BJCP British Journal of Clinical Pharmacology

DOI:10.1111/j.1365-2125.2008.03112.x

Letter to the Editors

Lean body mass normalizes the effect of obesity on renal function

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Descriptors of body size and renal function are the most important covariates in pharmacokinetic studies.

Several methods can be used to estimate glomerular filtration rate (GFR) [1], the most common being Cockcroft and Gault [2]. Studies of GFR in the obese population have shown both increases in GFR [3] and no change [4]. Methods based on creatinine (see for an overview [5]) may overestimate GFR due to its active secretion. In contrast, inulin is considered an accurate measure of GFR [6].

We hypothesize that GFR, when scaled by lean body weight, will not be different between obese and non-obese subjects.

GFR data were obtained from a previous study [7] undertaken at Tel Aviv University Medical School, Israel by one of the co-authors (A.C.). The dataset comprised 17 patients (seven male and 10 female), ranging in age from 23 to 46 years, of whom nine (three male and six female) were normal weight [body mass index (BMI) <25 kg m^{-2}] and eight (four male and four female) were obese (BMI >30 kg m^{-2}). All patients had normal serum creatinine concentration. GFR was determined by inulin clearance, which was 145 ± 38.5 ml min^{-1} (mean $\pm$ SD) and 89.8 ± 15.3 ml min^{-1} in the obese and lean population, respectively. The obese patients underwent gastroplasty after the initial renal function tests. Measurements of GFR were repeated at least 12 months after surgery and were 109.9 ± 20.6 ml min^{-1}. Only two individuals in the postsurgery obesity group achieved a BMI of <30 kg m^{-2}; the remaining six individuals, although achieving significant reductions in body mass, remained above the BMI cut-off. This provided 11 observations in the lean group (nine originally lean and two obese who became lean) and 14 observations in the obese group (eight originally obese and repeated measures on six who remained obese). The non-normalized values of GFR were compared between obese and non-obese individuals, as were GFR values when normalized by total body weight and lean body mass (see Figure 1). Lean body mass was calculated using the method of Janmahasatian [8], which is a function of total body weight, height and sex. Statistical comparisons were performed using repeated measures analysis of variance.

The (non-normalized) GFR values were higher by 42% in the obese compared with non-obese patients ($P = 0.003$) (Figure 1a) and 36% lower ($P = 0.002$) in obese than normal weight individuals when normalized by total body weight. In contrast, when normalizing GFR by lean body mass, there was no apparent difference in the GFR between obese and control individuals ($P = 0.27$) (Figure 1c).

Renal function, as defined by GFR, is increased in the obese population. Normalizing GFR to total body weight (to produce ml min^{-1} kg^{-1}) results in overcompensation of the effects and the conclusion that obese patients have a lower GFR (per kg) than non-obese patients. This suggests that the increase in excess adipose tissue does not contribute entirely to an increase in renal function. In contrast, normalizing GFR by lean body mass appears to explain 'apparent' differences between obese and non-obese individuals. Indeed, further support for the benefit of normalizing by lean mass was gained when the index variable, BMI, was randomly reassigned (thereby eliminating the true influence of obesity) in the data and the analysis re-performed many times. If lean body mass was seen as an appropriate descriptor then no dataset generated under this method should show a statistically significant difference between the reclassified 'lean' and 'obese' patients. No statistical differences in GFR when normalised by lean body mass were evident in any of the randomised datasets.

In conclusion, it appears that renal function is closely related to lean body mass, which should be used in preference to total body weight for estimating creatinine clearance.

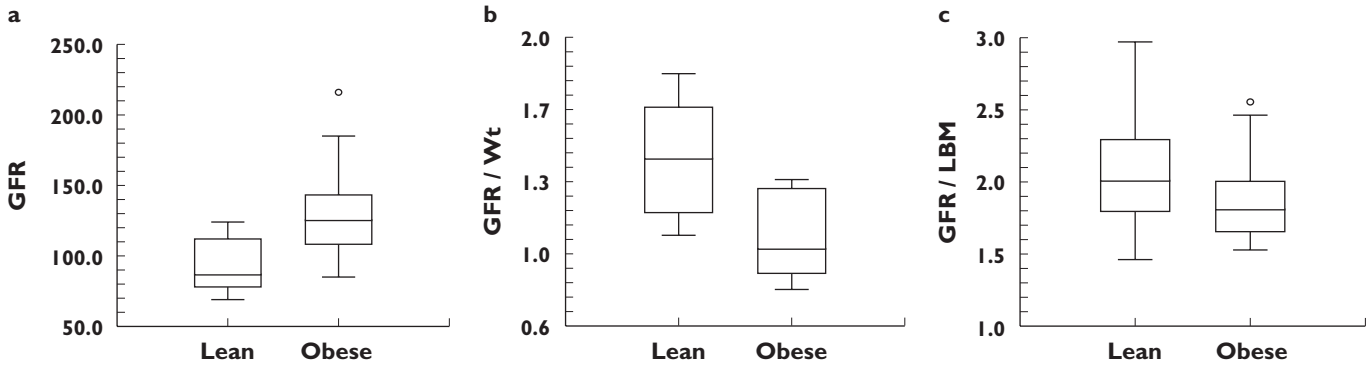

Figure 1

Box plots of glomerular filtration rate (GFR) for lean and obese subjects. In all figures there were 11 observations of GFR from lean subjects (nine from the original lean patients and two from patients who were obese and became lean after surgery) and 13 observations from obese subjects (eight from obese patients presurgery and six from the same cohort 12 months after surgery). (a) Non-normalized GFR ($P = 0.003$, repeated measures analysis of variance comparing lean with obese). (b) GFR normalized to total body weight ($P = 0.002$, repeated measures analysis of variance comparing lean with obese). (c) GFR normalized to lean body mass (LBM) ($P = 0.27$, repeated measures analysis of variance comparing lean with obese; power is approximately 0.65 to show 25% difference assuming same variability)

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RECEIVED

1 November 2007

ACCEPTED

20 December 2007

PUBLISHED *OnlineEarly*

15 February 2008

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