What is the best alternative to inulin clearance to estimate GFR in patients with decompensated alcoholic cirrhosis?

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Abstract

Background. Accurate evaluation of the glomerular filtration rate (GFR) in patients awaiting liver transplantation is important because they have a greater risk of impaired renal function. A major percentage of these patients have alcoholic cirrhosis, and the accuracy of bedside used GFR estimates have not been specifically evaluated in this group. The aim of this study was to evaluate the validity of the simplified Modification of Diet in Renal Diseases (MDRD) and Cockcroft and Gault (CG) formulas in patients with decompensated alcoholic cirrhosis in comparison to inulin clearance as the reference method.

Methods. GFR estimated by the simplified MDRD and CG formulas were retrospectively compared to the true GFR measured by inulin clearance in a single-centre cohort of 148 patients with decompensated alcoholic cirrhosis.

Results. Mean ± standard deviation of age, body mass index, inulin clearance and MDRD and CG estimates were 54.4 ± 6.9 years, 26.5 ± 4.7 kg/m², 76.9 ± 28.0 mL/min per 1.73 m², 99.4 ± 34.0 mL/min per 1.73 m² and 98.7 ± 32.0 mL/min per 1.73 m², respectively; 70% of the patients had a GFR, measured by inulin clearance, below 90 mL/min per 1.73 m². The difference between estimated GFR and true GFR were 23 ± 23 mL/min per 1.73 m² for MDRD and 22 ± 20 mL/min per 1.73 m² for Cockcroft and Gault.

Conclusions. The simplified MDRD and CG formulas largely overestimated GFR in patients with decompensated alcoholic cirrhosis. Results of such bedside formulas should be interpreted with caution in these patients.

Keywords: alcoholic liver cirrhosis; glomerular filtration rate; plasma creatinine

Introduction

Alcoholic liver cirrhosis is a major cause of morbidity and mortality in western countries. It is responsible for almost 25 000 deaths yearly in the USA [1]. In a recent retrospective study, abusive alcohol consumption was found to be the leading cause of liver transplantation in France, accounting for more than 30% of all liver transplantsations [2]. Several studies have demonstrated that chronic kidney disease (CKD) or renal failure is a frequent co-morbidity occurring in 15% to 50% of patients with severe cirrhosis before liver transplantation [2–6] and influenced negatively the outcome of the patients with liver allograft [2,4–11]. Therefore, there was clearly a need to assess accurately the renal function of patients with severe cirrhosis before transplantation.

Patients with alcoholic cirrhosis have an increased prevalence of diabetes mellitus. For example, Sharma et al. found 27% of diabetic patients in a cohort of 221 North-American cirrhotic patients at the time of liver transplantation [5]. Moreover, Karie-Guigues et al. found a prevalence of 13% for diabetes in a French retrospective cohort of 1508 cirrhotic patients [2]. This increased prevalence led to a potentially increased risk to develop CKD.

Several formulas estimating the glomerular filtration rate (GFR) have been developed for daily clinical practice. Among them, the Cockcroft and Gault (CG) formula and the Modification of Diet in Renal Diseases (MDRD) simplified formula are the most frequently used [12,13]. However, these equations have been determined for a specific population, and their external validity in cirrhotic patients is insufficiently documented [14].

In previous studies evaluating renal function before liver transplantation in adults, GFR was estimated by using plasma creatinine (PCR) alone, creatinine clearance (24-h urine
collection) or formulas (MDRD, CG) [7,9,11,15–17]. However, all of these estimations have a poor accuracy to predict reliably the true GFR [14,18–22]. The reference method for assessing the GFR is the measurement of renal clearances of an ideal marker of glomerular filtration, i.e. a marker that is freely filtered through the glomerulus and neither secreted nor reabsorbed by the tubule (e.g. inulin, iothalamate, EDTA and iohexol). However, these techniques based on exogenous markers are difficult to perform in clinical practice because of their complexity and cost [23,24].

To our knowledge, no study has tested the performance of CG and simplified MDRD formulas specifically in alcoholic patients.

The aim of this study was to evaluate the validity of estimated GFR (eGFR) calculated by both simplified MDRD and CG equations in comparison to the true GFR assessed with the reference method (i.e. inulin clearance) in patients with decompensated alcoholic cirrhosis before liver transplantation.

Materials and methods

Patients

Data from 148 consecutive candidates for liver transplantation with decompensated alcoholic cirrhosis and undergoing GFR measurement by inulin clearance between June 2004 and June 2008 were analysed in a single-centre retrospective cohort. All patients had severe cirrhosis (class C of the Child–Pugh classification) and were free of alcohol intake for at least 6 months.

Methods

GFR was measured by inulin clearance (polyfructosan infusion, Inutest, Fresenius Kabi, Graz, Austria), as previously described [25]. Briefly, a standard technique was used in fasting patients by a trained staff with a continuous infusion of polyfructosan (0.33 mg/kg per minute, diluted in mannitol or isotonic saline) after a load dose of polyfructosan (30 mg/kg in 10 min). The continuous infusion of polyfructosan consists of an initial equilibration period of 45 min following by at least three control periods of 30 to 45 min. The total duration of polyfructosan was 120 to 150 min. Water diuresis was induced by oral absorption of 5 mL/kg of water followed by 3 mL/kg every 30 min combined with an intravenous infusion of 0.9% sodium chloride or mannitol. This enabled the patients to spontaneously empty their bladder every 30 min. Three to four urine samples were collected, and a blood sample was drawn midway through each collection period. The clearance values were obtained from the mean values of the three to four clearance periods. Measurements of polyfructosan were performed with an enzymatic method using inulinase and gluco-oxidase.

Normal body mass index (BMI) was defined as a BMI between 18 and 24.9 kg/m², overweight patients as patients with a BMI between 25 and 30 kg/m² and obese patients as patients with a BMI above 30 kg/m². Arterial hypertension was defined as systolic blood pressure higher than 140 mmHg and/or diastolic blood pressure higher than 90 mmHg.

The local reference value for inulin clearance was (mean ± SD) 117 ± 22 mL/min per 1.73 m² and has been determined in 99 healthy renal donors (males 47%, age (mean ± SD) 37 ± 10 years).

Plasma creatinine was measured with a colorimetric compensated Jaffé kinetic, Modular, Roche Diagnostics, Meylan, France. Albuminuria was measured with a nephelemetric technique (Automat BN2, Dade Behring, Siemens SAS, St Denis, France). Albuminuria was considered significant when the albuminuria to creatininuria ratio was higher than 2 mg/mmol.

The CG and simplified MDRD formulas were used to calculate eGFRs, with the following equations: CG = (K* [140 – age (years) * weight (kg)] / [PCr (µmol/L)], with K = 1.23 for men and 1.04 for women [12] and MDRD = 186 * [PCr (mg/dL)]^{1.154} * (age (years)_{0.203}) * (1.212 if black people) * (0.742 if woman) [23]. The conversion factor for PCr from µmol/L to mg/dL was 88.4; eGFR calculated by CG equation was normalized to 1.73 m² of body surface area (BSA). BSA was calculated for each patient using Dubois formula: BSA = 0.007184 * (height)_{0.725} * (weight)_{0.425} (kg) [26].

The Model for End-Stage Liver Disease (MELD) score was calculated using the following equation: MELD = 10 * [0.957 * Ln(PCr (mg/dL))] + (0.378 * Ln(total bilirubin (mg/dL))] + (1.12 * Ln (INR)) + 0.643] [27]. When laboratory values were <1 mg/dL, they were rounded up to 1.

International normalized ratio (INR), total bilirubin, prothrombin time, factor V and plasmatic albumin were extracted from the database software of our institution.

Statistics

Statistical analysis was performed using the Statview software (Abacus Concepts, Berkeley, CA, USA). All data are given as mean ± standard deviation (SD). To compare eGFR and GFR, the following methods were used: calculation of Pearson correlation coefficient, absolute bias (average difference between eGFR and measured GFR), graphic representation with Bland and Altman method (allowing to show the scattering of the absolute bias and the extreme limits of agreement) and calculation of accuracies 10%, 30% and 50% [28]. For the comparison of two means, we used two-tailed unpaired Student t-test, assuming that the data were distributed following a normal law. Differences were considered significant if p was below 0.05.

Results

Patients

The characteristics of the 148 patients (males 77%) are summarized in Table 1. There were some missing data: INR and total bilirubin were available for 144 patients, prothrombin time (PT) for 141 patients, albumin for 140 patients and factor V for 130 patients. Finally, the MELD score has been calculated for 143 patients.

Sixty per cent of the patients had an elevated body mass index (BMI) with a prevalence of obesity of 22%. Only 1.4% of the patients had BMI below 18 kg/m². Ten patients (6.75%) had elevated blood pressure.

Mean GFR, measured by inulin clearance, was 76.9 ± 28 mL/min per 1.73 m² and was decreased by 34% in comparison to the healthy control population. Of the patients, 26.3% had measured GFR between 30 and 59.9 mL/min per 1.73 m², 39.2% had measured GFR between 60 and 89.9 mL/min per 1.73 m², 30.4% had measured GFR above or equal to 90 mL/min per 1.73 m² and finally, only 4.1% had measured GFR below 30 mL/min per 1.73 m².

Table 2 shows the values of GFR, Pcr, MELD score, serum total bilirubin and INR for men and women. GFR was lower in women than in men; however, PCr was higher in men than in women. Moreover, MELD score was higher in women than in men.

An increased PCr (defined arbitrarily as a PCr higher than 106 µmol/L in men and higher than 80 µmol/L in women) was observed in 5% of all patients with CKD stage 2 and 51% of all patients with CKD stage 3 or higher.

In men, PCr was increased in 5% of patients with CKD stage 2 and 38% of patients with CKD stage 3 or higher. In women, an increased PCr was observed in 7% of patients with CKD stage 2 and 51% of all patients with CKD stage 3 or higher. In the total cohort, the sensitivity of an increased PCr to detect stage 3 or higher CKD was 51%,
with a specificity of 97%. Albuminuria was observed in 15% of the patients.

**Comparison between eGFR and GFR**

Mean eGFR estimated by CG was 98.7 ± 32.0 mL/min per 1.73 m². Correlation between GFR estimated by CG and measured GFR is shown in Figure 1. The Pearson coefficient between eGFR and measured GFR was $r = 0.784$ ($P < 0.001$). The absolute bias was 22 ± 20 mL/min per 1.73 m² (~25 to 95), and the comparison between eGFR and GFR found significant higher values with CG ($P < 0.05$). The representation with the Bland and Altman plot highlighted a strong overestimation of the true GFR by the CG formula, with marked scattering of values (Figure 2). Accuracies 10%, 30% and 50% were 19%, 55% and 71%, respectively, for the CG formula.

Mean eGFR estimated by the simplified MDRD formula was 99.4 ± 34.0 mL/min per 1.73 m². Correlation between GFR estimated by MDRD and measured GFR is shown in Figure 3. The Pearson coefficient between eGFR and measured GFR was $r = 0.751$ ($P < 0.001$), and the absolute bias was 23 ± 23 mL/min per 1.73 m² (~16 to 87); the mean eGFR estimated by the MDRD formula was significantly higher than the true GFR ($P < 0.05$). The Bland and Altman representation showed a wide dispersion of values when comparing the values obtained with MDRD formula to the true GFR (Figure 4). Accuracies 10%, 30% and 50% were 22%, 57% and 69%, respectively, for the MDRD formula.

**Discussion**

The present study demonstrates the important overestimation of GFR when using standard bedside eGFR equations (CG and simplified MDRD) in patients with decompen-sated alcoholic cirrhosis comparatively to GFR measured by the reference method (i.e. inulin clearance).

Table 1. Characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>54.4 ± 6.9</td>
<td>34.2–68</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76 ± 16</td>
<td>30–131</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.85 ± 0.2</td>
<td>1.14–2.42</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.5 ± 4.7</td>
<td>13.8–42.3</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>112 ± 17</td>
<td>82–167</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>64 ± 10</td>
<td>39–94</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>66 ± 13</td>
<td>40–112</td>
</tr>
<tr>
<td>MELD Score</td>
<td>16.3 ± 5.3</td>
<td>6.4–30.2</td>
</tr>
<tr>
<td>INR</td>
<td>1.7 ± 0.5</td>
<td>1–3.5</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>3.7 ± 4.0</td>
<td>0.5–24.9</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>32 ± 6</td>
<td>20–46</td>
</tr>
<tr>
<td>Prothrombin time (%)</td>
<td>52 ± 15</td>
<td>23–97</td>
</tr>
<tr>
<td>Factor V (%)</td>
<td>57 ± 25</td>
<td>15–161</td>
</tr>
<tr>
<td>Plasma creatinine (µmol/L)</td>
<td>79 ± 28</td>
<td>33–194</td>
</tr>
<tr>
<td>Plasma area (mm²/L)</td>
<td>6.3 ± 4.0</td>
<td>2.1–34.4</td>
</tr>
<tr>
<td>Inulin clearance (mL/min per 1.73 m²)</td>
<td>99.4 ± 34.0</td>
<td>30–194</td>
</tr>
<tr>
<td>eGFR by simplified MDRD formula (mL/min per 1.73 m²)</td>
<td>99.4 ± 34.0</td>
<td>30–194</td>
</tr>
<tr>
<td>eGFR by Cockcroft and Gault formula (mL/min per 1.73 m²)</td>
<td>98.7 ± 32.0</td>
<td>35–198</td>
</tr>
</tbody>
</table>

**Performance of eGFR according to GFR levels**

For GFR lower than 60 mL/min per 1.73 m² ($n = 45$), mean absolute bias was 19 ± 25 for MDRD and 21 ± 19 mL/min per 1.73 m² for CG. Accuracies 10% and 30% were 11.1% and 40%, respectively, for MDRD and 8.9% and 33.3%, respectively, for CG. For GFR between 60 and 90 mL/min per 1.73 m² ($n = 58$), mean absolute bias was 25 ± 18 for CG and 27 ± 19 mL/min per 1.73 m² for MDRD, whereas accuracies 10% and 30% were 22.4% and 58.6%, respectively, for MDRD and 15.5% and 62.1%, respectively, for CG. Finally, for GFR higher than 90 mL/min per 1.73 m² ($n = 45$), mean absolute bias was 20 ± 25 for CG and 18 ± 23 mL/min per 1.73 m² for MDRD with accuracies 10% and 30% for MDRD at 31.1% and 68.9%, respectively, and at 33.3% and 68.9%, respectively, for CG.

**Table 2. Values of INR, serum total bilirubin, Model for End-Stage Liver Disease (MELD) score, plasma creatinine (PCr) and glomerular filtration rate (GFR) in men, women and in the whole population**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women ($n = 31$)</th>
<th>Men ($n = 112$)</th>
<th>All patients ($n = 143$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td>1.86 ± 0.5</td>
<td>1.66 ± 0.5</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
<td>Total bilirubin (µmol/L)</td>
<td>88.5 ± 89.0</td>
<td>56 ± 55.0</td>
<td>63.2 ± 65.0</td>
</tr>
<tr>
<td>MELD</td>
<td>18.9 ± 5.0</td>
<td>15.7 ± 5.0</td>
<td>16.3 ± 5.0</td>
</tr>
<tr>
<td>PCr (µmol/L)</td>
<td>74.7 ± 32.0</td>
<td>80.7 ± 27.0</td>
<td>79.3 ± 28.0</td>
</tr>
<tr>
<td>GFR (mL/min per 1.73 m²)</td>
<td>73.9 ± 26.0</td>
<td>77.8 ± 28.0</td>
<td>77 ± 28.0</td>
</tr>
</tbody>
</table>
have lowered blood pressure. We can also note that a large part of our patient population are overweight, probably because of increased extracellular volume.

In patients presenting with decompensated cirrhosis, ascites and oedema can be responsible for a significant overestimation of the patient’s ‘dry’ weight [13]. This can explain the overestimation of GFR described with the CG formula in these patients [19]. Moreover, their lean body mass is often decreased by malnutrition, resulting in an important inaccuracy of eGFR using the body weight in the formula (e.g. the CG one) [14]. In this setting, the MDRD formula (that does not include body weight) or the use of another filtration marker like cystatin C (that does not depend on muscle mass [31]) theoretically allows a more accurate evaluation of GFR because it does not include body weight in calculation.

Simplified MDRD equation is widely used in daily clinical practice. Its accuracy has been studied in normo-renal and in CKD patients [23], but to our knowledge, it has not yet been evaluated in patients with decompensated alcoholic cirrhosis.

Briefly, published studies performed in non-cirrhotic patients demonstrate that the MDRD formula provides a correct evaluation of the real GFR principally when GFR is below 60 mL/min per 1.73 m² [32]. Moreover, several studies have shown that the MDRD formula is more accurate than the CG one in patients with decreased GFR, especially in overweight and/or older patients [33–35]. However, studies in patients with normal or slightly decreased renal function find that the MDRD equation significantly underestimates true GFR [23]. Thus, in this setting, our results seem rather different from those obtained in healthy controls and non-cirrhotic CKD patients since we describe an important overestimation of GFR with the MDRD equation in patients with decompensated alcoholic cirrhosis. The bias observed for the MDRD formula can be explained by the specific features of our population in comparison to the patients included in the first MDRD study [13]. Indeed, the original population had probably a higher creatinine production rate.

There is also an important overestimation of GFR (22 ± 20 mL/min per 1.73 m²) with the CG formula. As suggested previously, this overestimation can be explained at least partly by an important proportion of overweight patients (BMI above 25), these later presenting with an increased extracellular volume [36].

Mean absolute bias were not statistically different between the two formulas in the three levels of GFR studied; however, our results show that the MDRD formula may have better accuracy when GFR is below 90 mL/min per
For GFR above 90 mL/min per 1.73 m². Moreover, our findings suggest that the two formulas had low accuracies for lower GFR.

To our knowledge, the accuracy of the MDRD formula has been evaluated in cirrhotic patients by only a few previous studies [29,30,37–39]. However, several limitations can be discussed in these reports: first, the population was heterogeneous with regard to the aetiology and the severity of cirrhosis. Second, these studies evaluated the MDRD formula in comparison to isotopic measurement of GFR that have a limited value in patients with fluid splanchnic sequestration because of an extra-renal clearance of the tracer [40]. Third, almost all of these studies included a relatively low number of patients [29,30,37,39]. By contrast, the study by Gonwa et al. was performed in 1,447 patients undergoing 125I-iodalumate clearance [37].

In this later study, the authors described an underestimation of eGFR with both the CG (−9 mL/min per 1.73 m²) and the simplified MDRD (−7 mL/min per 1.73 m²) [37]. These results seem conflicting when compared to the other studies and to ours [29,30]. These discrepancies could be explained by several differences between the studies (e.g. age, degree of renal failure, reference method of GFR measurement, aetiology and severity of cirrhosis) that could have influenced the final results [33–35]. The different aetiologies of cirrhosis may have played a role because patients with alcoholic cirrhosis have modifications in body composition [41], with severe protein-energy malnutrition [42] that could involve lower PCr comparatively to patients with cirrhosis of others aetiologies. The degree of malnutrition also seems positively correlated to the severity of cirrhosis, leading possibly to lower PCr in more severe cirrhosis [42]. In the study by Gonwa et al., when patients are split with a GFR cutoff value of 40 mL/min per 1.73 m², patients with a GFR below 40 mL/min per 1.73 m² exhibit an average overestimation of GFR of 24 and 22 mL/min per 1.73 m² with the CG and MDRD formulas, respectively [37]. In this group, these results are close to ours probably because a more important rate of patients with uncompensated alcoholic cirrhosis had a GFR below 40 mL/min per 1.73 m². Contrary to the results of the study by Gonwa et al., when we split our population for GFR cutoff value of 40 mL/min per 1.73 m², mean bias was slightly decreased in patients with lower GFR, for CG (18.9 versus 22) and for MDRD (17.9 versus 22.9).

However, the correlation coefficient between eGFR and measured GFR were decreased when GFR was below 40, with, for CG formula, $r^2 = 0.27$ (versus 0.53 when GFR was above 40 mL/min) and for MDRD formula, $r^2 = 0.04$ (versus 0.48). The discrepancies observed between our findings and those of Gonwa et al. concerning the change of mean absolute bias between the two subgroups of patients could be related to the several differences previously described between the population of the two studies. In addition, the interpretation of the results of our population subgroup with GFR below 40 mL/min was limited by the low number of patients ($n = 11$).

Other studies found an overestimation of eGFR with the MDRD formula. The study by Skluzacek et al. also showed a large overestimation of 18.7 mL/min per 1.73 m², while the average GFR was lower (58 mL/min per 1.73 m²) [29]. However, except for a comparable mean age at inclusion, this study presented several differences in comparison to ours: a small number of patients ($n = 19$), a wide heterogeneity of both aetiologies and clinical severity of cirrhosis and the use of isotopic clearance as the reference method for GFR measurement. In the study by Macaulay et al., a smaller bias was found for the MDRD formula, with an overestimation of 3 mL/min per 1.73 m²; however, the mean GFR (83 mL/min per 1.73 m²) was higher, the percentage of male patients was lower (60%), and the reference method for GFR assessment was different (isotopic clearance) [30]. Moreover, cirrhosis aetiologies were various, and alcoholic cirrhosis accounted for only 30% of the aetiologies. Chalongtias et al. found results similar to ours in 38 cirrhotic patients with isotopic measurement of GFR. Mean GFR was 85.4 mL/min per 1.73 m², mean absolute bias with simplified MDRD formula was +14.7 mL/min per 1.73 m², and correlation coefficient was $r = 0.64$ [38].

Finally, Poge et al. tested the performance of MDRD in 44 patients in comparison of GFR measured by Inulin clearance. Mean GFR was markedly low at 28.3 mL/min per 1.73 m², and the authors found an important overestimation of eGFR determined by CG formula and simplified MDRD formula (+51.7 and +43.8 mL/min per 1.73 m², respectively). The correlation coefficients and the accuracies 10% and 30% were low for the two formulas [39]. In the later study, performances of the formulas using cystatin C were better.

Another study has recently tested the performance of cystatin C based formulas (Xirochakis et al. Hepatology 2008;48 suppl 4:A1724) in comparison to the MDRD formula and isotopic measurement of GFR. The authors found that Hoek formula was the more accurate formula, but the agreement with measured GFR was moderate for all formulas. These data showed that, whereas cystatin C is a better marker of renal function than PCr in cirrhotic patients [31,43,44], the cystatin-C-based formulas have accuracies close to those of creatinine-based formulas in this group of patients.

An important strength of our study is the use of the reference standard for GFR measurement (i.e. inulin clearance) [23]. Indeed, inulin is the ideal glomerular filtration marker since it is freely filtered without being secreted nor reabsorbed [25,45]. It is a safe, accurate and reproducible method to measure GFR, but it is an expensive technique performed only in specialized centres [46].

To our knowledge, before this study, the only one evaluating the accuracy of PCr in a homogeneous cohort of alcoholic cirrhotic patients was the study published by Papadakis et al. [18]. This is relevant because abusive alcohol consumption is the leading cause of cirrhosis [1] and because the cirrhotic population is at increased risk to develop or to worsen CKD before and after liver transplantation [3,4,6,9,47].

Several studies have demonstrated that PCr was not an effective marker to accurately detect an impaired renal function in a general population. This is particularly true in patients with cirrhosis: indeed, several studies found that a high proportion of cirrhotic patients had normal PCr, whereas GFR was already impaired [18–20,48]. Therefore,
the risk to not detect renal dysfunction when using PCr alone or formulas based on PCr in patients with alcoholic cirrhosis seems important because of ‘falsely low’ PCr. This hypothesis was reinforced by our clinically relevant results: in men, an increased PCr was only observed in 5% of patients with stage 2 CKD and 38% of patients with stage 3 or higher CKD. In women, an increased PCr was more frequently observed in case of stage 2 CKD and stage 3 or higher CKD (61% and 97%, respectively). These findings are consistent with previous studies showing the inability of PCr in cirrhotic patients to detect the presence of CKD [18–20]. These results could be due to the arbitrarily selected cutoff values of plasma creatinine in our institution that could be inadequate, especially in cirrhotic patients. Moreover, that underlines the potential interest of the daily clinical use of cystatin C as a marker to detect CKD in the cirrhotic patients [31,43,44].

The systematic use of PCr as the reflection of renal function in cirrhotic patients has an important limit that should be underlined: in the era of MELD score for liver allograft attribution, the subgroups of patients with basically lower PCr (e.g., women and older patients) can be disadvantaged. Indeed, Cholongitas et al. had shown that despite lower PCr, cirrhotic women had lower renal function [38]. We demonstrated similar findings in our female patients. Consequently, their access to liver transplantation was negatively impacted because of the use of PCr in the determination of the MELD score, as previously described by Moylan et al. [49]. Moreover, because a low PCr can also indirectly reflect a more severe liver dysfunction as well as the presence of a more severe protein denutrition, the more severely ill patients could also have less easy access to liver transplantation.

In conclusion, the calculation of eGFR with both simplified MDRD and CG equations leads to an important overestimation of GFR in patients presenting severe alcoholic cirrhosis, and results of such bedside formulas should be interpreted with caution in these patients. Thus, surrogate markers of renal function, like cystatin C [31,43,44], should be further evaluated in these patients.

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Conflict of Interest statement. None to declare.

References

Tubulointerstitial nephritis and renal tubular acidosis of different types are rare but important complications of primary biliary cirrhosis

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Abstract

Background. A very few cases of biopsy-proven tubulointerstitial nephritis (TIN) in patients with primary biliary cirrhosis (PBC) have been reported. Although the clinical importance of this association has been suggested, information on its clinicopathological features and prognosis is limited.

Methods. We reviewed 5955 renal biopsies processed at our department, and identified four patients with TIN associated with asymptomatic PBC. We evaluated clinicopathological features and outcomes in these patients, and reviewed the previously reported cases of TIN associated with PBC.

Results. Our four patients were female. The patients’ age at the time of renal biopsy ranged from 36 to 77. Three patients had been treated with ursodeoxycholic acid. All patients had urinary abnormalities such as proteinuria and elevated levels of urinary β2-microglobulin, and three patients had renal insufficiency. All patients had distal renal failure.

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