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Estimating the prevalence of renal insufficiency in seniors requiring long-term care

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Background. Renal function declines with age, but little is known about the extent of renal insufficiency among the institutionalized elderly. The objective of this study was to estimate the prevalence of low glomerular filtration rate (GFR) in a large sample of elderly adults living in long-term care facilities, and to compare two commonly used methods for estimating GFR.

Methods. A total of 9931 residents aged 65 years and older participated in a retrospective cross-sectional study of 87 long-term care facilities in Ontario. GFR was estimated by the Cockcroft-Gault and Modification of Diet in Renal Disease Study (MDRD) equations. The prevalence of low GFR, using the Cockcroft-Gault equation (<30 mL/min), was compared with the MDRD equation (<30 mL/min/1.73 m^2).

Results. A total of 17.0% (95% CI 15.6 to 18.5) of men and 14.4% (95% CI 13.6 to 15.3) of women had a serum creatinine concentration above the laboratory reported upper reference limit of normal. The prevalence of both elevated serum creatinine and low GFR were observed to increase with age ($P < 0.0001$). The Cockcroft-Gault equation produced a consistently lower estimate of GFR than did the MDRD equation, a discrepancy most pronounced in the oldest residents. Among all men, a low GFR was more prevalent using the Cockcroft-Gault (10.3%, 95% CI 9.2 to 11.5) than MDRD (3.5%, 95% CI 2.8 to 4.2) equation, with a similar difference also seen in women (23.3%, 95% CI 22.4 to 24.3 versus 4.0%, 95% CI 3.6 to 4.5, respectively). Of all residents whose Cockcroft-Gault estimated GFR was under 30 mL/min, 14.7% (95% CI 13.2 to 16.3) were found to have GFR greater than 60 mL/min/1.73 m^2 according to the MDRD equation.

Conclusion. Age-associated renal impairment is common among elderly long-term care residents, but there exists a clear discrepancy between the Cockcroft-Gault and MDRD equations in predicting GFR. Consideration should be given to medication dose adjustment, based on a practical estimate of GFR. However clarification is needed about which method, if either, is most valid among the frail elderly. Complex patient and societal issues surrounding advanced care directives, treatments associated with renal insufficiency, and, if and when to initiate dialysis, require further attention.

Key words: nursing homes, mass screening, geriatric assessment, kidney diseases, glomerular filtration rate, cross-sectional studies, prevalence.

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Renal function declines with advancing age [1]. Knowledge about the prevalence of a low renal glomerular filtration rate (GFR) among elderly persons living in long-term care facilities has ramifications for drug prescribing, laboratory reporting, and the design of related randomized clinical trials. Although measured serum creatinine alone is often used to approximate GFR, its low accuracy in the frail and very elderly is well recognized [2]. Direct measurement of GFR (e.g., 24-hour urinary creatinine collection, inulin clearance) is often impractical, due to problems with incontinence, patient transport, and the expense of testing. Experts therefore recommend simple mathematical equations be used to estimate GFR in most adults [3], such as the Cockcroft-Gault [4] and Modification of Diet in Renal Disease Study (MDRD) [5] formulas.

Little is known about the prevalence of renal insufficiency in long-term care facilities. Previously conducted studies typically enrolled community-dwelling seniors [6, 7], and based their results on measured serum creatinine alone [8–10]. A preliminary study in long-term care facilities suggested that the prevalence of renal insufficiency might be higher than appreciated [11]. Moreover, it is unclear which of the recommended equations for the estimation of GFR should be used in clinical practice, and whether they generate accurate or like results. In the current study we estimated the prevalence of low GFR in a large sample of long-term care residents, and compared two well-known predictive equations of GFR [4, 5].

METHODS

In the province of Ontario approximately 56,600 adults live within 500 long-term care facilities [12]. The majority

are Caucasian (>95%) and female (73%), living in their seventh (22%), eighth (46%) and ninth (24%) decades of life. More than half of all residents are diagnosed with hypertension or heart failure, 16% with diabetes mellitus, 21% with visual or hearing impairment, 63% with cognitive impairment, and over 60% have persistent urinary and bowel incontinence. These individuals are prescribed an average of six regular medications at a given time. The following study examined 87 of the 500 long-term care facilities.

Each fall season, consultant pharmacists record each resident's age, weight, gender, and serum creatinine concentration, in order to suggest appropriate amantadine doses in the event of an influenza A outbreak. In the 2001 to 2002 season, serum creatinine was measured using the modified kinetic Jaffe assay (Johnson & Johnson Vitros 950 analyzer, Rochester, NY, USA), with a laboratory coefficient of variation of less than 1%. The adult serum creatinine references reported by the laboratory were 60 to 125 μmol/L (0.7 to 1.4 mg/dL) in men, and 50 to 110 μmol/L (0.5 to 1.2 mg/dL) in women. In the current study, GFR was estimated using both the MDRD and Cockcroft-Gault equations (see **Appendix**). Predicted GFR was categorized according to Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (i.e., >90, 60 to 89, 30 to 59, and <30 mL/min/1.73 m^2 [MDRD] or mL/min [Cockcroft-Gault]) [3]. The number and proportion of residents falling within each GFR category was stratified by gender and age. Prevalence ratios (PR) and 95% CI were used to compare the proportion of men and women whose estimated GFR was less than 30 mL/min/1.73 m^2 by MDRD, or less than 30 mL/min by Cockcroft-Gault, with the age group of 65 to 74 years as the referent. This approach considers the GFR threshold below which drug dose adjustments or avoidance of common renal handled medications are recommended [13], and highlights the relative risk of low GFR with advancing age. Chi-squared tests were used to examine differences between two proportions, and analysis of variance (ANOVA) with trend analyses was used to examine for differences between age groups in serum creatinine and weight. A P value less than 0.05 was considered significant. All analyses were conducted using SPSS 10.0 (SPSS, Inc., Chicago, IL, USA), and graphs were made using SPSS and Excel 2000 (Microsoft Corporation, Redmond, WA, USA). The Hamilton Health Science's Ethics Review Board approved the study.

RESULTS

Complete data were available for 9931 elderly aged 65 years and older (over 85% of eligible residents). Among the 2616 men and 7315 women studied, the respective mean age was 82 (SD 8) and 85 (SD 7) years, and the respective mean weight was 69.6 (SD 14.1) kg [153 (SD 31.0) pounds) and 57.7 (SD 13.6) kg [127 (SD 30.0) pounds]. Among males, the median serum creatinine was 99 μmol/L (1.1 mg/dL), and among females it was 77 μmol/L (0.9 mg/dL). In both men and women, each 5-year increase in age was associated with a mean increase in serum creatinine of between 1 to 9 μmol/L (0.01 to 0.1 mg/dL) ($P < 0.0001$), despite an associated 0.5 to 4 kg (1.1 to 8.8 pounds) decline in body weight ($P < 0.0001$). A total of 17.0% (95% CI 15.6 to 18.5) of men and 14.4% (95% CI 13.6 to 15.3) of women were found to have a serum creatinine concentration above the laboratory reported upper reference limit of normal (Fig. 1).

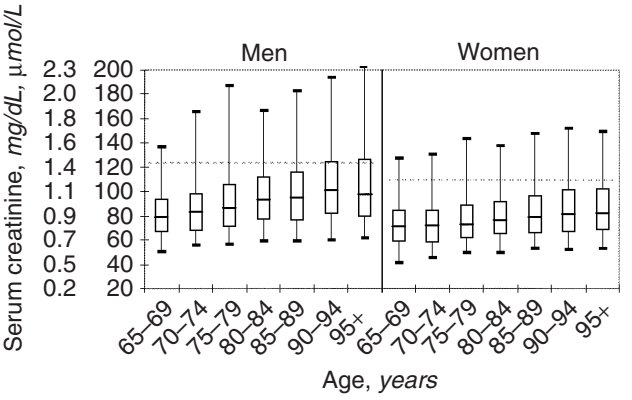

Fig. 1. Box-plots of serum creatinine for 9931 long-term care residents, according to age and gender. The interquartile range (upper and lower ends of each box) and median (solid line across each box) are presented. The whiskers extend to the upper 95th and lower 5th percentiles. The dashed horizontal lines represent the normal upper reference limit for men (125 μmol/L) and women (110 μmol/L) reported by the laboratory.

The predicted GFR within each age- and gender-specific stratum differed between the Cockcroft-Gault and MDRD equations (Fig. 2). Among all men, low GFR was considerably more prevalent using the Cockcroft-Gault equation (10.3%, 95% CI 9.2 to 11.5), compared to the MDRD equation (3.5%, 95% CI 2.8 to 4.2) (Fig. 2) (Table 1). A similar difference was also seen in women (23.3%, 95% CI 22.4 to 24.3 versus 4.0%, 95% CI 3.6 to 4.5, respectively). Relative to those aged 65 to 74 years, the prevalence ratio of low GFR increased with advancing age in both men and women, but more dramatically so using the Cockcroft-Gault equation (Table 1).

Out of 385 men and women whose MDRD-estimated GFR was less 30 mL/min/1.73 m^2, none had a Cockcroft-Gault estimated GFR greater than 60 mL/min. Conversely, of the 1978 residents whose Cockcroft-Gault predicted GFR was less than 30 mL/min, 14.7% (95% CI 13.2 to 16.3) had a MDRD estimated GFR greater than 60 mL/min/1.73 m^2.

DISCUSSION

In a large sample of elderly long-term care residents, both elevated serum creatinine and low estimated GFR

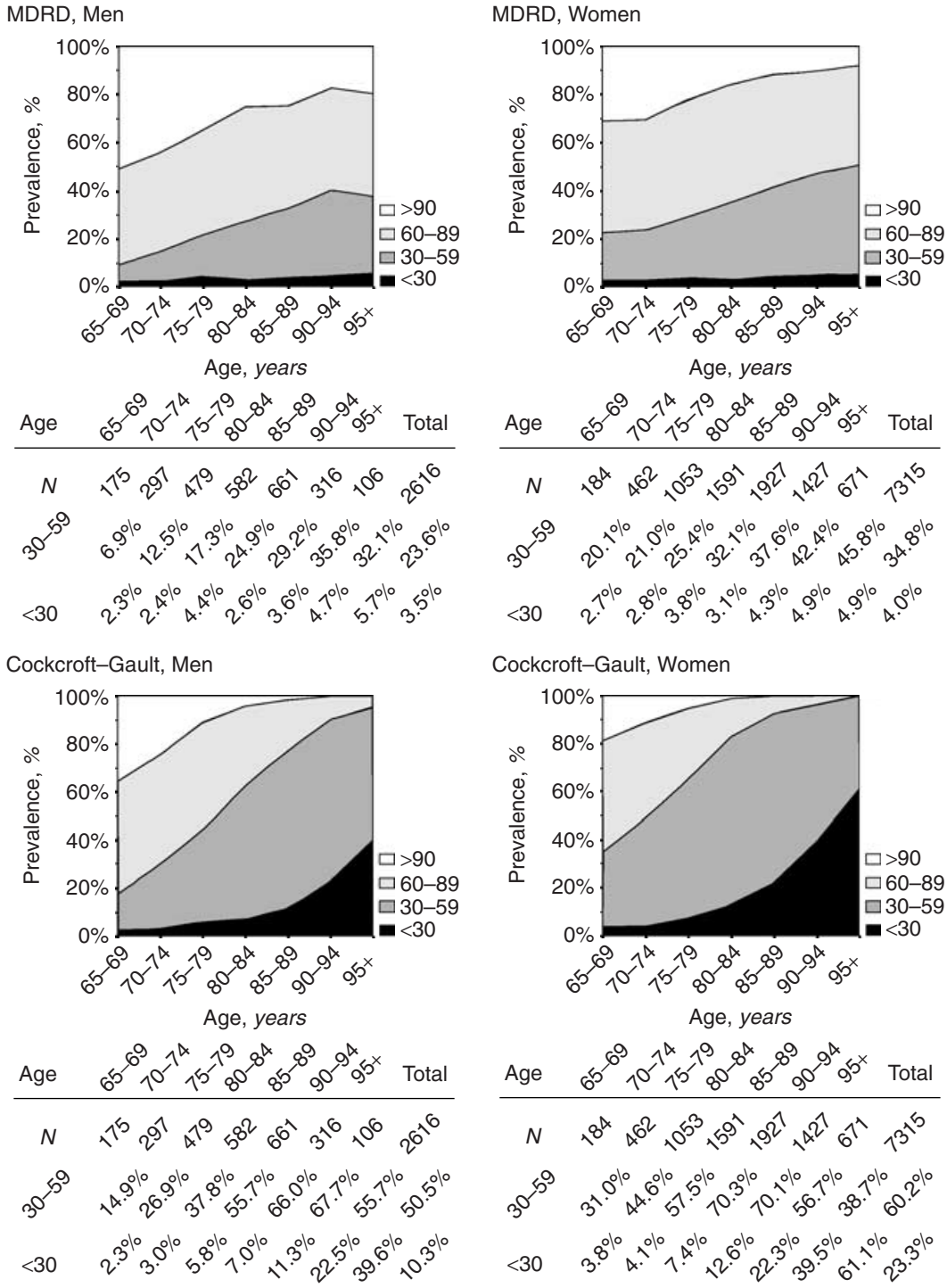

Fig. 2. Prevalence of categorized glomerular filtration rate (GFR) according to age and gender, estimated by the Modification of Diet in Renal Disease (MDRD (mL/min/1.73 m^2) and Cockcroft-Gault (mL/min) equations. Below each figure is the number of individuals studied and the GFR category prevalence estimates.

were commonly observed. The risk of having low GFR increased with age, but depended upon whether the Cockcroft-Gault or MDRD equation was used.

Nearly 40% of long-term care residents in our study were found to have renal insufficiency, based on an MDRD-estimated GFR of less than 60 mL/min/1.73 m^2 (Fig. 2). Extrapolating these estimates to the population at large, 21,000 of all 56,600 long-term care residents in Ontario [12], 95,000 of all 250,000 residents in Canada [14], and 570,000 of those 1.5 million residents in the

Table 1. Age-related prevalence and prevalence ratio of low glomerular filtration rate (GFR) among elderly long-term care residents, estimated by the Modification of Diet in Renal Disease (MDRD) (<30 mL/min/1.73 m^2) and Cockcroft-Gault (<30 mL/min) equations

			MDRD equation		Cockcroft-Gault equation	
	Age *years*	Number of persons evaluated	Prevalence of low GFR %	Prevalence ratio (95% CI) of low GFR	Prevalence with low GFR %	Prevalence ratio (95% CI) of low GFR
Men	65–74	472	2.3	1.0 (Referent)	2.7	1.0 (Referent)
	75–84	1061	3.4	1.5 (0.7–2.8)	6.8	2.4 (1.3–4.2)
	85–94	977	4.0	1.7 (0.9–3.3)	14.9	5.4 (3.1–9.5)
	95+	106	5.7	2.4 (0.9–6.4)	39.6	14.4 (8.0–25.8)
	All	2616	3.5	—	10.3	—
Women	65–74	646	2.8	1.0 (Referent)	4.0	1.0 (Referent)
	75–84	2644	3.4	1.2 (0.7–2.0)	10.5	2.6 (1.8–3.9)
	85–94	3354	4.5	1.6 (1.0–2.6)	29.6	7.4 (5.0–10.8)
	95+	671	4.9	1.8 (1.0–3.1)	61.1	15.2 (10.4–22.2)
	All	7315	4.0	—	23.3	—

United States [15] could meet the definition of having chronic kidney disease [3]. Moreover, this estimate would nearly double if Cockcroft-Gault–derived estimates were used.

These results are in stark contrast to healthy older participants in the Baltimore Longitudinal Study on Aging [1, 16]. The Baltimore study documented a mean creatinine clearance (by 24-hour urine) of 97 mL/min in healthy octogenarians and 146 mL/min in participants aged 30 to 39 years, with an average decline in creatinine clearance of 0.75 mL/min per year after the third decade of life.

The limitations of solely using serum creatinine as an indirect measure of GFR are well recognized, since serum creatinine is related to muscle mass, and to a lesser extent dietary protein intake and renal tubular secretion. Despite an age-related increase in serum creatinine, we saw a more pronounced age-associated decline in body weight in this sample of elderly persons living in a long-term care setting, relative to that observed in a previous study of community-dwelling seniors [7]. Within-person [17], and both intra- and inter-laboratory variability [18, 19] of serum creatinine further complicate an accurate assessment of renal function among institutionalized elderly. Predictive equations that consider serum creatinine in conjunction with gender, age, and body mass represent an attractive and practical alternative for GFR assessment in this population. Both the Cockcroft-Gault and MDRD equations were previously validated in middle-aged adults with renal disease [5], raising concerns about their "transportability" to a long-term care setting. Here we have shown that there is a clear discordance between the two equations when applied to the frail elderly.

The MDRD equation reports GFR as mL/min/1.73 m^2, which differs substantially from the Cockcroft-Gault equation, which estimates GFR in mL/min, using patient weight. Furthermore, both equations may underestimate gold standard GFR in elderly persons [20], with this underestimate being larger with the Cockcroft-Gault than MDRD formula. This partly artifactual association

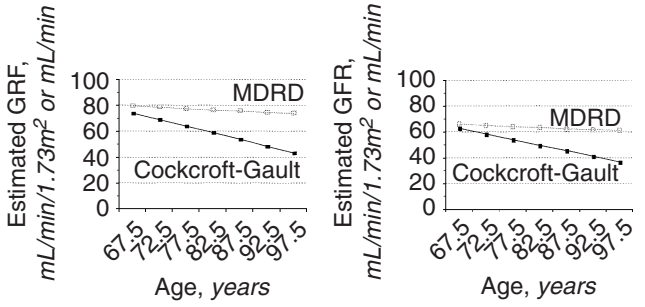

Fig. 3. Mathematical relationship between advancing age and estimated glomerular filtration rate (GFR), comparing the Modification of Diet in Renal Disease (MDRD) (top line) and Cockcroft-Gault (bottom line) equations. The figure on the left represents the hypothetical change in GFR for an aging man, at a fixed body mass of 72 kg and a serum creatinine of 88 μmol/L (1.0 mg/dL). The figure in the right represents an aging woman, at a fixed body mass of 65 kg and serum creatinine of 80 μmol/L (0.9 mg/dL).

between increasing age and declining GFR may be due to the presence of mathematical coupling. In our study, men aged 65 to 69 years had a mean body mass of 72 kg and a mean serum creatinine of 88 μmol/L (1.0 mg/dL), with corresponding values of 65 kg and 80 μmol/L (0.9 mg/dL) among women of similar age. Hypothetically, assuming that body mass and serum creatinine remained unchanged with advancing age, the Cockcroft-Gault equation would estimate a more rapid decline in GFR than the MDRD equation (Fig. 3). These points do not necessarily validate one method over the other, but highlight the need for clarification about which method, if either [21–23], is most valid. Future diagnostic and prognostic studies are needed to validate these equations against inulin clearance and the development of adverse events, including drug toxicity, anemia, malnutrition, and end-stage renal disease.

In a previous study conducted in four long-term care facilities, we observed a high rate of inappropriate drug prescribing for estimated Cockcroft-Gault GFR [24]. Many

residents are often prescribed several medications over lengthy periods of time. Allopurinol, metformin, glyburide, digoxin, nonsteroidal anti-inflammatory drugs, H_2-receptor antagonists and magnesium hydroxide are each associated with rare, but serious side effects in the presence of low GFR. Whether a program aimed at medication dose adjustment in the presence of low GFR is cost saving remains to be determined. Similarly, the automatic reporting by clinical laboratories of both serum creatinine and estimated GFR, based on age, gender, and/or body mass, requires evaluation, in terms of its impact on clinical care and drug prescribing.

Finally, in the United States, 0.3% of long-term care residents receive routine dialysis [25], and this estimate is projected to increase within aging populations [26]. Complex patient and societal issues surrounding advanced care directives, treatments associated with renal insufficiency, and if and when to initiate dialysis, require further attention.

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APPENDIX: MODIFICATION OF DIET IN RENAL DISEASE (MDRD) AND COCKCROFT-GAULT EQUATIONS FOR ESTIMATING THE GLOMERULAR FILTRATION RATE (GFR)

MDRD equation

$$\text{GFR (mL/min/1.73 m}^2) = 186 \times (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if African American})$$

Cockcroft-Gault equation

$$Cl_{creat}\ (\text{mL/min}) = \frac{(140 - \text{age years}) \times (\text{weight kg})}{(72)\ (\text{serum creatinine mg/dL})} \times 0.85 \text{ if female}$$

To convert serum creatinine from μmol/L to mg/dL divide by 88.4. To convert from pounds to kilograms, divide by 2.2.

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