) and bw (R^2_{adj}=0.29, p<0.0001), respectively. Also the RMSE% associated with the prediction of TSH from R (17%) was lower than that

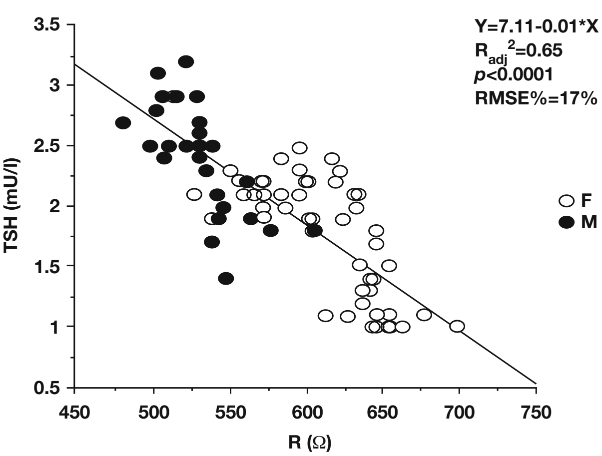

Fig. 1 - *Relationship between TSH and body resistance in the pooled sample. F: females; M: males; R: body resistance at 50 kHz; R^2_{adj}: adjusted coefficient of determination; RMSE%: percent root mean square error. Standard errors are 0.43 and 0.001 for intercept and slope respectively.*

associated with its prediction from RI (22%) and bw (24%). The TSH-R relationship is given in Figure 1. After the contribution of R to TSH was taken into account, anthropometric variables were not able to explain any additional part of TSH variance (*p*=NS, stepwise regression; data not shown).

DISCUSSION

Thyroid size is known to be related to anthropometric dimensions and this relationship may partly explain the differences in thyroid volume observed between sexes (1). However, this correlation is only low to moderate and even if it is useful to work out reference values for thyroid size (1, 15), there is a need for more accurate predictors of thyroid volume and, most importantly, function. As this latter is concerned, it is to be noted that the correlation existing between thyroid size and TSH in healthy subjects is too low [r=-0.26, *p*=0.001, n=296 (1)] for thyroid volume to be considered a good proxy of thyroid function. FFM may be a better "denominator" for thyroid function than weight because it comprises the most metabolically active tissues of the body (2). R offers a qualitative assessment of fat-free tissues because of its inverse relationship with TBW, which is the major constituent of FFM (5, 12). This simple use of BIA avoids the problems connected with the population-specificity of quantitative algorithms and the fact that many of them include bw among the predictors (3).

In this study of healthy subjects, we found that R was a better predictor of TSH than anthropometry. We studied healthy subjects because we were interested to know whether a physiological relationship existed between TSH and R. Moreover, since hyperthyroid subjects have often suppressed levels of TSH, the study of the TSH-R relationship as a continuous one would have been difficult in conditions of thyroid disease [besides the fact that physiological relationships between thyroid function and fat-free tissues may be lost during thyroid disease (7)]. The relationship between TSH and R was an inverse one (Fig. 1) and since R is inversely proportional to FFM, this relationship can be interpreted as showing a direct relationship between TSH and FFM, which is biologically sound. It is of interest however that R was a better predictor of TSH than RI. Since RI is generally a better predictor of FFM than R (5, 16), this suggests that factors other than the relationship of R with body composition may explain the greater power of R in estimating thyroid function as compared to RI and anthropometry.

The limitations of this study should be kept in mind. It was performed in a convenience sample that is not representative of the general population. For instance, the average BMI of our subjects was 21 kg/m^2, which is substantially lower than the average national BMI. Since there is some evidence that the relationship between anthropometry and thyroid size may be different in obese subjects (3), future studies should investigate this relationship also in overweight (and underweight) subjects. It is also possible that sample-related characteristics may be responsible for the great association between BIA and TSH in our study. However, this seems unlikely in view of the fact that body composition relationships in homogenous samples such as that employed in our study, are commonly less strong than in heterogeneous samples and this is especially true for BIA (6, 16).

In conclusion, this study of healthy subjects of both sexes shows that bioelectrical resistance may be a better indicator of thyroid function than anthropometry, possibly because of its more direct relationship with fat-free tissues. Further studies are needed to test whether this relationship held in under- and over-weight subjects. The question whether FFM is a better predictor of TSH than bw awaits a final answer from the employment of reference models for the assessment of FFM.

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