· Advances in Medical Sciences · Vol. 58(2) · 2013 · pp 376-381 · DOI: 10.2478/ams-2013-0020

Creatinine or cystatin C – which is a better index of renal function in morbid obesity?

Mysliwiec P[1,*], Jasiewicz P[2], Hady HR[1], Choromanska B[1], Mroczko B[3], Mysliwiec H[4], Siemiatkowski A[2], Dadan J[1], Szmitkowski M[3]

1 1st Department of General and Endocrinological Surgery, Medical University of Bialystok, Bialystok, Poland
2 Department of Anaesthesiology and Intensive Care, Medical University of Bialystok, Bialystok, Poland
3 Department of Biochemical Diagnostics, Medical University of Bialystok, Bialystok, Poland
4 Department of Dermatology and Venereology, Medical University of Bialystok, Bialystok, Poland

* CORRESPONDING AUTHOR:
1st Department of General and Endocrinological Surgery,
Medical University of Bialystok,
M. Sklodowskiej-Curie 24a,
15-276 Bialystok, Poland
Tel.: +4885 746 8672
Fax: +4885 746 8620
e-mail: mpiotr@umb.edu.pl (Piotr Mysliwiec)

Received: 21.01.2013
Accepted: 27.05.2013
Advances in Medical Sciences
Vol. 58(2) 2013 · pp 376-381
DOI: 10.2478/ams-2013-0020

ABSTRACT

Purpose: The most important index of renal function is estimated glomerular filtration rate (eGFR) which can be calculated from creatinine or cystatin C concentration in serum. There is uncertainty, which formula is best suited to assess renal function in morbidly obese patients. The aim of this study was to evaluate eGFR in patients with morbid obesity using formulas: Modification of Diet in Renal Disease (MDRD), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Grubb, Le Bricon, Hoek, Larsson, and to compare the obtained results.

Material and Methods: In 40 morbidly obese patients, serum concentration of cystatin C and creatinine were assayed. Values of eGFR were calculated using the above-mentioned formulas.

Results: The mean value of eGFR ranged from 85.9 to 111.1 ml/min/1.73m^2, depending on the formula. The biggest difference between the obtained values was 29% (Grubb vs. Hoek $p<0.01$). After calculation of eGFR from creatinine concentration (MDRD), 7 patients were qualified to the 2nd and 3rd stage of chronic renal disease, while application of Hoek's formula, based on cystatin C concentration, allotted 27 patients to 2nd and 3rd stage of chronic renal disease. Le Bricon formula gave eGFR values, that correlated best with albuminuria.

Conclusion: eGFR calculated using Le Bricon formula based on the cystatin C concentration was significantly lower than eGFR calculated from creatinine concentration and was more closely associated with albuminuria. Relying only on creatinine concentration to estimate glomerular filtration rate can lead to underestimation of renal malfunction in obese patients.

Key words: Morbid obesity, glomerular filtration, creatinine, cystatin C

INTRODUCTION

Obesity is a constantly growing health issue worldwide [1]. Obese patients have increased risk of metabolic syndrome [2] and kidney function impairment [3]. Hypertension and type 2 diabetes are etiologic factors of 70% cases of end-stage renal disease, while the obesity is the main risk factor for these disorders [4]. Even in apparently healthy men, a correlation between body mass index and renal diseases was observed [5]. Glomerular filtration rate (GFR) is the basic determinant of kidney function. Clearance of exogenous substances is the most precise, however, difficult and expensive method of evaluating GFR [6]. In practice, creatinine clearance is usually assessed. A number of formulas based on the concentration of creatinine in serum have been proposed: Cockcroft-Gault [7], Modification of Diet in Renal Disease (MDRD) [8] and group Collaboration formula (CKD-EPI) [9].

Aforementioned formulas are not suitable for quickly increasing renal malfunction and are inadequate for patients without chronic renal disease [6]. Using body mass as a

determinant of muscle mass in Cockcroft-Gault's formula leads to overestimation of GFR in patients with oedema, overweight and obesity. Those equations are also inadequate for evaluation of GFR >60 ml/min [10].

Besides creatinine, eGFR can also be calculated from cystatin C concentration. Cystatin C is a polypeptide produced constantly in the same volume by all nucleated cells of the body. Because of its low molecular mass, it is easily filtrated by kidneys and it was suggested superior to creatinine for glomerular filtration assessment. Cystatin C was shown to be unaffected by age, gender or muscle mass [11]. Many authors proposed formulas based on cystatin C concentrations for estimating GFR: Grubb et al. [12], Larsson et al. [13], Le Bricon et al. [14] and Hoek et al. [15].

The aim of this study was to evaluate eGFR in patients with morbid obesity using formulas based on creatinine and cystatin C and to compare the obtained results.

MATERIALS AND METHODS

We studied 40 morbidly obese patients awaiting bariatric surgery in the 1st Department of General and Endocrinological Surgery, Medical University of Bialystok, Poland. The study protocol was approved by the local Bioethics Committee (approval Nr: R-I-002/371/2010). Informed written consent was obtained from all patients. Patients with previously diagnosed renal disease, signs of acute inflammation or history of malignancy were excluded from the study.

Venous blood samples from all of the patients were drawn before treatment. All blood samples were allowed to clot before centrifugation. Sera were removed, aliquoted and stored at -80° C until assayed. Serum concentration of cystatin C was measured using enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Abingdon, England) according to the manufacturer's instructions. The serum samples were diluted 30-fold for the determination of cystatin C. Serum cystatin C was assessed using ELISA immunoenzymatic assay from R&D with MiniBOS Dia-Sorin analyzer. Measurements were performed twice. The intra-assay coefficient of variation (CV%) of cystatin C is reported by the manufacturer to be 3.1 % at a mean concentration of 29.9 ng/ml, standard deviation (SD)=0.92. In the literature, the units of cystatin C concentration have uniformly been mg/l, and for this reason we decided to use these units in the present study. Serum creatinine was measured using kinetic method by Jaffe with picric acid on the Abbott Architect i8000 analyzer. 24-hour urine sample was collected for albumin measurement.

Estimated GFR was calculated according to MDRD [8], CKD-EPI [9], Grubb et al. [12], Larsson et al. [13], Le Bricon et al. [14] and Hoek et al. [15] formulas.

MDRD formula containing four variables (serum creatinine, age, race and gender):

$eGFR = 175 \times [Cr]^{-1.154} \times age^{-0.203} \times 1.212$ (if black) x 0.742 (if female)

[Cr] – creatinine concentration [8]

CKD-EPI formula contains variables for creatinine concentration in serum, age, gender and race (*Tab. 1*).

Grubb et al. [12] analysed the relation of the concentration of cystatin C assessed using immunoturbidimetric method and GFR was obtained from iohexol clearance in 536 patients. The authors developed formula:

$eGFR = 84.69 \times CysC^{-1.680}$ (x1.384 if children<14 years old); CysC - cystatin C concentration.

Larsson et al. [13], after the examination of 100 patients, compared GFR obtained from iohexol clearance with cystatin C and creatinine concentration. They reached better correlation of GFR with cystatin C (r=0.91) than with creatinine (r=0.84). For cystatin C concentration obtained by turbidimetric method they proposed the formula:

$eGFR = 99.43 \times CysC^{-1.5837}$; CysC - concentration of cystatin C.

Unlike all other methods used in our paper, formula of Larsson et al. [13] gives results in ml/min and not in ml/min/1.73m^2.

Among 25 patients after renal transplantation, Le Bricon et al. [14] compared GFR obtained from ^{51}Cr-EDTA clearance with cystatin C concentration obtained by nephelometric method and creatinine concentration. They developed a formula:

$eGFR = 78/CysC + 4$; CysC - concentration of cystatin C.

Among 123 patients, mostly with kidney diseases and type 2 diabetes, Hoek et al. [15] compared GFR obtained from iothalamate clearance with creatinine clearance obtained from Cockcroft-Gault's formula and with cystatin C concentration obtained by nephelometric method. They proved correlation between GFR and cystatin C concentration (r=0.873) and Cockcroft-Gault's formula (r=0.876). More precise estimation of GFR was reached after application of formula:

$eGFR = -4.32 + 80.35 \times 1/CysC$; CysC - concentration of cystatin C,

than after using Cockcroft-Gault's formula.

The data were analysed using nonparametric tests. For visual representation we used median, range between 25 and 75 percentile, minimal and maximal values. Kruskal-Wallis ANOVA, Mann-Whitney and Spearmann's tests were applied. $P < 0.05$ was assumed as statistically significant. Statistical analysis was conducted using Statistica 10.0.