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# Evaluating the non-evidence based practice of rounding serum creatinine in the elderly and the impact on medication dosing

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**Evaluating the non-evidence based practice of rounding serum creatinine in the elderly and the impact on medication dosing**

A Thesis

Presented to the College of Pharmacy and Health Sciences

and

The Honors Program

of

Butler University

In Partial Fulfillment

of the Requirements for Graduation Honors

Kelly Lynn Roden  
April 22, 2015

## **Evaluating the non-evidence based practice of rounding serum creatinine in the elderly and the impact on medication dosing**

Kelly Roden, PharmD Candidate; Cathy Ramey, PharmD, CGP

**Background:** The Cockcroft and Gault equation is widely accepted in practice as the most appropriate way to calculate an estimated creatinine clearance. Geriatric patients often present with reduced muscle mass, and therefore lower creatinine production, due to normal changes in body composition associated with aging. Because serum creatinine and creatinine clearance are inversely proportional using the Cockcroft and Gault equation, a lower serum creatinine may falsely overestimate renal function in the elderly population. Rounding to a normal serum creatinine is believed by some practitioners to prevent over estimation of creatinine clearance and renal function.

**Objective:** The objective of this study is to identify and compare medications that require renal dose adjustment when using the patient's measured serum creatinine, if less than 1 mg/dL, versus a rounded serum creatinine of 1 mg/dL in the Cockcroft and Gault equation.

**Methods:** Each patient's estimated creatinine clearance was calculated using the patient's measured serum creatinine and a rounded value of 1 mg/dL in the Cockcroft and Gault equation. Once both creatinine clearances had been calculated, an evaluation was completed to determine how many of the patient's medications required renal dose adjustment based on either the measured or rounded creatinine clearance. The number of dosing discrepancies was then assessed, in addition to creatinine clearance values, to look for trends or patterns regarding the amount of dosing discrepancies and the effects of rounding to a serum creatinine of 1 mg/dL.

**Results:** A total of 32 patients (6 male, 26 female) were evaluated for renal dose adjustments based on the measured and rounded creatinine clearance. Seven patients were identified as having discrepancies, all of which were female patients. The average difference between the measured and rounded creatinine clearance in female patients was 16 mL/min. A total of 12 discrepancies were found affecting 9 different medications. The average number of discrepancies per patient that presented with a discrepancy was 1.71 discrepancies. Five of the 12 discrepancies affected both the measured creatinine clearance and the rounded creatinine clearance, while 7 of the 12 discrepancies affected only the rounded creatinine clearance.

**Conclusion:** Results of the study show that patients in CKD Stage 3, or in CKD Stage 2 but within approximately 16 mL/min of CKD Stage 3, are more likely to present with renal dosing discrepancies, and that the discrepancies identified were not localized to particular medications or therapeutic areas.

Word Count: 2248

Key Phrases: serum creatinine, creatine clearance, elderly, renal dosing discrepancies

## BACKGROUND

Physiologically, muscle tissue uses creatine, a nutrient produced primarily by the liver and kidneys, as a source of energy. The breakdown of creatine by muscle tissue results in a waste product called creatinine. Creatinine is then released from muscle tissue into the blood stream and cleared, almost exclusively, by the kidneys. As a result, creatinine clearance can be used to assess renal function. The Cockcroft and Gault equation is widely accepted in practice as the most appropriate way to calculate an estimated creatinine clearance and is the standard equation used for drug dosage adjustments.<sup>1</sup> This equation accounts for the patient's age, ideal body weight, gender, and serum creatinine level. Over time, it has been adapted into practice to use the patient's actual body weight when it is less than the patient's ideal body weight. The following is the Cockcroft and Gault equation:

$$\text{CrCl (mL/min)} = [(140 - \text{age}) \times \text{IBW} (\times 0.85 \text{ for females})] / (\text{SCr} \times 72).$$

Normal serum creatinine levels in adults range from 0.6-1.2 mg/dL. Geriatric patients often present with reduced muscle mass, and therefore lower creatinine production, due to normal changes in body composition associated with aging. Because serum creatinine and creatinine clearance are inversely proportional using the Cockcroft and Gault equation, a lower serum creatinine indicates a higher creatinine clearance and increased renal function. A normal creatinine clearance ranges from 90 to 130 mL/min. Questions have arisen about how to assess renal function in geriatric patients using the Cockcroft and Gault equation when low serum creatinine is due to decreased muscle mass and not due to increased renal creatinine clearance.

Accurately estimating renal function in this population is imperative for proper dosing. Both over and under dosing medications have consequences that impact quality of care and patient outcomes. For example, a patient presenting with decreased muscle mass, decreased serum creatinine, and decreased renal function may have an estimated creatinine clearance that appears normal via the Cockcroft and Gault equation. Overdosing of medications in this patient increases the risk for adverse drug effects and toxicities. In practice, some clinicians routinely round a serum creatinine level of less than 1 mg/dL to 1 mg/dL for use in the Cockcroft and Gault equation in older adults. Rounding to a normal serum creatinine is believed by some to more accurately predict renal function and prevent over estimation of creatinine clearance and renal function.

## **PREVIOUS STUDIES**

Hu et al assessed the relationship between estimating creatinine clearance and drug dosing errors in the elderly and found that patients with a lower estimated creatinine clearance experienced more dosing errors and that “physicians routinely overestimate renal function in older patients.”<sup>2</sup> This overestimation of renal function is a result of using measured serum creatinine levels in the Cockcroft and Gault equation when decreased measured serum creatinine is not a result of sufficient renal function, but rather a result of reduced muscle mass. The practice of rounding to 1 mg/dL has been adapted to prevent this overestimation, although it is not an evidence based method. However, there are other studies that assess the practice of rounding the serum creatinine to 1 mg/dL and the results have not proven to be better at accurately assessing renal function.

Dowling et al found that using a rounded serum creatinine of 1 mg/dL, as opposed to a measured serum creatinine, lead to a significantly lower estimation of creatinine clearance when using the Cockcroft and Gault equation.<sup>3</sup> In addition, when both estimates were compared to a patient's actual creatinine clearance via 24 hour urine collection, the rounded value more significantly underestimated renal function. This study recommends that the practice of rounding be avoided due to the underestimation of renal function which leads to sub-therapeutic dosing errors.<sup>3</sup> This recommendation is further supported by Smythe et al. However, Smythe also addressed the degree of the measured serum creatinine below 1 mg/dL and the impact on estimating creatinine clearance. The study found that "bias was greater and precision less when SCr concentrations of < 0.7 mg/dL were rounded than when SCr concentrations of > 0.7 mg/dL were rounded. Furthermore, "a consistent effect on precision of rounding the SCr concentration was not evident."<sup>4</sup>

## **NEED FOR FURTHER STUDY**

There is an ongoing need to assess the clinical practice of rounding serum creatinine to 1 mg/dL in geriatric patients and its effects on accurately estimating renal function. This non-evidence based practice can lead to dosing errors for medications requiring renal dose adjustments. There is need to study the prevalence of dosing errors when assessing patients renal function from calculating an estimated creatinine clearance from measured serum creatinine versus rounded serum creatinine. Furthermore, there is a need for establishing evidence based guidelines for when rounding may be considered appropriate. Although the objective of this study is not to establish guidelines, there will be an evaluation of common medications with dose discrepancies.



## **OBJECTIVE**

The objective of the study is to evaluate geriatric patients at a designated long term care facility in Indiana. For those patients with a serum creatinine less than 1 mg/dL, a review will be completed to assess how many of their current medications require renal dosage adjustment using their measured serum creatinine versus a serum creatinine rounded to 1 mg/dL in the Cockcroft and Gault equation. The number of medications that require dosage adjustment using both methods will be compared. Common medications that present discrepancies in renal dose adjustment when comparing measured vs. rounded serum creatinine will be identified.

Here after, the estimated creatinine clearance calculated using the patient's measured serum creatinine value in the Cockcroft and Gault equation will be referred to as the measured creatinine clearance; similarly, the estimated creatinine clearance calculated using a rounded serum creatinine value of 1 mg/dL in the Cockcroft and Gault equation will be referred to as the rounded creatinine clearance.

## **METHODS**

This study is a retrospective chart review of geriatric patients residing in the Brownsburg Health Care Center, a long term care facility in Indiana. Inclusion criteria for this study are patients residing in the long term care facility, patients age 65 and older, patients with a measured serum creatinine of less than 1 mg/dL, and patients receiving at least one scheduled medication. Exclusion criteria for this study are patients on dialysis, patients with any form of amputation, patients with a serum creatinine greater than or equal to 1 mg/dL, and patients with a height less than or equal to 60 inches. Only

scheduled medications (including oral medications, injectable medications, and patches) were evaluated. This study excluded all “as needed” medications, topical medications (including creams, ointments, ear/eye drops, enemas, etc.), inhalers and aerosol solutions, and multivitamins. This study received IRB approval through Butler University due to collection of patient information including: age, gender, height, weight, serum creatinine, and current medications. Once all data were collected, each patient’s estimated creatinine clearance was calculated using the Cockcroft and Gault equation using both the patient’s measured serum creatinine and a rounded value of 1 mg/dL. Once both creatinine clearances had been calculated, an evaluation was completed to determine how many medications of the patient’s current medications required renal dose adjustment based on either the measured or rounded creatinine clearance. The number of dosing discrepancies was then assessed, in addition to creatinine clearance values, to look for trends or patterns regarding the amount of dosing discrepancies and the effects of rounding to a serum creatinine of 1 mg/dL.

## **RESULTS**

### *Patient Characteristics*

A total of 89 patients were residing in the Brownsburg Health Care Center at the time of data collection. Of that, 32 patients met the study criteria and were subject to evaluation. The population group was predominately female with 26 females of the 32 total patients (81.25%). The average age in years and average number of medications for female patients was 78.5 and 9.7 respectively. Furthermore, the average difference between the measured and rounded creatinine clearance was 16 mL/min for female

patients. Figure 1 details all the patient characteristics and the comparisons between the male and female patients.

### *Discrepancies*

Of the 32 patients evaluated, 7 patients presented with renal dosing discrepancies. All 7 patients that presented with discrepancies were female. Among the 7 female patients, a total of 12 discrepancies were identified giving an average of 1.71 discrepancies per patient. The 12 discrepancies presented from 9 various medications. Seven of the 12 discrepancies (58.3%) affected only the rounded creatinine clearance, while 5 of the 12 discrepancies (41.7%) affected both the measured and rounded creatinine clearance. Additionally, the discrepancies presented with a variety of renal dosing recommendations including recommendations to: decrease dose (4/12; 33.3%), decrease frequency (3/12; 25%), decrease dose and frequency (1/12; 8.3%), and decrease dose or frequency (1/12; 8.3%). Furthermore, 3 of the 12 discrepancies (25%) identified that the medication was contraindicated based of the patient's renal function. A full list of the medications, discrepancies, and dosage recommendations can be found in Figure 2.

Further analysis was done to identify if there was any relationship between the discrepancies and creatinine clearance values. Three of the 7 patients that presented with a discrepancy had a measured creatinine clearance  $> 60$  mL/min; however, this value was then reduce to 30-60 mL/min after calculating the patient's rounded creatinine clearance. The remaining 4 patients that presented with discrepancies had a measured creatinine clearance of 30-60 mL/min, and the rounded creatinine clearance remained in that range.

A full depiction of the breakdown of patients by creatinine clearance ranges can be seen in Figure 3.

## **DISCUSSION**

### *Creatinine Clearance Values*

The creatinine clearance ranges detailed in Figure 3 were identified to give insight into the Chronic Kidney Disease (CKD) Stage of the patient, whether that patient's CKD Stage would change after calculating a rounded creatinine clearance, and if there was any relationship between the patients that presented with discrepancies and their CKD Stage. The CKD Stages, as defined by the KDOQI Clinical Practice Guidelines are as follows: Stage 1 (normal function;  $> 90$  mL/min), Stage 2 (mild dysfunction; 60-89 mL/min), Stage 3 (moderate dysfunction; 30-60 mL/min), Stage 4 (severe dysfunction; 15-30 mL/min), and Stage 5 (failure;  $< 15$  mL/min).<sup>5</sup> The 3 patients that presented with discrepancies and a measured creatinine clearance  $> 60$  mL/min (as seen in Column 2 of Figure 3) would be categorized into CKD Stage 1 or 2 depending on the patient's exact creatinine clearance value; however, these patient were then re-categorized into CKD Stage 3 after calculating a rounded creatinine clearance of 30-60 mL/min. Keeping in mind that the average difference between the measured and rounded creatinine clearance for female patients identified in this study was 16 mL/min, then patients with a measured creatinine clearance between approximately 60-76 mL/min in CKD Stage 2 would be at the highest risk for being re-categorized into CKD Stage 3. The remaining 4 patients that presented with discrepancies (as seen in Column 3 of Figure 3) met the criteria for CKD Stage 3 based on both the measured and rounded creatinine clearances. These findings

give insight to practitioners that patients in CKD Stage 3, or in CKD Stage 2 but within approximately 16 mL/min of CKD Stage 3, are more likely to present with renal dose discrepancies. This helps identify for which patients it may be beneficial to calculate both a measured and rounded creatinine clearance using the Cockcroft and Gault equation and evaluate the risks and benefits of the different renal dosing recommendations.

### *Clinical Implications*

A practitioner's decision to use a measured vs. rounded creatinine clearance to determine renal dosing of medications can ultimately affect the patient and the quality of their care. The following are examples of medications that were identified in this study as having discrepancies and the clinical implications of the renal dose adjustment recommendation. Keppra (Levetiracetam) was identified as having a discrepancy between the prescribed dosage and both the measured and rounded creatinine clearances. The renal dose adjustment recommendation is to decrease the frequency of administration. If that recommendation is accepted, the patient may be at an increased risk of inadequate seizure management; conversely, if the recommendation is declined and the practitioner continues the prescribed dose, the patient may be at an increased risk of central nervous system and cardiovascular side effects.<sup>6</sup> Similarly, Viread (Tenofovir), a medication indicated for the treatment of HIV or Hepatitis C, was identified as having a discrepancy between the prescribed dosage and the rounded creatinine clearance. If the practitioner uses the measured creatinine clearance, then there is no dose adjustment required. However, if the practitioner uses the rounded creatinine clearance, the renal dose adjustment recommendation is to decrease the frequency of administration. If that recommendation is accepted, the patient may be at an increased risk of inadequate viral

suppression and disease progression; conversely, if the recommendation is declined and the practitioner continues the prescribed dose, the patient may be at an increased risk of central nervous system and endocrine side effects.<sup>7</sup> In summary, the clinical implications of implementing the renal dose adjustment recommendations must be carefully considered for patients that present with discrepancies, and clinical judgement must be made on a case-by-case basis. A full list of the medications, discrepancies, and dosage recommendations can be found in Figure 2 and more examples of clinical implications can be found in Figure 4.

## **CONCLUSION**

In conclusion, the results of this study show that patients in CKD Stage 3, or in CKD Stage 2 but within approximately 16 mL/min of CKD Stage 3, are more likely to present with renal dosing discrepancies, and that the discrepancies identified were not localized to particular medications or therapeutic areas.

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# FIGURES

Figure 1 – Patient Characteristics

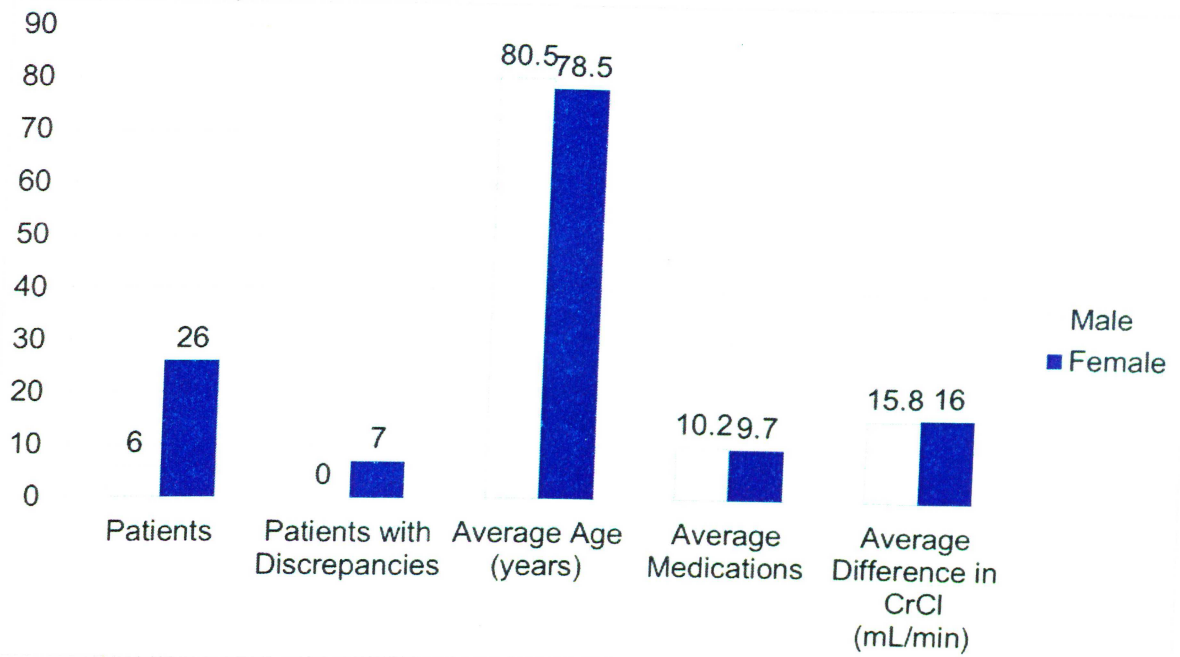


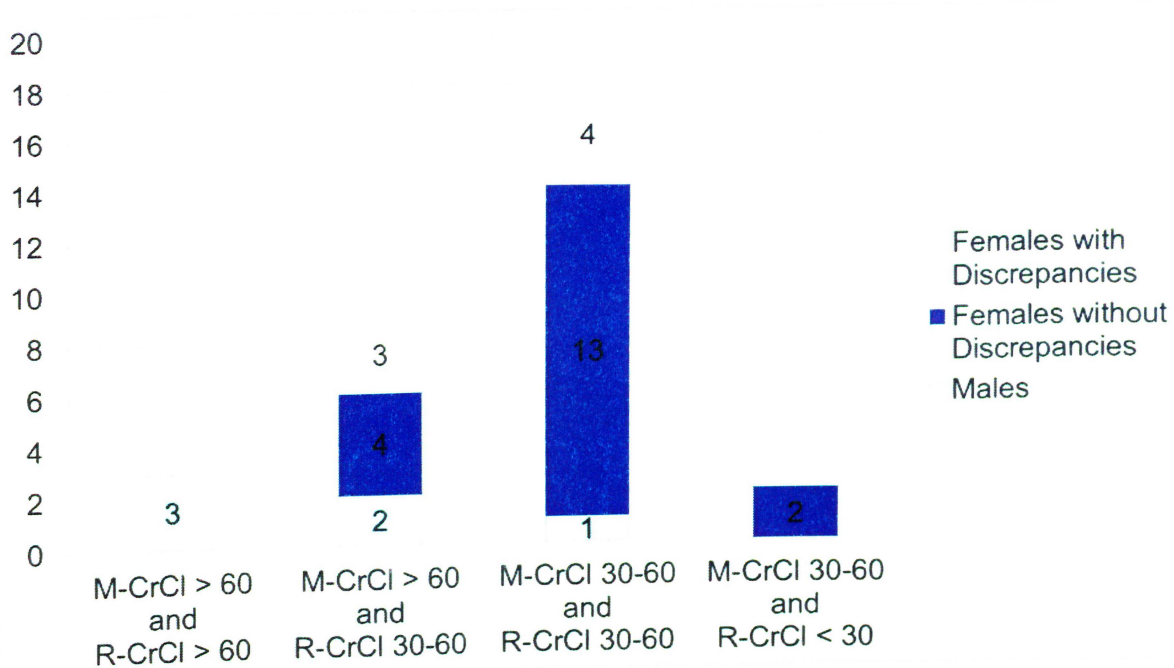


Figure 2 – Discrepancies

Medication	Dosage	M-CrCl Dosage Recommendation	R-CrCl Dosage Recommendation
Keppra (Levetiracetam)	500mg po TID	250-750mg po BID	250-750mg po BID
Macrobid (Nitrofurantoin)	100mg po QHS	Contraindicated	Contraindicated
Macrobid (Nitrofurantoin)	100mg po BID x 10 days	Contraindicated	Contraindicated
Pepcid (Famotidine)	20mg po BID	N/A	Administer 50% of dose or increase to q 36-48 hrs
Lyrica (Pregabalin)	100mg po BID	N/A	50mg po BID
Zantac (Ranitidine)	300mg po QHS	150mg po daily	150mg po daily
Zantac (Ranitidine)	150mg po BID	N/A	150mg po daily
Aldactone (Spironolactone)	50mg po daily	12.5-25mg po daily	12.5-25mg po daily
Aldactone (Spironolactone)	50mg po BID	N/A	12.5-25mg po daily
Viread (Tenofovir)	300mg po daily	N/A	300mg po q 48 hrs
Combivir (Lamivudine/ Zidovudine)	150/300mg po BID	N/A	Fixed-dose combination product not recommended
Januvia (Sitagliptin)	100mg po daily	N/A	50mg po daily

M-CrCl = Measured Creatinine Clearance; R-CrCl = Rounded Creatinine Clearance

**Figure 3 – Measured vs. Rounded Creatinine Clearance Ranges**



M-CrCl = Measured Creatinine Clearance; R-CrCl = Rounded Creatinine Clearance

Figure 4 – Clinical Implications

<b>Drug</b>	<b>Recommendation</b>	<b>Accept</b>	<b>Decline</b>
Keppra	↓ Frequency	Risk of inadequate seizure management	↑ Risk of CNS and CV effects
Macrobid	Contraindicated	New ABX	Untreated UTI
Lyrica	↓ Dose	Risk of inadequate pain, seizures, etc. management	↑ Risk of CNS effects
Viread	↓ Frequency	Risk of inadequate viral suppression	↑ Risk of CNS and endocrine effects
Januvia	↓ Dose	Risk of inadequate blood glucose control	↑ Risk of ADRs