

# Comparison of Modification of Diet in Renal Disease and Cockcroft-Gault Equations in Detection of Glomerular Filtration Rate Alterations in Coronary Artery Visualized Patients

*Koroner Arter Görüntülemesi Yapılan Hastaların Glomerular Filtrasyon Hızı Değişikliği Tespitinde Modification of Diet in Renal Disease ve Cockcroft-Gault Denklemlerinin Karşılaştırılması*

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## ABSTRACT

**Objective:** Contrast induced nephropathy (CIN) may arise after the use of contrast agents. Estimation of real glomerular filtration rate (GFR) is very important in order to prevent CIN. The most used GFR estimating equations are Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) but their superiority to each other is unknown in contrast media used patients.

**Material and Methods:** Total of 165 patients were enrolled to our study. Serum urea, creatinine and cystatin C levels of all patients were measured just before and fifth day of coronary angiography/angioplasty procedure. Alteration in serum cystatin C level was accepted as reference and GFR changes according to both equations were compared with serum cystatin C level variations.

**Results:** Decreased GFR values according to both formulas were related with an increasing in serum cystatin C levels ( $p=0.042$ ). However, there wasn't any superiority of formulas to each other in terms of GFR alterations ( $r= -.276$  and  $r= -.275$  for CG and MDRD equations respectively).

**Conclusion:** Both CG and MDRD equations are useful to detect the GFR changes in coronary angiography performed patients and there was no superiority of them to each other. To our knowledge, this is the first study about the comparison of MDRD and CG equations in coronary artery visualized patients.

**Key Words:** Glomerular filtration rate, MDRD, Cockcroft-Gault, Coronary angiography

## ÖZET

**Amaç:** Kontrast madde kullanımının ardından kontrast nefropatisi (KN) görülebilmektedir. KN'nin önlenmesi için gerçek glomerüler filtrasyon hızının (GFR) hesaplanması oldukça önemlidir. GFR hesaplamada en çok kullanılan Cockcroft-Gault (CG) ve Modification of Diet in Renal Disease (MDRD) denklemleridir ancak koroner anjiyografi yapılan hastalarda GFR değişikliğinin tespitinde birbirine olan üstünlüğü bilinmemektedir.

**Gereç ve Yöntem:** Çalışmaya 165 hasta dahil edildi. Koroner anjiyografi işlemi öncesi ve beşinci gününde tüm hastaların serum üre, kreatinin ve sistatin C düzeyleri ölçüldü. Serum sistatin C düzeyindeki değişiklik referans olarak alındı ve her iki formüle göre olan değişiklik referans değişiklik ile karşılaştırıldı.

**Bulgular:** İşlem sonu serum sistatin C düzeyindeki artış her iki denklemdeki GFR düşüşü ile ilişkili bulundu ( $p=0.042$ ). Ancak GFR değişikliğini tespit etme açısından denklemler birbirine üstün bulunamadı (CG ve MDRD denklemleri için sırasıyla  $r= -.276$  ve  $r= -.275$ ).

**Sonuç:** Koroner anjiyografi uygulanan hastalarda GFR değişikliği tespitinde hem CG hem de MDRD denklemleri kullanışlı olup birbirine üstünlükleri yoktur. Literatür kayıtlarına göre çalışmamız koroner arter görüntülemesi yapılan hastalarda GFR değişikliğinin tespiti adına MDRD ve CG denklemlerini karşılaştıran ilk çalışma özelliğini taşımaktadır.

**Anahtar Sözcükler:** Glomerular Filtrasyon Hızı, MDRD, Cockcroft-Gault, Koroner Anjiyografi

## Introduction

Contrast media utilization is frequent in most part of clinical cardiology and radiology in order to get a

precise diagnose and treatment. Some complications such as allergic reactions, contrast induced nephropathy, cerebrovascular events etc. may arise due to the usage of contrast agents. Lower incidence

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rate of mentioned complications and absence of systemic risk analysis about this issue may overlook prevention, diagnosis and early treatment of contrast media related complications. Contrast induced nephropathy (CIN) develops after the usage of contrast agents and is a third common reason of in hospital acute renal failure. 0,5 mg/dl or 25% elevation of serum creatinine in the first 48 hours after an administration of contrast media defined as CIN (1). A greatest risk to the development of CIN is an impaired initial renal function or a lower glomerular filtration rate (GFR). Therefore, evaluation of GFR before procedure is crucial but there is no gold standard test to measure the GFR in a daily practice. Inulin measurement is very valuable method for this purpose but difficulties in practice and cost of the test are restrictions for its usefulness. In this sense, the most used equations are Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) to estimate near real GFR value. The precision and superiority of these equations to each other is unknown in contrast media used patients. Therefore, we aimed to reveal the superiority of these two most used equations to each other in patients whose coronary arteries were visualized by contrast media.

## Materials and Methods

In this trial, 165 adult patients (78 men) were included. The trial was approved by the number 1 local Ethic Committee with a reference number of B-014. All patients were informed about the study and their written consents were obtained. Patients were classified to four groups according to their GFR. GFR level in group I was > 90 milliliters (ml) per minute per 1.73 m<sup>2</sup> (ml/min/1.73 m<sup>2</sup>), 89-60 ml/min/1.73 m<sup>2</sup> in group II, 59-30 ml/min/1.73 m<sup>2</sup> in group III and 29-15 ml/min/1.73 m<sup>2</sup> in group IV. Dialysis required patients were excluded. All of their medications continued without any interruption. Information about age, weight, smoking, chronic diseases and medications were recorded. Isoosmolar (308 mOsm/L) 94 ± 18 ml of contrast media was administered to coronary arteries for their visualization. All patients consumed 2000 ml of water after the procedure. *Evaluation of renal function changes:* Serum urea, creatinine and cystatin C levels of all patients were measured in coronary angiography/angioplasty performed patients just before the procedure. Serum creatinine was measured by using the kinetic method according to Jaffé method without deproteinisation (Roche Diagnostics, Mannheim, Germany). Serum cystatin C levels were measured with a particle-enhanced immunonephelometric method (Dade Behring,

Marburg, Germany). The GFR was calculated before and fifth day of procedure according to both MDRD and CG equations. Serum cystatin C was also measured before and fifth day of procedure. MDRD formula and CG formulas are standardized for a body surface area of 1.73 m<sup>2</sup>. MDRD and CG equations were like as shown below;

$$\text{GFR (MDRD)} = 175 \times \text{Serum Cr}^{-1.154} \times \text{age}^{-0.203} \times 1.212 \text{ (if patient is black)} \times 0.742 \text{ (if female)} \text{ (2) and}$$

$$\text{GFR (CG)} = (140 - \text{age}) \times (\text{Weight in kilogram}) \times (0.85 \text{ if female}) / (72 \times \text{Cr})$$

Initial and fifth day of serum cystatin C levels were measured. In addition, GFR values were calculated according to both formulas at the same days. Changes in GFR values and serum cystatin C levels in past 5 days calculated and presented as percentage (%). Alterations in serum cystatin C levels accepted as reference value in each patient and change of GFR levels according to both formulas compared with the changing of serum cystatin C levels. The closer relationship between serum cystatin C percentage change and GFR percentage change according to each equation was accepted as superior.

**Statistical Analysis:** Descriptive statistics for the continuous variables were presented as Mean, Standard deviation, minimum and maximum values while count and percentages for categorical variables. Paired t test was used to compare periods (Before and after). For determination linear relations among the variables, Pearson correlation analysis was carried out. Statistical significance level was considered as 5% and SPSS (version: 13) statistical program was used for all statistical computations.

## Results

Mean age and weights of patients were 58.65 ± 11.65 years and 77.09 ± 15.40 kilograms respectively. 54, 114, 63, 111 and 132 patients had diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease and chronic kidney disease respectively. 65 patients were smoker. Chronic kidney disease (CKD) stages of patients before and fifth day of procedure according to both formulas were showed in table 1 and table 2. GFR levels of patients were decreased after a procedure but dialysis was not required in any patient. The highest decrease of GFR was seen in patients who CKD stage I. Although it was only 2.382 % and 3.275 % of average GFR reduce according to CG and MDRD equations respectively. At the same time, average serum cystatin C level was increased only 2.469 % in the patients of mentioned group. The change in average serum cystatin C level was found statistically significant (p=0.049). However, reducing

**Table 1.** GFR levels of patients before procedure according to both equations

Equation	CKD stage	N*	%
CG	I	65	49.2
CG	II	50	37.9
CG	III	14	10.6
CG	IV	3	2.3
MDRD	I	65	49.2
MDRD	II	49	37.1
MDRD	III	12	9.1
MDRD	IV	6	4.5

\* Number of patients

MDRD: Modification of Diet in Renal Disease

Disease CG: Cockcroft-Gault

CKD: Chronic Kidney Disease

**Table 2.** GFR levels of patients on fifth day of procedure according to both formulas

Equation	CKD stage	N*	%
CG	I	57	43.1
CG	II	55	41.7
CG	III	14	10.6
CG	IV	6	4.5
MDRD	I	48	36.4
MDRD	II	67	50.1
MDRD	III	12	9.1
MDRD	IV	6	4.5

\* Number of patients

MDRD: Modification of Diet in Renal

CG: Cockcroft-Gault

CKD: Chronic Kidney Disease

in average GFR values after procedure which calculated by both equations were not found statistically meaningful (table 3). Although there was correlation between increasing of average serum cystatin C level and decreasing of GFR values which calculated by both MDRD and CG formulas ( $p=0.042$ ). However, there was not superiority of equations to each other in detection of GFR alterations ( $r= -0.276$  and  $r= -0.275$  for CG and MDRD equations respectively, see table 4).

## Discussion

CIN is the third common or 10% reason of in hospital acute renal failure (3). A pathophysiology of CIN is very complex; adenosine metabolism, glomerular flow, alterations in endothelin and prostaglandin metabolism and oxidative stress take a role (4,5). Additionally, there is role of hemodynamic deterioration, atheroembolism and drug toxicity during percutaneous coronary intervention (PCI) in the development of acute renal failure (6,7). Most favorite reason of CIN is renal tubular ischemia

during the use of contrast media (8). In most health centers, patients leave the hospital after many hours or one day of cardiac catheterization and actually it hides the real incidence of CIN. On the other hand, its incidence is approximately 1 % in the presence of normal kidney functions and greater than 50 % in the existence of impaired renal functions (9). It was only 5.54 % in our study group patients may be as a result their near normal renal functions. Rihal et al. (10) reported 3.3 % incidence of acute renal failure in their study and emphasized independent risk factors such as basic high level of creatinine, amount of used contrast media, acute myocardial infarction and the presence of shock status. Mehran et al analyzed prospective data of 9726 PCI performed patients and created a new risk score model. It contains eight independent parameters. These risk factors are; presence of chronic renal disease, diabetes mellitus, female gender, intervention after acute coronary syndrome, < 40 % of left ventricular ejection fraction, 150 ml or above use of contrast agent, 70 years or

**Table 3.** Preprocedural and fifth day values of average serum cystatin C and GFR levels

	Before		Fifth Day		p
	Average	SD	Average	SD	
Cystatin C	,81	,30	,83	,27	,049
CG	93,21	30,65	91,00	30,18	,205
MDRD	85,49	20,80	82,69	19,55	,109

MDRD: Modification of Diet in Renal Disease

CG: Cockcroft-Gault

SD: Standart Deviation

p: p value

**Table 4.** Correlation of serum cystatin C and GFR changes according to both equations

	Cystatin C (%)		CG (%)	
	r	P	r	p
CG (%)	-,276	,042		
MDRD (%)	-,275	,042	,999	,001

MDRD: Modification of Diet in Renal Disease

CG: Cockcroft-Gault

p: p value

over age and the use of intraaortic balloon pump. There was a linear relationship between the summit of these risk factors and occurrence of CIN (11). We were also determined more decrease of GFR in patients who diagnosed with diabetes mellitus. Conversely, Toprak et al. (12) reported absence of relation between left ventricular ejection fraction and CIN in coronary angiography performed patients. Necessity of hemodialysis was 1% in the study of McCullough et al. (13) but none of our patients was required to hemodialysis.

On the other hand, Aras et al. (14) compared MDRD and GC equations in elderly population in order to detect ideal GFR estimating equation and they found the MDRD as superior equation than CG. Similarly, in the study of Mahajan et al. (15) MDRD and CG equations were compared in healthy population and they revealed that MDRD results were more accurate than the results of CG. Furthermore, in patients with acute kidney disease the GFR values calculated by MDRD were more accurate the results of CG equation and it may suggest the usefulness or superiority of MDRD even in patients with acute renal failure (16). However, we have not discovered the superiority of equations to their each other. We have used  $94 \pm 18$  ml of contrast media to visualize coronary arteries and it is lower than the usual dose in real practice. Additionally, many of our patients have had stage I and II CKD or normal renal functions. Because of all these situations there was no high load to kidneys of our patients and therefore, the real prediction values of equations may not have appeared.

To our knowledge, this is a first study which compares the MDRD and CG equations in coronary artery visualized patients. Certainly, we need additional studies to find the best equation in the detection GFR alterations in the use of contrast media.

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