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SHORT COMMUNICATION

The appropriate whole-body index on which to base standardized uptake value in 2-deoxy-2- ^{18}F fludeoxyglucose PET

^{1,2}G KERAMIDA, MD, ¹J HUNTER, BAppSci, ^{1,2}S DIZDAREVIC, MD and ²A M PETERS, DSc

¹Clinical Imaging Sciences Centre, Brighton Sussex Medical School, University of Sussex, Brighton, UK

²Department of Nuclear Medicine, Brighton Sussex University Hospitals NHS Trust, Brighton, UK

Address correspondence to: Dr Georgia Keramida

E-mail: G.Keramida@bsms.ac.uk

Objective: Tissue uptake of 2-deoxy-2-fluorine-18 fludeoxyglucose (^{18}F -FDG) is routinely quantified as standardized uptake value (SUV), which in general is the fraction (F) of administered activity per millilitre of tissue multiplied by an index of body size, usually weight (W), i.e. $\text{F/ml} \times \text{W} = \text{SUV}$ or $\text{F/ml} = \text{SUV} \times (1/\text{W})$. Other indices have been suggested as preferable to W, especially lean body mass (LBM) and body surface area (BSA). The second equation mentioned above shows that the reciprocal of the ideal index should correlate closely with F/ml and give a regression line through the origin. The purpose of this study was to determine which of these three indices best meets these criteria.

Methods: Data were evaluated from 49 males and 51 females undergoing routine ^{18}F -FDG positron emission

tomography/CT. A 3 cm diameter region of interest was drawn over the liver and F/ml recorded. LBM and BSA were estimated from height and weight.

Results: Based on all patients, the reciprocals of the three indices gave similar correlation coefficients with F/ml, but only 1/LBM gave regressions close to the origin. Intercepts were significantly higher for females for 1/W and 1/BSA, consistent with females having more body fat, but there was no significant difference with 1/LBM.

Conclusion: LBM is the best index on which to base SUV because adipose tissue accumulates less ^{18}F -FDG than other soft tissues.

Advances in knowledge: The value of this study lies in its use of a novel, more rational approach than previously to confirm that SUV should be based on LBM.

INTRODUCTION

In positron emission tomography (PET) using 2-deoxy-2-fluorine-18 fludeoxyglucose (^{18}F -FDG) for cancer management, quantification of tumour ^{18}F -FDG uptake is essential in order to monitor treatment. This is most often performed by calculation of the standardized uptake value (SUV), which is the fraction of the administered activity per unit volume of tissue multiplied by an index of body size to account for dilution of the tracer throughout the body.

The appropriate index of body size needs to be consistent with the effective distribution volume of the ^{18}F -FDG, which is the administered activity divided by average tissue concentration of tracer throughout the whole body. The effective distribution volume for ^{18}F -FDG is unknown but will vary from subject to subject. Although the most frequently used index of size is body weight (W; giving SUV_w), it has been suggested that lean body mass (LBM; giving SUV_{lbm}) is more appropriate,^{1–3} because adipose tissue in general accumulates less ^{18}F -FDG than do other

soft tissues. Body surface area (BSA, giving SUV_{bsa}) has also been suggested.²

It has been claimed that, because SUV_w correlates positively with body weight, SUV should not be based on weight.^{2,3} SUV_{bsa} correlated negatively with body weight.² By contrast, SUV_{lbm} showed no correlation with weight,^{2,3} suggesting that LBM is the best index on which to base SUV.^{1–3} A difficulty with this approach, however, is that when the dependent and independent variables of any relationship contain the same variable, correlation coefficient will be spuriously increased, unless the variable is measured with absolute accuracy. Therefore, in order to compare weight and LBM as indices of body size, SUV_{lbm} should have been correlated with LBM rather than with weight. Several different equations have been developed to estimate LBM, but, in general, they show rather poor agreement;^{4,5} therefore, the accuracy with which LBM is estimated is questionable. The choice of whole-body index for SUV is analogous to the choice of the ideal whole-body scaling variable for glomerular filtration rate (GFR), which, as pointed

Table 1. Regression equations for $100 \times \text{F/ml}$ (y-axes) against reciprocals of body size indices (x-axes). Correlation coefficients are shown in brackets

Body size indices	All ($n = 100$)	Males ($n = 49$)	Females ($n = 51$)
100/W	$0.84 + 1.60x$ (0.75) ^a	$0.75 + 1.54x$ (0.64)	$1.51 + 1.26x$ (0.72) ^c
100/LBM	$0.14 + 1.52x$ (0.81)	$-0.77 + 2.10x$ (0.65)	$-0.27 + 1.68x$ (0.78)
1/BSA	$-0.96 + 7.48x$ (0.79) ^b	$-0.91 + 7.16x$ (0.65)	$-0.15 + 6.22x$ (0.76) ^c

BSA, body surface area; LBM, lean body mass; W, weight.

^aSignificantly greater than corresponding intercept for 1/LBM ($p < 0.001$).

^bSignificantly less than corresponding intercept for 1/LBM ($p < 0.001$).

^cSignificantly higher than corresponding intercept for males ($p < 0.001$ for 1/W; $p < 0.01$ for 1/BSA).

out by Delanaye *et al*,⁶ should show no correlation with GFR scaled to that whole-body variable. Better, still, a comparison avoiding any tendency towards an artificial correlation should be adopted.

The aim of this small study, therefore, was to compare weight, LBM and BSA as scaling indices for SUV, using a novel, more rational approach so that certain organs should normalize to a relatively standard value across patients.

METHODS

Theory

If mSUV is the average SUV throughout the body, then

$$\left(\frac{\text{F}}{\text{ml}}\right) \times V = \text{mSUV} = 1 \quad (1)$$

where F/ml is the fraction (F) of administered activity per millilitre of “average” tissue, and V is the effective volume of distribution of ¹⁸F-FDG. This volume includes an equivalent related to ¹⁸F-FDG excreted in the urine up to the time of imaging, usually 60 min.

If average tissue density is taken as 1 g ml^{-1} , V can be substituted with weight (W) or LBM, so that

$$\left(\frac{\text{F}}{\text{ml}}\right) \times W = \text{mSUV} = 1 \quad (2)$$

or

$$\left(\frac{\text{F}}{\text{ml}}\right) \times \text{LBM} = \text{mSUV} = 1 \quad (3)$$

Rearranging and substituting SUV_w or SUV_{lbm} for mSUV:

$$\left(\frac{\text{F}}{\text{ml}}\right) = \text{SUV}_w \times \left(\frac{1}{W}\right) \quad (4)$$

or

$$\left(\frac{\text{F}}{\text{ml}}\right) = \text{SUV}_{\text{lbm}} \times \left(\frac{1}{\text{LBM}}\right) \quad (5)$$

If weight is equivalent to the appropriate distribution volume, then plotting F/ml against $1/W$ would give a straight-line graph

passing through the origin (*i.e.* no intercept) with a gradient equal to the SUV_w of the tissue from which F/ml was derived and, similarly, for 1/LBM and 1/BSA (even though BSA is not a volume). Therefore, the aim of this study was to determine which body size index best meets these criteria.

Patients

This was a retrospective clinical study aiming to inform on the optimal whole-body scaling variable for the measurement of SUV. Data were gathered from 49 male patients and 51 female patients attending our department for routine clinically indicated ¹⁸F-FDG PET/CT, mainly for management of cancer. All patients gave informed consent for publication of any data arising from their PET/CT studies.

Imaging

A Siemens (Erlangen, Germany) Biograph 64-slice PET scanner with immediate non-enhanced CT scanning (120 kVp/50 mA, Care Dose 4D®; slice 5 mm; pitch 0.8; rotational speed 0.5 s^{-1}) was used. Arms were up, as arms down may result in artificial elevation of the liver ¹⁸F-FDG signal owing to beam-hardening effects. Emission data were acquired at 3 min per bed position. Imaging was performed 60 min after injection of approximately 400 MBq.

Image analysis

A circular region of interest of 3 cm diameter was drawn over the centre of the right lobe of the liver in a midsection slice and maximum and average SUVs (SUV_{max} and SUV_{ave}) were recorded. Patients with visible suspicious focal hepatic pathology were not included.

Data analysis and statistics

The PET CT computer is programmed to generate SUV as SUV_w . SUV_w was therefore divided by the same value of weight from which SUV_w was calculated to give F/ml. This was then plotted against 100/W, 100/LBM and 1/BSA. This was performed for both genders combined and for males and females separately.

LBM was estimated from height and weight using the gender-specific formulae of Boer.⁷ BSA was estimated from height and weight using the gender-non-specific formula of Haycock *et al*.⁸

Relations between variables were quantified using Pearson's linear regression analysis. The standard errors (SE) of the intercepts of the resulting regression equations were calculated.⁹

Figure 1. Linear correlation between $100 \times \text{F/ml}$ and $100/\text{weight}$ (upper panel), $100/\text{lean body mass (LBM)}$ (middle panel) and $1/\text{body surface area (BSA)}$ (lower panel); closed circles: men (faint continuous regression line; $n = 51$); open circles: women (dashed regression line; $n = 49$). The regression line for all patients is bold. Regression equations and correlation coefficients are shown in Table 1.

The significance of the difference between any pair of intercepts was calculated using Student's unpaired t -testing, where

$$t = \frac{\text{intercept}_1 - \text{intercept}_2}{(\text{SE}_1^2 + \text{SE}_2^2)^{0.5}}$$

Similarly, the significance of the difference between an intercept and zero was calculated from:

$$t = \frac{\text{intercept}}{\text{SE}}$$

The significance was rejected if $p > 0.05$.

RESULTS

In general, the relationships of F/ml with the reciprocals of the body size indices were linear. Correlation coefficients were all higher with respect to SUV_{ave} than SUV_{max} for males, females and both genders combined for all three body size indices. Results are therefore given only for SUV_{ave} .

The regression equations of F/ml against the reciprocals of the three body size indices are given in Table 1 and illustrated in Figure 1. When genders were combined, $100/\text{W}$ gave an intercept that was significantly > 0 ($p < 0.001$), whereas $1/\text{BSA}$ gave an intercept that was significantly < 0 ($p < 0.001$). $100/\text{LBM}$, by contrast, gave an intercept close to and not significantly different from zero.

When the genders were separated, the intercepts given by $100/\text{W}$ and $1/\text{BSA}$ were significantly greater for females than for males ($p < 0.01$), but there was no significant difference with respect to $100/\text{LBM}$ (Table 1).

Correlation coefficients were marginally higher for $100/\text{LBM}$ than for $100/\text{W}$ and $1/\text{BSA}$ for females, males and both genders combined (Table 1).

DISCUSSION

The effective distribution volume of ^{18}F -FDG is complex and influenced by many factors that include time allowed for uptake, the presence or absence of tumour, the amount of body fat and the extent to which fat accumulates ^{18}F -FDG, the ^{18}F -FDG blood clearance rate (which is influenced by blood glucose) and renal function. Therefore, no index of whole-body size would be able to accurately and consistently define the volume of distribution in a heterogeneous population of patients.

Adipose tissue accumulates ^{18}F -FDG but less than does lean tissue. ^{18}F -FDG has been shown to enter adipose tissue to an extent that is positively associated with obesity.¹⁰ SUV based on weight should therefore be overestimated to an extent that depends on percentage body fat, and its reciprocal should give a positive intercept when correlated with F/ml , as we observed.

Because surface area increases in proportion to the radius squared while volume increases at a rate proportional to radius

cubed, BSA in large individuals is relatively low, explaining the negative intercept seen when F/ml is regressed on 1/BSA.

SUV based on LBM will be underestimated to an extent that depends on how much ^{18}F -FDG accumulates in adipose tissue and, if significant, also on body fat percentage. The insignificant positive intercept observed with 100/LBM for genders combined suggests that adipose tissue in general accumulates minimal ^{18}F -FDG.

The differences in the intercepts observed between males and females are consistent with the above conclusions. Thus, females have approximately 10% more fat than males,¹¹ and, accordingly, the intercepts with respect to 100/W and 1/BSA were significantly higher in females. By contrast, because of the exclusion of body fat, there was no significant gender difference with respect to 100/LBM.

These three whole-body indices have advantages and disadvantages. The advantage of weight is that it is easily and accurately measured. Its disadvantage is that adipose tissue in general accumulates less ^{18}F -FDG than does lean tissue. Apart from potentially underestimating SUV, LBM has the disadvantage of uncertainty in its estimation. Thus, there are several

equations described in the literature between which several groups have found poor agreement.^{4,5} Uncertainty in the estimation of LBM will attenuate any correlation between SUV_{LBM} and weight, such as those observed previously,¹⁻³ thereby weakening the claim that, on this basis, SUV_{LBM} is more reliable than SUV_{W} . Estimation of LBM may also be more difficult in a cancer population because of the relatively high prevalence of cachectic patients. Nevertheless, despite these apparent disadvantages, 100/LBM correlated marginally better than 100/W and 1/BSA with F/ml (Table 1). BSA has no apparent advantages but has several disadvantages, including its two-dimensional nature and that the equations for its estimation are not gender specific. BSA is lower, relative to the body mass, in larger individuals than in smaller individuals, accounting for its negative intercepts in the present study and in the finding of Sugawara et al² that SUV_{BSA} correlates negatively with body weight.

In conclusion, this study has adopted a rational and simple approach and confirmed that LBM is the preferred body size index on which to base SUV and should be taken up in routine clinical practice. LBM however is not perfect, reflecting the uncertainty of the effective distribution volume of ^{18}F -FDG, the inadequacy of equations for estimating LBM and the uptake of ^{18}F -FDG, albeit limited, in fatty tissues.

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