Estimation of lean body mass in children

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Editor’s key points

- Lean body mass (LBM) is often used to guide anaesthetic drug doses in adults.
- The relationship between LBM, body weight, and extracellular fluid volume in children is unclear.
- This study shows that these relationships are similar in adults and children.
- Therefore, estimated LBM may be better than body weight to guide drug dosing in children.

Background. In adults, dosages of some anaesthetic agents are based on lean body mass (LBM) rather than body weight. Our aim was to derive an equation for estimating LBM in children.

Methods. Patients comprised three groups: prospective kidney transplant donors from two separate centres (centres 1 and 3) and children referred to a further centre (centre 2) for the routine clinical measurement of glomerular filtration rate (GFR). GFR and extracellular fluid volume (ECV) were measured using Cr–51-EDTA. LBM was directly estimated (eLBM) in adults using an equation based on height and weight. ECV in children was estimated (eECV) from another equation based on height and weight, converted to eLBM using the relationship between eLBM and ECV determined in the adults from centre 1 and then compared with adult data from centre 3.

Results. In children, the ratio of eECV to ECV was 1.04 (so 0.18). In centre 1, eLBM (kg) was 3.81 (so 0.55) times greater than ECV (litres) in men (n = 50) and 3.77 (0.77) times greater in women (n = 51). eLBM in children was therefore derived by multiplying eECV by 3.8. In children, eLBM showed a close linear correlation with measured ECV (eLBM = 3.50ECV + 2.0; R2 = 0.857), similar to adults (eLBM = 2.82ECV + 14.5; R2 = 0.582). In all groups, eLBM/weight correlated inversely with weight.

Conclusions. In terms of the relationships between eLBM, ECV, and weight, children are similar to adults. Therefore, drug dosage in children should also be based on eLBM rather than weight.

Keywords: drug therapy, drug dosage calculations; children; pharmacokinetics; pharmacology, clinical

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The doses of some anaesthetic agents, especially water-soluble drugs, are routinely based on lean body mass (LBM), estimated from height and weight using equations that are different for men and women.1 2 However, these equations, which are based on previously described relations between total body water (TBW), LBM, height and weight,3 4 are not applicable to children, often giving nonsensical estimates for LBM, including negative values.

An equation based on height and weight has been described previously for estimating extracellular fluid volume (ECV) in children.5 Taking this a step further and assuming that the relation between ECV and LBM is the same in children as in adults, we present here an equation based on height and weight for estimating LBM in children. This required us to first establish the relation between ECV and LBM in adults.

Methods

Subjects and study design

Pre-existing anonymous clinical data sets of subjects from three separate institutions were retrospectively analysed.

The opinion of the Local Research Ethics Committee was that this study is in the domain of service improvement rather than research and therefore did not require formal ethical review by an NHS REC. Patient characteristics are summarized in Table 1.

The principle underpinning the study design is the assumption that ECV is proportional to LBM in both adults and children. If the proportionality constant (conversion factor) could be determined in adults, it could be used to multiply an estimate of ECV (eECV) to give LBM in children, because an equation has previously been described for estimating ECV in children from height and weight.5

The three patient groups consisted first of an adult group from one institution (centre 1) in which the conversion factor was determined using measured ECV and LBM estimated from height and weight (eLBM); secondly, a group of children in which the conversion factor was then used to derive eLBM from eECV; and thirdly, a further adult group with which to compare childhood eLBM with adult eLBM and their respective relationships with measured ECV in order to validate the conversion factor.
The adults from centre 1, in whom the conversion factor was derived, comprised 101 healthy prospective kidney transplant donors (50 men and 51 women). The children (aged up to and including 13; $n = 69$; all with non-cancerous conditions) to whom the conversion factor was applied were from another institution and referred for the routine clinical measurement of glomerular filtration rate (GFR). Only children with a $\text{GFR/ECV} \geq 4.5$ ml min$^{-1}$ litre$^{-1}$ (range 4.5–10.4 ml min$^{-1}$ litre$^{-1}$) were included. [Note that in children, GFR is more appropriately scaled to ECV rather than to body surface area (BSA).] The second group of adults comprised 195 healthy prospective kidney transplant donors (93 men and 102 women) from a third institution (centre 3). In order to avoid bias, the adult data from centre 1 were used only to establish the relationship between $eLBM$ and measured ECV for the purpose of estimating LBM in the children and thereafter not further utilized.

Measurement of GFR and ECV

GFR was measured from three or four blood samples obtained between 120 and 240 min after bolus injection of Cr-51-EDTA using the conventional slope–intercept method. It was scaled to a BSA of 1.73 m$^2$ (GFR/BSA), using the equation of Haycock and colleagues to calculate the BSA from height and weight, and corrected for the single-compartment assumption using separate Brochner-Mortensen equations for adults and children. Using BSA, corrected GFR/BSA was then ‘descaled’ to give absolute, one-compartment-corrected GFR.

GFR per unit ECV ($\text{GFR/ECV}$) was expressed exclusively as the terminal rate constant ($\alpha_2$) of the same Cr-51-EDTA clearance curve with correction for the single-compartment assumption using the equation described by Bird and colleagues:

$$\text{corrected } \text{GFR/ECV} = \alpha_2 + (\alpha_2^2 \times 15.4) \text{ ml min}^{-1} \text{ ml}^{-1}$$

(1)

(Note that whilst one-compartment GFR overestimates ‘true’ GFR, $\alpha_2$ underestimates true GFR/ECV.) Then,

$$\text{ECV} = \frac{\text{GFR}}{(\text{GFR/ECV})}$$

(2)

In a recent study, this method gave ECV in good agreement with ECV simultaneously and independently measured in the same individual from multisample iohexol clearance.

Estimation of LBM

LBM was estimated in both groups of adults from height ($H$; cm) and weight ($W$; kg) using the equations described by Boer:

$$\text{Men : } eLBM = 0.407W + 0.267H - 19.2 \text{ (kg)}$$

(3)

$$\text{Women : } eLBM = 0.252W + 0.473H - 48.3 \text{ (kg)}$$

(4)

LBM was also estimated using the formulae of James:

$$\text{Men : } eLBM = 1.1W - 128 \left( \frac{W}{H} \right)^2 \text{ (kg)}$$

(5)

$$\text{Women : } eLBM = 1.07W - 148 \left( \frac{W}{H} \right)^2 \text{ (kg)}$$

(6)

It was shown by Boer that ECV, measured as the bromide space, displays a linear, proportionate relation with $eLBM$. The current study confirms this for adults with respect to $eLBM$ based on both the Boer equations and the James equations (Fig. 1).

For the estimation of LBM in children, it was assumed that the observation of Boer with respect to the proportional relationship between ECV and LBM in adults can be extrapolated to children. Using the Boer equations, the proportionality constants (conversion factors) were found to be 3.81

<table>
<thead>
<tr>
<th>Centre 1</th>
<th>Centre 2 (children; n = 69)</th>
<th>Centre 3</th>
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<tr>
<td>Men (n = 50)</td>
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<tr>
<td>Age (yr)</td>
<td>44 (14) (19–70)</td>
<td>5.9 (3.5) (0.5–13)</td>
<td>48 (12) (21–76)</td>
<td>48 (12) (24–69)</td>
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<tr>
<td>Weight (kg)</td>
<td>81 (12) (60–114)</td>
<td>21.5 (10.7) (4.3–48)</td>
<td>68 (12) (52–103)</td>
<td>86 (11) (55–120)</td>
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<td>Height (cm)</td>
<td>179 (6) (169–191)</td>
<td>1.1 (0.2) (0.6–1.6)</td>
<td>164 (7) (149–176)</td>
<td>179 (6) (164–191)</td>
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<tr>
<td>BMI (kg m$^{-2}$)</td>
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<td>16.5 (3.2) (12.6–26.7)</td>
<td>25 (4) (20–37)</td>
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<td>48 (12) (24–69)</td>
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<td>Weight (kg)</td>
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<td>70 (7) (62–110)</td>
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<td>Height (cm)</td>
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<td>48 (12) (24–69)</td>
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<td>Weight (kg)</td>
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<td>Height (cm)</td>
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<td>BMI (kg m$^{-2}$)</td>
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<td>27 (3) (19–35)</td>
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<td>Women (n = 102)</td>
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<td>Weight (kg)</td>
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<td>BMI (kg m$^{-2}$)</td>
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</table>
Lean body mass in children

Using the James equations for LBM, the corresponding values for men and women were 3.86 (0.54) and 3.81 (0.83), respectively. Exclusion of obese subjects (BMI > 30 kg m\(^{-2}\); 4/50 men and 7/51 women) had little effect on these values, which became, using Boer’s equations, 3.84 (0.55) and 3.86 (0.79). Given these near-identical values between the two sets of equations (Fig. 1), the Boer equations were subsequently used for estimating LBM in children, inserting a value of 3.8 into the equation that estimates ECV (litre) from height (H; cm) and weight (W; kg):\(^5\)

\[
e_{\text{ECV}} = 0.0215 \times W^{0.6469} \times H^{0.7236}
\]

and so

\[
e_{\text{LBM}} = 3.8 \times e_{\text{ECV}}
\]

Although not used, it is re-assuring to note that the corresponding conversion factors based on the adults from centre 3 and Boer’s equations were 4.03 (0.46) and 3.73 (0.51) in men and women, respectively, similar to the values recorded from centre 1. Corresponding values with the exclusion of subjects with BMI > 30 kg m\(^{-2}\) in this population (15/93 men and 13/102 women) were 4.06 (0.47) and 3.78 (0.48), respectively.

Results

Extracellular fluid volume

In children, there was good agreement between eECV and measured ECV (Fig. 2), with a mean ratio of 1.04 (\(\pm\) 0.18), supporting the validity of equation (7). Adult ratios were also close to unity with mean values in centres 1 and 3 of 1.02 (0.19) and 1.05 (0.13), respectively. Mean measured ECV/weight in children was 0.222 (0.038) litre kg\(^{-1}\), significantly higher (\(P<0.001\)) than in both men and women from centre 3, in whom corresponding values were 0.187 (0.011) and 0.184 (0.015) litre kg\(^{-1}\), respectively. Mean measured ECV/eLBM in children was 0.259 (0.042) litre kg\(^{-1}\), intermediate between men and women in whom the corresponding values were 0.251 (0.011) and 0.274 (0.015) litre kg\(^{-1}\), respectively.

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*Fig 1* Dependence of measured ECV on eLBM in adults from centres 1 (left panels) and 3 (right panels). eLBM was estimated using Boer’s equations (upper panels) and James’ equations (lower panels). Results between the two centres are similar. The two sets of equations gave almost identical values. Note the linear and proportionate (regression lines pass close to origins) relationships between ECV and eLBM.
Lean body mass

Across children and adults from centre 3, there was a non-linear relation between weight and eLBM that approached identity in very small individuals (Fig. 3A). Childhood data appeared continuous with data from women but men had a higher eLBM per unit weight and per unit measured ECV (Fig. 3A and B).

In children, measured ECV showed a close linear correlation with eECV [from equation (7)] and therefore, from inspection of equation (8), inevitably also with eLBM [eLBM = 3.50(ECV) (litre) + 2.0 kg; \( R^2 = 0.857 \); Fig. 3]. Importantly, the relationship between measured ECV and eLBM in children was similar to the corresponding relation in adults [eLBM = 2.82(ECV) (litre) + 14.5 kg; \( R^2 = 0.582 \); Fig. 3].

In all three subject groups, eLBM/weight showed strong negative correlations with weight (Fig. 4), as would be anticipated from inspection of Figure 3A.

Discussion

Several techniques have been described for estimating LBM in children, including sophisticated techniques that measure TBW or use dual absorption X-ray absorptiometry, to simple techniques, such as waist circumference and skin fold thickness, as summarized by Ellis\(^9\) and by Wells and Fewtrell.\(^10\) The current paper, however, is the first to estimate LBM in children from an equation based exclusively on height and weight. This is of potential value, as the adult equations based on height and weight are not applicable to children, giving negative values, for example, in very small children (data not shown).

Because it assumes that LBM is directly proportional to ECV, the described technique is analogous to estimating LBM from TBW.\(^3\) Its validity therefore depends on the accuracy of the data from the adults from centre 1, in whom the relationship between measured ECV and eLBM was first established. ECV per unit eLBM (ECV/eLBM) in these adults was 268 ml kg\(^{-1}\) in men and 275 ml kg\(^{-1}\) in women, with respective coefficients of variation (so/mean) of 14.6% and 17.6%. These values of ECV/eLBM are lower than the corresponding values of 303 and 302 ml kg\(^{-1}\) obtained using bromide in men and women by Boer,\(^2\) but this can be explained by the bromide space being higher than the distribution volume of Cr-51-EDTA. Boer’s coefficients of variation, however, were lower at 5.3% and 6.3%, respectively. The corresponding coefficients of variation for the men and women from centre 3 were 10.8% and 14.6% (see the Results section). The estimation of LBM may become inaccurate in obese subjects,\(^1\) but the exclusion of these (BMI > 30 kg m\(^{-2}\)) had little effect on the conversion factor used in equation (8).
Lean body mass in children

In a recent previous study, a conversion factor of 3.9, based on Boer’s equations, was reported. However, although close to the factor reported in the current study, this value was obtained on a population of adults referred for clinical measurement of GFR rather than a healthy population; moreover, women and men were not separated.

The validity of the current technique depends on the validity of the assumption that the relationship between ECV and LBM is the same in children as in adults. It is highly likely that the relationship between LBM and TBW is the same between children and adults, so the critical assumption is that TBW is distributed between intracellular and extracellular spaces in an identical manner. There are limited data on this point, but support is provided in the current study by the data illustrated in Figure 3, which show the continuity that exists between children and women with respect to the relationship between eLBM and measured ECV, arising at a body weight of ~50 kg, another potential cut-off point.

In conclusion, it is suggested that the dosages of drugs that are based on eLBM in adults should also be based on eLBM in children, obtained using equation (8), given above.

Conflict of interest
None declared.

References
9. Ellis KJ. Selected body composition methods can be used in field studies. J Nutr 2001; 131:15895–955

Fig 4 Relationships between eLBM/weight (y) and weight [x (kg)] in children (bold line: y=0.91–0.0026x; R²=0.241; P<0.001), women (lower fine line: y=0.95–0.0039x; R²=0.541) and men (upper fine line: y=1.03–0.0033x; R²=0.785). As in Figure 3, eLBM was based on Boer’s equations in adults and equation (8) in children.