Original Research

Evaluation of Renal profile in liver cirrhosis patients: impact of muscle mass and sex

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ABSTRACT:
Background: The current study was carried out to evaluate renal profile among subjects having liver cirrhosis. **Material and methods**: This study included 100 consecutive cirrhotic patients who underwent Cr-ethylenediamine tetra acetic acid (EDTA) (as a mGFR) and abdominal computed tomography (CT). The eGFR was calculated using creatinine or cystatin C. Muscle mass was assessed in terms of the total skeletal muscle at L3 level using CT. **Results:** Modification of diet in renal disease (MDRD)-eGFR was overestimated in 49% of patients. A multivariate analysis showed that female sex, Child B and C vs. A (aOR 1.69 and 1.84) and skeletal muscle mass (aOR 0.89) were independent risk factors associated with overestimation. Interestingly, the effect of skeletal muscle mass on overestimation varied based on sex. Decreased muscle mass significantly enhanced the risk of overestimation of MDRD-eGFR in male patients, but not in female patients. Cystatin C-based eGFR showed a better correlation with mGFR than MDRD-eGFR; it was also better at predicting overall survival and the incidence of acute kidney injury than MDRD-eGFR. **Conclusions:** The risk factors associated with overestimation included female sex, impaired liver function, and decreased muscle mass in males. In particular, eGFR in male patients with sarcopenia should be carefully interpreted. Creatinine-based eGFR was overestimated more often than cystatin C-based eGFR, with overestimation of eGFR closely related to poor prognostic performance.
Key words: Cirrhosis, Muscle mass

INTRODUCTION

Liver cirrhosis (LC) is a worldwide health problem that is associated with various complications and high mortality. Although, in the past four decades, the incidence of hepatitis B continuously decreased and a promising cure for hepatitis C was developed, LC remains a formidable challenge in clinical practice due to the ever-increasing incidences of alcoholic and non-alcoholic fatty liver diseases, autoimmune-related liver disease and drug-induced liver disease.[1-3] It is well known that cirrhosis is often accompanied by decreased renal function, resulting in poor outcomes even in stage I acute kidney injury (AKI).

Creatinine (Cr), the most frequently used parameter for the evaluation of renal function, is a very powerful prognostic biomarker in cirrhotic patients, and an important element of the model for end-stage liver disease (MELD) scoring system.[4] However, renal function estimated by the Cr-based formula is relatively inaccurate considering endogenous synthesis and metabolism. The actual renal function is likely to be overestimated rather than undervalued, especially in patients with liver cirrhosis because of poor nutritional status and reduced muscle mass. Since Cr is produced in liver and stored in muscle following phosphorylation, its serum concentration is inevitably associated with liver function and muscle mass.[5] It is also known to be affected by age, gender, and race, which are reflected in Cr-based formulas. In fact, it has been reported that Cr-based equations (e.g. MDRD-4 equation) overestimate the true renal

71

function by less than 30% to as much as 50%, especially, in patients with poor liver function or low glomerular filtration rate (GFR).[6,7] However, few studies correlated the true GFR with potential markers in large series of cirrhotic patients.[8]

In this study, we investigated the extent of overestimation of 2 common estimated GFR (eGFR) calculations using Cr and cystatin C, compared with measured GFR (mGFR) using 51Cr-EDTA, and identified the impact of low muscle mass on over/underestimation of renal function.

Material and methods

In this study, 100 successive cirrhotic patients underwent abdominal computed tomography (CT) and 51Cr-ethylenediamine tetraacetic acid (EDTA) (as a measure of GFR). Utilizing either creatinine or cystatin C, the eGFR was computed. At the L3 level, muscle mass was calculated using the total skeletal muscle.

Results

There were overall 100 subjects having cirrhosis out of which 89 were males and 11 were females.

Modification of diet in renal disease (MDRD)-eGFR was overestimated in 38% of patients. A multivariate analysis showed that female sex, Child B and C vs. A (aOR 1.12 and 1.45) and skeletal muscle mass (aOR 0.54) were independent risk factors associated with overestimation. Interestingly, the effect of skeletal muscle mass on overestimation varied according to sex. Decreased muscle mass significantly enhanced the risk of overestimation of MDRD-eGFR in male patients, but not in female patients. Cystatin C-based eGFR showed a better correlation with mGFR than MDRD-eGFR; it was also better at predicting overall survival and the incidence of acute kidney injury than MDRD-eGFR.

Table 1: Gender-wise distribution of subjects

Gender	Number of subjects	Percentage
Males	89	89%
Females	11	11%
Total	100	100%

Discussion

Skeletal muscle is vital to mobility, posture, strength and balance as it allows the performance of physical activities of daily living.[9] In addition, it is also a pivotal metabolic and homeostatic organ, via crosstalk with other organs systems.[10] Most importantly, it plays a key role in protein metabolism as a source of amino acids when protein intake is insufficient, thus preserving the protein content of other essential organs.[10,11] However, when muscles undergo chronic catabolism to supply amino acids for other metabolic purposes, a reduction in lean body mass (LBM) is observed. This has potentially serious clinical consequences such as muscle weakness, impaired physical function, increased morbidity and mortality.[12] In fact, as low as 10% loss of LBM is associated with increased risk of death, due to impaired immune response and increased susceptibility to infections, while a 40% reduction is incompatible with life.[13]

In this study it was discovered that decreased muscle mass significantly enhanced the risk of overestimation of MDRD-eGFR in male patients, but not in female patients. Cystatin C-based eGFR showed a better correlation with mGFR than MDRD-eGFR; it was also better at predicting overall survival and the incidence of acute kidney injury than MDRD-eGFR. Modification of diet in renal disease (MDRD)-eGFR was overestimated in 49% of patients. A multivariate analysis showed that female sex, Child B and C vs. A (aOR 1.12 and 1.45) and skeletal muscle mass (aOR 0.54) were independent risk factors associated with overestimation. Groothof, D et al explored effects of 24-h height-indexed creatinine excretion rate (CER index) on GFR estimated with creatinine (eGFRCr), muscle mass-independent cystatin C (eGFRCys), and the combination of creatinine and cystatin C (eGFRCr-Cys) and predicted probabilities of discordant classification given age, sex, and CER index. They included 8076 adults enrolled in the PREVEND study. Discordant classification was defined as not having eGFRCr <60 mL/min per 1.73 m2 when eGFRCys was <60 mL/min/1.73 m2. Baseline effects of age and sex on CER index were quantified with linear models using generalized least squares. Baseline effects of CER index on eGFR were quantified with quantile regression and logistic regression. Effects of annual changes in CER index on trajectories of eGFR were quantified with linear mixed-effects models. Missing observations in covariates were multiply imputed. Mean (SD) CER index was 8.0 (1.7) and 6.1 (1.3) mmol/24 h per meter in male and female participants, respectively (P difference < 0.001). In male participants, baseline CER index increased until 45 years of age followed by a gradual decrease, whereas a gradual decrease across the entire range of age was observed in female participants. For a 70-year-old male participant with low muscle mass (CER index of 2 mmol/24 h per meter), predicted baseline eGFRCr and eGFRCys disagreed by 24.7 mL/min/1.73 m2 (and 30.1 mL/min/1.73 m2 when creatinine was not corrected for race). Percentages (95% CI) of discordant classification in male and female participants aged 60 years and older with low muscle mass were 18.5% (14.8–22.1%) and 15.2% (11.4–18.5%), respectively. For a 70-year-old male participant who lost muscle during follow-up, eGFRCr and eGFRCys disagreed by 1.5, 5.0, 8.5, and 12.0 mL/min/1.73 m2 (and 6.7, 10.7, 13.5, and 15.9 mL/min/1.73 m2 when creatinine was not corrected for race) at baseline, 5 years, 10 years, and 15 years of follow-up, respectively. Low muscle mass may cause considerable overestimation of single measurements of eGFRCr.[14]

Conclusion

The risk factors associated with overestimation included female sex, impaired liver function, and decreased muscle mass in males. In particular, eGFR in male patients with sarcopenia should be carefully interpreted. Creatinine-based eGFR was overestimated more often than cystatin C-based eGFR, with overestimation of eGFR closely related to poor prognostic performance.

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