

Comparison of Modification of Diet in the Renal Disease (MDRD) and Cockcroft-Gault (CG) Formulas for Estimating Glomerular Filtration Rate (GFR) in Patients Metabolic Syndrome

Metabolik Sendromlu Hastalarda Glomerüler Filtrasyon Hızının (GFH) Modification of Diet in the Renal Disease (MDRD) ve Cockrof-Gault(CG) Formülleri ile Karşılaştırılması

ABSTRACT

OBJECTIVE: Comparison of Glomerular Filtration Rate (GFR), by Cockcroft-Gault (CG) and Modification of Diet in the Renal Disease (MDRD) formulas in metabolic syndrome patients.

MATERIAL and METHODS: 999 patients attending hypertension unit were studied retrospectively. 627 patients had MS parameters. MS was diagnosed according to the International Diabetes Federation. Renal function calculated with two formulas with creatinine, age, gender and Weight. Analysis was performed using SPSS 15.0. The significance level was $P < 0,05$.

RESULTS: Many patients were MS 627 (63%); non MS 372 (37%). In comparison MDRD and CG ; the proportion, according GFR < 60 ml/min/1.73 m², in MS was high ($p=0.015$). In MS concerning of GFR were significant ($p<0.001$), in non MS was not different ($p=0.027$). In MS we observe a negative correlation between MDRD and uric acid ($p<0.001$), with CG it was not ($p=0.555$), between MDRD and albuminuria was not observed a correlation ($p=0.263$), with between CG and albuminuria there was an incorrect positive relationship.

CONCLUSION: In patients with MS, we recommend using the MDRD equation to predict Evaluation of glomerular filtration rate from serum creatinine concentration, because it is the most accurate in population MS and easily applicable in clinical practice.

KEY WORDS: Metabolic syndrome, Glomerular filtration rate

ÖZ

AMAÇ: Metabolik sendromlu (MS) kişilerde, Glomerüler Filtrasyon Hızının (GFH) Cockcroft-Gault(CG) ve Modification of Diet in the Renal Disease(MDRD) formüllerine göre karşılaştırılması.

GEREÇ ve YÖNTEMLER: Hipertansiyon polikliniğinde takip edilen 999 hastanın dosyası geriye dönük olarak incelendi. 627 hasta MS ölçütlerine sahipti. MS tanımı Uluslararası Diyabet Federasyonu kriterlerine göre yapıldı. Böbrek fonksiyonlarının tahmini, kreatinin, yaş, cinsiyet ve kiloya göre, iki formüle göre hesaplandı. Değerlendirilme SPSS 15,0 kullanılarak yapıldı. Anlamlılık düzeyi $P < 0,05$ olarak tespit edildi.

BULGULAR: Hastaların çoğu, 627 (%63) MS kriterlerini taşıyordu, MS olmayanlar 372 (%37) idi. MDRD ve CG karşılaştırıldığında; hasta oranları, GFH hızı < 60 ml/min/1,73 m² ye bağlı olarak hesaplandığında MS grupta anlamlı farklılık bulundu ($p<0,015$). MS grupta GFH hesaplanması anlamlı farklı idi ($p<0,001$), MS olmayanlarda ise anlamlı değildi ($P=0,027$). MS grupta ürik asitle MDRD formülü arasında negatif bağlantı gözlemlendi ($p<0,001$), CG ile bağlantı yoktu($p=0,555$). Albuminüri ile MDRD formülü arasında bağlantı yoktu ($p=0,263$), CG ile bağlantı yanlış.

SONUÇ: MS'lu hastalarda, Glomerüler filtrasyon hızı hesaplanmasında, daha doğru ve klinik uygulamada kullanılması kolay olduğu için MDRD formülünün kullanılmasını öneriyoruz.

ANAHTAR SÖZCÜKLER: Metabolik sendrom, Glomerüler filtrasyon hızı

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Received : 22.05.2014

Accepted : 16.07.2014

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INTRODUCTION

Metabolic syndrome (MS) is a group of situations marked by excess body fat with abdominal obesity, a high blood pressure, dyslipidemia and a high blood sugar. MS this is a important factor for chronic kidney disease. A close association has been found between the MS and the risk for renal impairment, clinically expressed in the form of albuminuria (AU) and CKD (1). The most used methods for GFR estimation are the Cocroft-Gault (CG) Formula and Modificaiton of Diet in the Renal Disease (MDRD) equation. In any case, the exactitude of this evaluate is limited, because the creatinin level is influenced by factors other than creatinin filtration (2). To minimise these obstacles, diverse formulas have been created to calcule creatinie clearance from serum creatinine level, age, sex and anthropometric size. People with MS are obese, and therefore, according to people normal, rate of fat tissue is much more compared to muscle tissue. The Guidelines and The American Diabetes Association recommends estimation of GFR by either the MDRD equation or the CKD-EPI(Chronic Kidney Disease Epidemiology Collaboration) in all patients with diabetes (3). Depending to obesity, hypertension, diabetes incidence and CKD is an increasing public health problem (4). In fact, here essentially fatty tissue is in question weight increase is not connected to the muscle tissue. For MDRD only age for CG formula age with weight are considering as influence factors. CG Formula perceives fatty tissue as muscle and GFR calculation are more optimistic. AU and uric acid are two parameters on kidney function. In comparison, greater uric acid levels had a significant indicator of kidney disease (5). AU is well recognized as an independent marker of early renal failure in patients with diabetes mellitus and hypertension. The presence of AU is a powerful predictor of renal and cardiovascular risk in patients with type2 diabetes and hypertension (6). The aim of this study was to evaluation of GFR by CG formula, MDRD equation and comparison with AU, uric acid in people with MS.

PATIENTS and METHODS

A total of 999 adult patients (644 women, 355 men) attending our hypertension clinical unit (Internal Medicine Department, Sisli Etfal hospital Istanbul, Turkey) were studied retrospectively, from January 2009 to December 2012. Mean age 53.81 ± 11.63 years (range 20-92), body mass index (BMI) 30.89 ± 5.63 kg/m² (17.30-59.11), creatinine 0.85 ± 0.23 mg/dl (0.40-3.22), acid uric 5.12 ± 1.38 mg/dl (1.40-10.20) albumin excretion rate 29.56 ± 76.07 mg/24h (1.02-957). Since the facility was a hypertension clinic, all the patients were continuously followed and they were also under the anti-hypertensive treatment. All analyses have been done based on patients' documentation. Exclusion criteria were being pregnant, taking glucocorticoids, liver disease and with no known history of renal failure or other renal disease and with recording in the clinical

history of all of them. 627 patients had MS parameters. MS was diagnosed according to the International Diabetes Federation definition. For a patient to be qualified as having MS they must the condition are; waist circumference ≥ 94 cm for men , ≥ 84 cm for women and any two of the next four elements: reduced high density lipoprotein <40 mg/dl in males and < 50 mg/dl in females, triglyceride level ≥ 150 mg/dl, exceed (7) fasting plasma glucose (FPG) ≥ 100 mg/dl , or previously diagnosed type 2 diabetes, raised blood pressure: systolic blood pressure ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension. Creatinine, uric acid and AU were performed in the same laboratory. Blood and urine samples were obtained simultaneously. After the explanation given to all the patients in the hospital of how they collect their urine and the urine is collected, AU was measured from a 24-hour urine collection, applying an immunonephelometric procedure (Behring Nephrometer 2) with an concenient kit (Namtiserum VO human albumin;Date Behring). Creatininemia was measured on a multiparameter apparatus (Olympus AU 640; Olympus Optical, Tokyo, Japan),applying the Jaffé method with dichromatic calculations applying to the manufacture's statemnts and daily calibration of the apparatus. The creatinine measurement gap of the laboratory method used was 0.2 – 15 mg/dl, coefficient of variations was 2.8% and it was standardized against the standard reference material (ID/MS). Serum uric acid was determined by enzymatic in vitro test for the quantitative determination of uric acid in human serum (Roche/Hitachi modular analytics). Estimation of renal function calculated according the two formulas that we studied to predict GFR from serum creatinine, age and weight.

Creatinine-based formula:

Cockroft-Gault GFR (ml/min/1.73m²)= (140—age (years)) x weight (kg)/(0.814 x creatinine(mg/dl)) x 0.85 (if female)

MDRD GFR (ml/min/1.73 m²) We used the simplified equation= $186.3 \times (\text{creatinine(mg/dl)})^{-1.154} \times \text{age(years)}^{-0.203} \times 0.742$ (if female) x 1.212 (if black) (8).

Renal failure according to a GFR < 60 ml/min/1.73m² was defined.

There is an inverse relationship between serum uric acid level and renal function (9). AU is a marker for kidney damage (10). Using uric acid level and AU we compared the MDRD and CG GFR results.

Statistical analysis; Data analysis and management were performed using the statistical software SPSS 15.0. In the bivariate analysis of normal distributions, a test for independent samples was used for quantitative variable, and a Chi-square test for categorical variables. A non-parametric Mann-Whitney U test was used in the bivariate study of variables with a non-normal distribution. The significance level was fixed at $P < 0.05$.

RESULTS

A total 999 patients were included and divided into two groups; having MS criteria and non MS. Table I shows baseline characteristics of two group patients. Women represented 64% of the sample. Many Patients were MS 627 (63%), non MS subjects were 372 (37%). The proportion of subject, according GFR < 60 ml/min/1.73 m², calculated with MDRD and CG formulas we observed significant difference in MS

group (p=0.015). Renal failure subject was height. But in non MS was not different (p=0.027) (Table II). When comparison is made according the MDRD and CG formula concerning of GFR, in MS group we observe significant differences (p<0.001) (Table III). A total AU measured in 826 patients and 686 subject (83%) were normoalbuminuric and in 140 patients (17%) were with AU ≥ 30 mg/24h. In MS group 93 (17%) and in non MS group 47 (15%) patient had AU ≥ 30 mg/24h. In MS group, as

Table I: Baseline characteristics of patients.

n=999	With MS (n=627)	Without MS (n=372)	p
MDRD GFR (ml/min/1.73 m²)	87.87±20	89.45±22	0.233
C-G GFR(ml/min/1.73 m²)	111.09±34	94.20±29	<0.0001
Age (years)	53.77±10	53.88±12	0.853
Waist circumflex (cm)	99.90±10	90.61±11	<0.0001
Fasting glucose (mg/dl)	100.83±16	93.68±17	<0.0001
Triglycerides (mg/dl)	175.79±99	118.37±66	<0.0001
HDL-C (mg/dl)	47.77±13	57.52±16	<0.0001
LDL -C (mg/dl)	128.99±48	126.33±35	0.598
Height (cm)	159.94±9	161.57±8	0.003
Weight (kg)	82.79±14	73.75±13	< 0.0001
Albumiuria (mg/24h)	31.61±81	26.129±66	0.013
Acid uric (mg/dl)	5.27±1	4.87±1	<0.0001
Creatinine (mg/dl)	0.83±0	0.86±0	0.067
Insulin (UI/mL)	10.43±6	6.81±4	<0.0001
BMI (kg/m²)	32.42±5	28.31±4	<0.0001
WHR	0.62±0	0.56±0	<0.0001
SBP (mm/hg)	142.07±20	142.27±22	0.58
DBP (mm/hg)	87.34±11	86.30±10	0.23

HDL-C: High density cholesterol, **LDL-C:** Low density cholesterol, **BMI:** Body mass index, **WHR:** Waist-hip ratio, **SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure

Table II: Proportional distribution of patients according normal and renal failure state.

	All patients			MS			non MS		
	Normal	Renal failure	p	Normal	Renal failure	p	Normal	Renal failure	p
MDRD	925(93%)	74(7%)	0.26	586(93%)	41(7%)	0.015	339(91%)	33(9%)	0.27
CG	934(93.5%)	65(6.5%)		601(96%)	26(4%)		333(90%)	39(10%)	

Renal failure: GFR<60 ml/min/1.73 m², normal: GFR > 60 ml/min/1.73 m²

Table III: Comparison of means GFR.

	MDRD (ml/min/1.73 m ²)	CG (ml/min/1.73 m ²)	P
MS	87.87±20.67	111.09±34.84	p<0.0001

MS: Metabolic syndrome

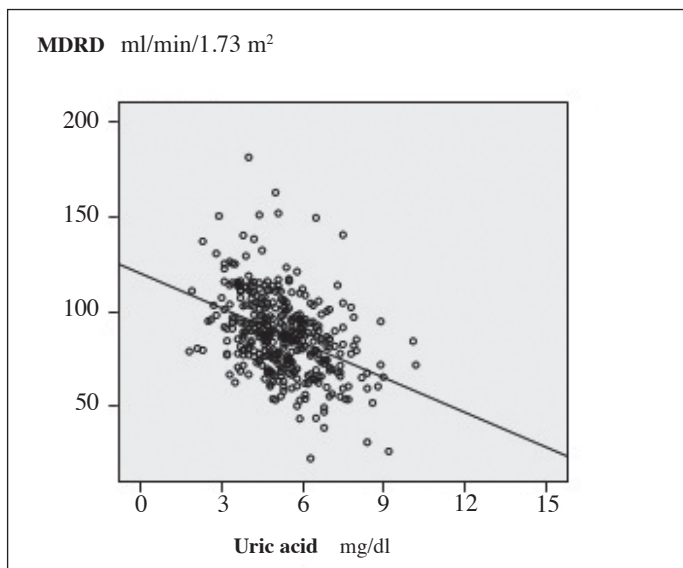


Figure 1: In with MS patients correlation between MDRD and uric acid.

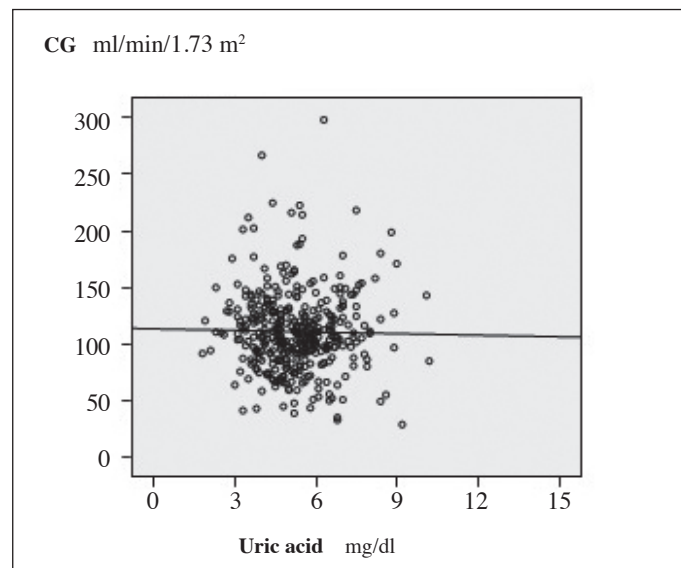


Figure 2: In with MS patients correlation between CG formula and uric acid.

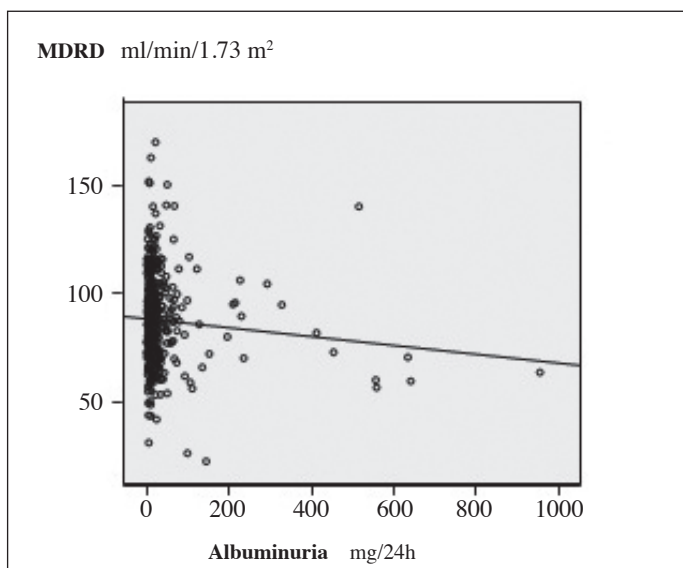


Figure 3: In with MS patients correlation between MDRD formula and AU.

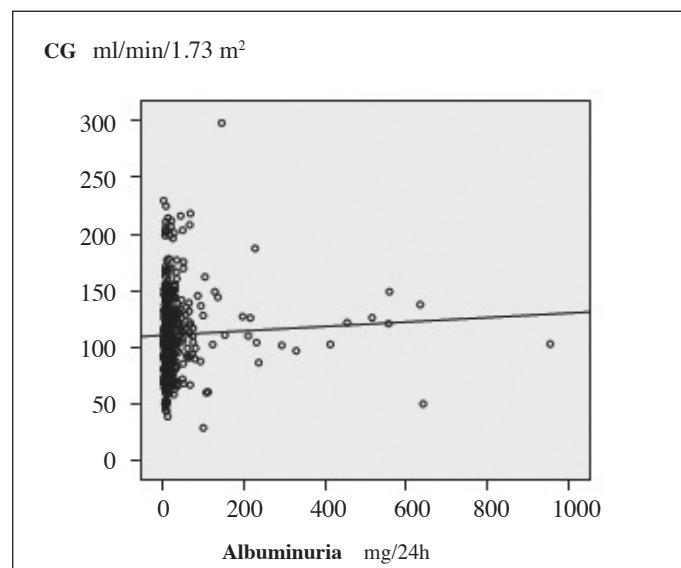


Figure 4: In with MS patients correlation between CG formula and AU.

is seen in the figure form and correlation calculate, we observe a negative correlation between MDRD formula and uric acid ($p<0.001$) Figure 1. But with CG it was not correlation ($p=0.555$)

Figure 2. In group MS between MDRD and AU we not observed a correlation ($p=0.263$) Figure 3, but with between CG and AU there was a incorrect positive relationship ($p=0.001$)= Figure 4.

DISCUSSION

In this study, we evaluated the performances of the CG and MDRD formulas for estimating GFR in patients with and without MS. Uric acid and levels of urinary albumin excretion, such measurements, particularly when combined with assessment of estimated GFR, have utility as biomarkers for enhanced risk of all-cause mortality, cardiovascular events, progressive chronic kidney disease, and end-stage renal disease in diabetic and nondiabetic subjects. Formula-derived estimated GFR results have become widely used in clinical practice. The CG and MDRD equation have been validated in patients with CKD and are currently used to stratify CKD. However, these equations do have recognized limitations, including a tendency to significantly underestimate higher levels of GFR and their accuracy is still debated (11). In practice it may be important to calculate GFR by using clearance procedures comprise extremes of age, body size, obesity, important malnutrition, muscle diseases, paraplegia, vegetarian diet, rapidly changing renal function, measurement of the dose of potentially toxic drugs that are eliminated by kidneys. It is suggest that metabolic syndrome is a significant determinant of CKD(12). It is know that variability in prognostication on renal capacity depend gender, age and BMI. For that reason, contradictory data in precedent studies concerning exactitude of equations may have reasoned differences in the distribution of gender, age and BMI between the cohorts in the studies. In our investigate of newly recording and follow-up for hypertension and in MS subjects, we observe, statistically significant correlations between estimated GFR derived by the MDRD formula with acid uric (Figure 1). In our analysis, we observe that performances of the MDRD, the CG were different in various subgroups of subjects. The greatest lack of precision was observed for subject who having MS state. In contrast to the MDRD, the CG includes a coefficient for body weight to correct the prediction of inter-individual differences in creatinine generation (muscular mass) due to body mass. It is considered there is relative error of predictions were significantly associated with body weight for predictions with CG formula, but not with MDRD (13). For CG, the relative error was linearly associated with BMI, with a large overestimate in obesity. They may be interpreted by the power that weight factors of the CG do not distinguish between muscular weight (related to creatinine production) and without muscular tissue (not related to creatinine production). Consequently, the CG modify any weight variance into a variance in envisaged renal function and have a propensity to exaggerate renal function in obese. Previously, Cockcroft and Gault proposed a rectification to tilt weight should be applied for the CG in the situation of obesity; but, did not describe data presenting the effects of excess fat on calculation. A factor to tilt weight for the CG is rarely well-respected and would necessitate additional estimation and calculation to regulate for age, gender, disease and different factors. Instead, the overweight and obese subjects with having lowered muscular mass than the overweight and obese subjects

GFR should be calculated with MDRD. The U.K. the National Service Framework for Renal Services now recommends the use of GFR for renal assessment in all diabetic patients. This may be problematic in MS subjects, because MS include parameters such as weight circumflex, diabetes, hypertension and dyslipidemia. Therefore in MS population we believe that GFR should be done to calculate with MDRD. In our study, we found that in a population with MS, the Evaluation of GFR with the MDRD and CG formula vary extensively, MDRD Formula give much higher estimate of GFR than the CG. At the time that we did not realize a GFR measurement, we cannot say which equation is the more correct for GFR calculation in MS patients. Right evaluation of GFR is not easy in routine practice and in outpatient condition. The obtained results suggest the estimation of GFR based on MDRD is better than CG. Estimation of GFR based on CG formula is significantly affected by obesity. Incorrect evaluation of renal function can conduct to misdiagnose the onset of renal failure and end stage renal insufficiency and dosing of drugs correctly. The 4-Variable MDRD study equation has now been validated extensively in multiple samples with and without chronic kidney disease. In general, these studies show good performance in people with MS. Two studies, comparing the CG and MDRD formulae to a measured GFR, found that the MDRD formula was more precise and accurate than the CG formula in people with MS (14). In comparing with the normal population, MS is accepted like a independent risk factor for CKD. According our results, use of these formulas for screening, CG formula overestimate number of in MS patients renal impairment. In present analyse, 4% of patient had GFR < 60 ml/min/1.73m² with CG versus 7% with MDRD. In patients diabetic, 72% sensitivity for the MDRD formula and 66 % for the CG formula to detect GFR values < 60 ml/min/1.73m² (15). Our results are in agreement with the latter study. We found, as did others, that the magnitude of the difference between the two formulae is influenced by weight particularly. Although it is not ideal the MDRD formula should be calculated in MS individuals. The influences of hyperglycemia (16) and weight related bias have led most analyzer to desist from the CG Formula in recent studies (17,18). As the CG Formula estimates GFR relative to weight, it significantly exaggerate overweight subjects. This predisposition is probably to increase because the the obesity is increasing in general population. Because a high BMI appear to be an significant risk component for renal disease (19) this mistake is inappropriate. Replacing the CG with the MDRD formula is not necessarily the solution but it is less than at least an incorrect technique. In addition, several practical details limit GFR estimation using the CG equation. First, it is more difficult to use the MDRD study equation because it requires measurement of weight. Second, it estimates creatinine clearance rather than GFR. Third, The clinical laboratory creatinine assays cannot easily be calibrated to the laboratory that performed the assays on samples used to drive the CG equation. We showed, In such population, the discrepancy between the

two estimates leads to an absence of concordance and may cause misclassification of patients in term of renal failure. In patients with MS, we recommend routinely using the MDRD to predict GFR from serum creatinine concentration, because it is most accurate in population MS and easily applicable in clinical practice. Patients with MS population represent a This article is not a population-based prevalence analyse and cannot be generalized. The inappropriate of this analyse is that were achieved under the treatment of hypertension, the number of female patients was high and the number of non MS patients was less. In conclusion, the MDRD formula furnish more confident estimations of kidney function than the CG Formula. specific challenge especially with overweight.

There is no conflict of interest among the authors.

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