

# Differences between GFR Estimates using Cockcroft and Gault and MDRD Equations: Implications for Drug Dosing

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## Background

- ❖ The MDRD formula has been shown to have greater accuracy and precision for estimation of the GFR (eGFR) when compared to the Cockcroft and Gault formula (C&G) for patients with renal impairment.
- ❖ However currently in Australia the majority of drug dosing advice is based on C&G<sup>1,2,3</sup>
- ❖ With a recommendation for the routine reporting of an eGFR with every serum creatinine request<sup>4</sup>, it is important to evaluate the differences between these two methods for GFR estimation.

## Aims

- ❖ To describe the population characteristics presenting to a private pathology service in Australia for creatinine measurement.
- ❖ To compare these characteristics with the population used to define the MDRD formula<sup>5</sup>.
- ❖ To investigate the relationship between estimates of GFR from the MDRD and Cockcroft and Gault formulae in this population.

## Methods

- ❖ A data set of over 31,000 results for patients presenting at Southern.IML Pathology for routine creatinine testing were available for analysis.
- ❖ Patients' age, sex, height and weight were also collected. Patients were measured wearing clothes but without shoes.
- ❖ Creatinine was measured using the rate-blanked, compensated Jaffe method from Roche Diagnostics.
- ❖ The following variables were considered:
  - Using actual weight and ideal body weight estimated from height in C&G calculations.
  - MDRD "uncorrection" for BSA to give actual GFR.
- ❖ Note that no gold standard for GFR was available so the study is comparative only.

## Formulae

**MDRD** - the abbreviated, or "4 variable" version of the MDRD was used.

$$eGFR = 186 \times \{ [S_{Cr} (\mu\text{mol/L}) \times 0.0113]^{-1.154} \} \times (\text{age})^{-0.203} \\ (\times 0.742 \text{ if female}). \text{Units: mL/min/1.73m}^2$$

### Cockcroft and Gault

$$\text{Creatinine Clearance} = (140 - \text{age}) \times \text{Wt (kg)} \times 0.85 \text{ if female} / 0.813 \times \text{SCr (}\mu\text{mol/L)}.$$
 Units: mL/min.

$$\text{Ideal Body Wt (kg)} = 50 + 0.9 \times (\text{Ht (cm)} - 150) \text{ (-5 kg if female)}$$

AMH version<sup>2</sup>: use lower of actual and ideal body weight

Therapeutic Guidelines version<sup>3</sup>: use actual weight unless BMI > 30, then use ideal body weight.

## Patient Demographics

- ❖ The patient demographics for the data set are shown in table 1.

**COMMENT:** It can be seen that overall the patient age, height, weight and BSA are very similar to those from the study where the MDRD equation was derived<sup>5</sup>.

	Centile	age (years)	weight (kg)	height (cm)	creatinine (umol/L)	BSA (m2)	MDRD (mL/min/1.73m2)	C&G(wt) (mL/min)
TOTAL n=31218	2.5th	23	51	149	53	1.48	41.8	37.9
	Median	58	78	166	79	1.87	81.1	92.2
	97.5th	82	120	185	136	2.34	122.0	181.2
FEMALE n=16737	2.5th	22	48.2	147	50	1.43	42.0	36.4
	Median	57	71	160	70	1.74	80.9	88.9
	97.5th	82	113	174	117	2.18	123.9	182.3
MALE n=14479	2.5th	24	60.6	159	65	1.66	41.6	39.7
	Median	59	85	174	90	2.00	81.3	96.3
	97.5th	82	125	188	153	2.42	120.1	180.1
MDRD Average		51	80	170	203	1.91	39.8	*

\* Not supplied

Table 1. Patient demographics for data set

## Cockcroft and Gault Formula

- ❖ The Cockcroft and Gault (C&G) formula is an estimate of creatinine clearance rather than of GFR.
- ❖ There is considerable variability in the result of the C&G equation depending on the estimate of patient weight used. Figure 1 shows the correlation between C&G based on actual body weight and C&G based on ideal body weight.
- ❖ Figure 2 shows the variation caused by two methods of choosing when to use ideal as opposed actual body weight.

**COMMENT:** The criteria for choice of weight in C&G estimates can significantly affect the results.

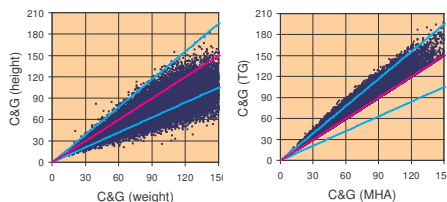


Figure 1. Effect of weight estimate on C&G results. The pink line is the line of identity and the pale blue lines are +/- 30% limits.

## MDRD v C&G

- ❖ A direct comparison of MDRD and C&G results is shown in figure 2a and table 1a.
- ❖ Figure 2b and table 1b show the relationship between MDRD "uncorrected" for BSA and C&G.
  - In both cases the AMH convention on weight estimate for C&G is used.
- ❖ The tables show the concordance of the 2 methods in assigning a stage of reduced GFR.

### COMMENTS:

- ❖ MDRD values are consistently higher than C&G values for results in the mild to moderate renal impairment range.
- ❖ The brown boxed in the tables show the percent that would be classified in a higher GFR classification if MDRD was used rather than C&G for drug dosing.
- ❖ "Uncorrecting" for BSA has little overall effect.

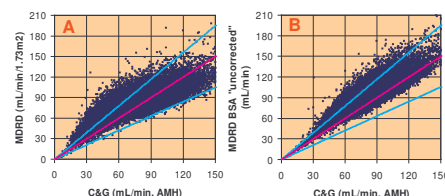


Figure 2. MDRD v C&G. MDRD, B MDRD "uncorrected for BSA"

C&G - AMH mL/min	n	eGFR (mL/min/1.73m <sup>2</sup> ) - MDRD					
		1 - 15	16 - 30	31 - 60	61 - 90	>90	
>90	8166	0%	0%	0%	26%	74%	
60-90	13880	0%	0%	1%	75%	24%	
30-60	8409	0%	0%	34%	63%	3%	
15-30	716	1%	24%	72%	2%	0%	
<15	44	75%	23%	2%	0%	0%	

C&G - AMH mL/min	n	eGFR (mL/min) - MDRD "uncorrected for BSA"					
		1 - 15	16 - 30	31 - 60	61 - 90	>90	
>90	8166	0%	0%	0%	5%	95%	
60-90	13880	0%	0%	0%	55%	45%	
30-60	8409	0%	0%	29%	69%	2%	
15-30	716	0%	25%	74%	1%	0%	
<15	44	73%	27%	0%	0%	0%	

Table 2. Classification of GFR reduction, MDRD v C&G. Yellow boxes – concordant results; brown boxes – MDRD relative over-estimation.

## Effect of Age

- ❖ The effect of various factors on the relationship between MDRD and C&G was explored. Age was the factor most associated with discrepancy between the formulae. As age increases the relative over-estimation of the MDRD compared to C&G increases (figure 3).

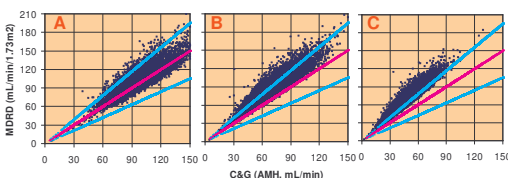


Figure 3. MDRD v C&G. Effect of age. A 18 to 50 years. B 50 to 70 years. C >70 years.

## Conclusions

- ❖ The population characteristics of patients attending for routine pathology in Australia closely resemble those in the population used to derive the MDRD formula.
- ❖ Current information for drug dosing is largely based on C&G based estimates of GFR however this estimate can be significantly affected by the choice of weight estimate.
- ❖ The use of the MDRD eGFR in place of the C&G will often lead to higher doses of drugs which are prescribed on the basis of renal function.
- ❖ The overestimation of MDRD relative to C&G is most marked in the elderly.
- ❖ Drug dosing should remain based on C&G until detailed review of prescribing advice is available.

## References

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