Comparison of performance of improved serum estimators of GFR to $^{99m}$Tc-DTPA GFR methods in patients with hepatic cirrhosis

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Running title: GFR measurements in patients with cirrhosis
Abstract

Rationale: GFR measurements are critical in patients with hepatic cirrhosis, but potentially erroneous when based on serum creatinine. New equations for estimated GFR (eGFR) have shown variable performance in cirrhotics, possibly due to inaccuracies in reference methods for measured GFR (mGFR). The primary objective was to compare the performance of 4 improved eGFR equations to a 1-compartment, 2-sample plasma slope intercept $^{99m}$Tc-DTPA mGFR method to determine whether any of the eGFR calculations could replace plasma $^{99m}$Tc-DTPA mGFR in patients with cirrhosis. The secondary objective was to test the hypothesis that mGFR utilizing voluntary voided urine collections introduce error compared to plasma-only methods.

Methods: 54 patients with hepatic cirrhosis underwent mGFR determinations from 2 plasma samples at 1 and 3h following intravenous administration of 185 MBq $^{99m}$Tc-DTPA. GFR was also generated by an UV/P calculation derived from blood and urine samples. These mGFR’s were compared to the eGFR’s generated by 4 estimating equations: MDRD, CKD-EPI (SCr), CKD-EPI (CysC) and CKD-EPI (CysC+Cr). eGFR’s were compared to mGFR’s by Pearson correlation, precision, bias, percent bias, and accuracy (eGFR’s varying by < 10% [p10], < 20% [p20] or < 30% [p30] from the corresponding mGFR).

Results: All eGFR’s showed poorer performance when the UV/P $^{99m}$Tc-DTPA mGFR was used as the reference, than when plasma $^{99m}$Tc-DTPA mGFR was employed.
When compared to the plasma $^{99m}$Tc-DTPA mGFR method, the performance of all eGFR equations was superior to most published reports. There was a moderately good positive correlation between eGFR’s and mGFR’s. When compared to plasma $^{99m}$Tc-DTPA mGFR, precision of eGFR’s was in the range of 14-20 ml/min and showed a negligible bias. Compared to the plasma $^{99m}$Tc-DTPA mGFR, CKD-EPI (CysC+SCr) showed the best overall performance and accuracy, at 85.19% (p30), 75.93% (p20) and 42.59% (p10).

**Conclusions:** Estimating equations for measuring eGFR performed better than in most published reports, attributable to use of plasma $^{99m}$Tc-DTPA mGFR method as a reference. CKD-EPI (CysC+SCr) eGFR showed best overall performance. However, more discriminating methods may be required when very accurate GFR measurements are necessary. mGFR measurements using urine collections may introduce error compared to plasma only methods.

**Key words:** $^{99m}$Tc-DTPA, glomerular filtration rate, MDRD, CKD-EPI, cirrhosis, creatinine, Cr, GFR
**Introduction**

Glomerular filtration rate (GFR) is an important parameter of renal function in patients with acute and chronic kidney disease. Patients with hepatic cirrhosis are susceptible to reversible as well as chronic kidney dysfunction due to altered hemodynamics, volume shifts and comorbidities (1-3). Accurate measurements of GFR are critical in these patients and affect both management and outcome. Many drugs with kidney clearance and liver metabolism or clearance require adjustments in the face of renal and hepatic insufficiency. Renal insufficiency portends a poor prognosis in cirrhosis (4,5). Renal function, typically measured by serum creatinine, also plays an important component in the Model for End-Stage Liver Disease score, which is utilized in prioritizing patients being considered for liver transplantation.

The most common clinical estimates of GFR are based on serum creatinine, often by the Cockcroft-Gault formula (6), and on 24h urinary creatinine clearance. It is widely recognized that the use of these creatinine-based estimates may significantly overestimate GFR in patients with hepatic cirrhosis. This is due to decreased hepatic production of creatinine, decreased muscle mass and malnutrition. These factors often coexist in patients with cirrhosis. Serum cystatin C has been proposed as a novel biomarker of renal function. It is found in nearly all tissues and body fluids, undergoes clearance by glomerular filtration and its levels are unaffected by race, age, muscle mass or liver disease (7). In recent years, improved equations have been developed for estimating GFR. These include MDRD (from the Modified Diet in Renal Disease Study)
and 3 formulas developed by the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) that utilize both serum creatinine (SCr) and cystatin C (CysC). These include CKD-EPI (SCr), CKD-EPI (CysC) and CKD-EPI (CysC+SCr) (8,9). These improved equations for determining estimated GFR (eGFR) have gained popularity and acceptance in the general population (10). In a limited number of studies in patients with cirrhosis, the cystatin C equations tend to show better results than methods based solely on serum creatinine. However, the published performance of the equations is variable, creating uncertainty as to whether these equations may obviate the need for more accurate methods for measuring GFR in cirrhotics (11-15).

The most accurate test for determining GFR in the United States has traditionally been plasma and/or urinary clearance of inulin. This method represents a significant technical challenge to routine clinical use. 99mTc-diethylenetriaminepentaacetic acid (DTPA) is a renal imaging agent that is excreted entirely by glomerular filtration and has been used clinically to measure GFR both by camera-based and plasma clearance methods. Camera based methods are hampered by attenuation factors, leading to general a preference for plasma clearance methods. Methods for measuring GFR have been developed using a single intravenous injection of 99mTc-DTPA, followed either by single and multiple plasma samples (16,17). The single injection, 1-compartment, 2-sample slope-intercept clearance method is widely utilized. A correction factor, such as that described by Bröchner-Mortensen, is often applied to recover the early compartment area under the curve (AUC) (16,18,19). The plasma 99mTc-DTPA clearance method
requires two venous access lines, several hours to completion, and careful attention to laboratory technique. Nonetheless, it is easier to implement than inulin clearance. In many centers throughout the United States and Europe, plasma $^{99m}$Tc-DTPA clearance has become a commonly employed method for GFR determinations when accurate measurements are required.

A number of publications have addressed the value of improved prediction equations for estimating GFR in patients with hepatic cirrhosis (11-15,20 review). However, these reports have compared to performance of the estimated GFR (eGFR) equations to very disparate reference methods for measured GFR (mGFR). None of these studies utilized the 1-compartment, 2-sample $^{99m}$Tc-DTPA plasma clearance method as a reference. The performance of the estimating equations was quite variable in many of these studies and, in most cases, less than optimal. Technical problems with the reference mGFR methods could compromise assessments of the value of the improved estimating equations for eGFR. This is particularly true when single injection GFR determinations involve timed, voluntary urine collections (21). The purpose of this study was to compare the performance of the MDRD, CKD-EPI (Cr), CKD-EPI (CysC) and CKD-EPI (CysC+Cr) estimating equations to that of the 2-sample plasma $^{99m}$Tc-DTPA clearance method for mGFR to determine whether any of the eGFR equations perform sufficiently well as to replace plasma $^{99m}$Tc-DTPA methods in patients with hepatic cirrhosis. A secondary objective was to test the hypothesis that performance of
the eGFR equations will be less favorable when compared to mGFR derived from a conventional methodology that incorporates voluntary timed voiding urine collections.

**Materials and Methods**

**Subjects:**

54 adult patients with hepatic cirrhosis were enrolled under a research protocol approved by the Investigational Review Board (IRB) of the University of Utah, Salt Lake City, UT and were able to complete all portions of the study. Of these, 17 were female and 37 were male, all Caucasian. The mean age was 57 years (range 37-72).

**Measured (reference) GFR methods:**

The reference, or measured GFR (mGFR) was determined by two separate methods following a single injection of 5.0 mCi (185 MBq) $^{99m}$Tc-DTPA. The plasma $^{99m}$Tc-DTPA method employed 2 plasma samples obtained at 1 and 3 hours following the intravenous administration of $^{99m}$Tc-DTPA (16, 17). Each sample was ultrafiltered to remove plasma proteins by a described method (21). The single-injection, two-sample plasma $^{99m}$Tc-DTPA mGFR is a monoexponential slope-intercept method that neglects the early (fast) exponential phase of what is, in reality, a biexponential clearance curve (16,18). To correct for this, the final GFR was corrected by the Bröchner-Mortensen quadratic formula, which is applicable to both adults and children (16,18,20). For this method, the Haycock method was used for estimating body surface area (BSA) from height and weight (22). However, the final plasma $^{99m}$Tc-DTPA mGFR was reported as gross GFR (ml/min, not BSA corrected).
As described by Vivier et al, mGFR was also measured by a method that utilizes both urine and plasma samples (UV/P method) (23). Following injection of $^{99m}$Tc-DTPA (the same dose as above) and observance of a 1-hour equilibrium period, two 90-minute voluntary voided urine collections were obtained at 150 and 240 min post injection. Blood samples were collected 60, 150, and 240 min after the injection. Urinary clearance was computed as follows: mGFR = $\frac{U}{P}$, where $U$ is the cpm/ml of urine sample, $V$ is the urine flow rate in ml/min, and $P$ is the log average of cpm in serum samples bracketing each urine collection. UV/P mGFR was expressed as gross GFR (ml/min, not BSA corrected).

**Estimated GFR equations:**

Measured GFR generated by both DTPA methods was compared to the estimated GFR (eGFR) values generated by 4 different prediction formulas recommended by the National Kidney Foundation that utilize serum creatinine and/or cystatin C (8,9). These include MDRD (from the Modified Diet in Renal Disease Study), which was calculated using 6 variables (serum creatinine, age, race, gender, albumin, and urea nitrogen) and 3 formulas developed by the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) including CKD-EPI (SCr), CKD-EPI (CysC) and CKD-EPI (CysC+SCr). Blood tests for the eGFR prediction formulas were obtained on the same day as the mGFR procedures were performed. The eGFR values were expressed as gross GFR (ml/min, not BSA corrected).

**Statistical analysis**
The parameters for assessment of the performance of an eGFR test in comparison to mGFR were based on Kidney Disease: Improving Global Outcomes (KDIGO) and National Kidney Foundation Kidney Disease Outcome Quality Initiative K/DOQI practice guidelines \((10,24)\). Pearson correlation was utilized to generate the correlation coefficient \((r\) statistic\) between mGFR and eGFR values. Precision of eGFR tests was defined as the root mean square error between the eGFR and mGFR values as determined by linear regression. Bias (mean mGFR-eGFR) and percent bias (mean of absolute value of \([mGFR-eGFR]/[mGFR]\)) were determined by the Altman Bland agreement test. Accuracy was measured as the percent of eGFR’s varying by < 10\% (p10), < 20\% (p20) or < 30\% (p30) from the corresponding mGFR value.

**Results**

The descriptive statistics (mean, standard deviation, range) for the GFR values derived from the two mGFR measurements (plasma and UV/P \(^{99}\)Tc-DTPA methods) as well as from the eGFR’s derived from the 4 estimating equations are shown in Table 1. Results for performance of the estimating equations in comparison to the two mGFR methods are summarized in Table 2. Plots of mGFR vs. eGFR values are shown in Figures 1 and 2.

**Comparison of plasma \(^{99}\)Tc-DTPA mGFR with eGFR’s**

The mGFR and each of the eGFR measurements was first confirmed to assume a roughly normal distribution, based on a frequency plot with a normal histogram overlay. There was a moderately strong positive correlation between each of the eGFR and the
plasma $^{99m}$Tc-DTPA mGFR values, but strongest for CKD-EPI (CysC+SCr), at +0.79 (95% CI 0.66 to 0.87). When compared to the $^{99m}$Tc-DTPA mGFR, the precision of eGFR-estimating formulas ranged from 14.18 ml/min (CKD-EPI [CysC+SCr]) to 19.59 ml/min (CKD-EPI [CysC]). Precision was most favorable for CKD-EPI (CysC+SCr). The bias was negligible (< -2.69 to 1.54 ml/min) for the eGFR values when compared to $^{99m}$Tc-DTPA mGFR. The percent bias was least for MDRD (2.53%). Accuracy was measured at three levels, as the percent of eGFR values that differ by <30% (p30), <20% (p20) or <10% (p10) of the corresponding mGFR values. The CKD-EPI (CysC+Cr) showed the best overall accuracy, at 85.19% (p30), 75.93% (p20) and 42.59% (p10), respectively. MDRD eGFR showed slightly higher accuracy than CKD-EPI (CysC+SCr), at p30 (88.89%), but slightly lower accuracy at p20 (68.52%) and p10 (35.19%). Accuracy was lower for both CKD-EPI (SCr), at 83.33% (p30) and CKD-EPI (CysC), at 77.78% (p30).

**Comparison to UV/P $^{99m}$Tc-DTPA mGFR with eGFR**

For each of the estimating equations, performance was less favorable when the UV/P $^{99m}$Tc-DTPA mGFR was used as the reference method, than when the plasma $^{99m}$Tc-DTPA mGFR was used (Table 1). When compared to the UV/P $^{99m}$Tc-DTPA mGFR method, precision of the eGFR measurements ranged from 16.45 to 25.55 ml/min. The eGFR equations gave higher GFR values than the UV/P $^{99m}$Tc-DTPA, with a bias ranging from -6.23 (MDRD) to -10.46 (CKD-EPI SCr), Accuracy was also considerably poorer when the UV/P 99mTc-DTPA mGFR method was used as a
reference than when the plasma $^{99m}$Tc-DTPA mGFR was used. For the least
discriminating measurement (p30), eGFR accuracies ranged from 55.56% (for CKD-EPI
[SCr]) to 61.11% (for CKD-EPI [CysC+SCr]) when compared to the UV/P as a reference
method.

Discussion

Patients with hepatic cirrhosis present a particular challenge in accurately
measuring GFR. Renal function is often impaired in this population due to a combination
of factors, including hypovolemia caused by hypoalbuminemia and large volume ascites,
renal ischemia caused by bleeding varices, drug toxicity and hepatorenal syndrome (1-
3). In this population, factors other than renal function can falsely lower the serum
creatinine. These factors include impaired production of creatinine by the liver, reduced
muscle mass and malnutrition. This results in an overestimation of glomerular filtration
with methods that use creatinine alone. Accurate measurements of renal function are
particularly critical in patients with hepatic cirrhosis. First, renal functional has substantial
prognostic significance in these patients (4,5) with a 7-fold increase in mortality in
cirrhotic patients that have reduced renal function (25). Pharmacokinetics can be altered
both by hepatic and renal disease. Adjustments in dosing of medications require an
accurate knowledge of the magnitude of renal dysfunction. The Model of End Stage Liver
Disease score is an important determinant in prioritizing patients for liver transplantation
but has been criticized in that it utilizes serum creatinine. Improved and more accurate
methods to measure GFR in patients with hepatic cirrhosis would greatly facilitate their
medical management and may provide a more informed methodology for the allocation of liver transplants.

It is recognized that improved estimating equations for GFR offer significant theoretical advantages over serum creatinine or urinary creatinine clearance estimators (10). These include MDRD and CKD-EPI equations that utilize both serum creatinine and cystatin C. However, whether the performance of these improved estimating formulas are sufficiently accurate in patients with cirrhosis as to obviate the necessity for more accurate but laborious methods for measuring GFR remains debatable. In accurately evaluating the performance of the estimating equations it is critical that the reference method utilized for mGFR be scrupulously accurate. Single injection GFR methods that utilize voluntary timed voided urine collections are potentially fraught with inaccuracy unless exceptional steps are taken to insure complete emptying of the bladder. Patients at risk for, or with a history of urinary retention may require bladder catheterization. Ultrasound conducted after each episode of voiding can insure complete emptying of the bladder. However, these maneuvers are rarely utilized and technical details regarding assurances of bladder emptying are seldom discussed in the published reports utilizing reference GFR methods.

In the current report, we tested and confirmed the hypothesis that inaccuracies are introduced by the addition of voluntary timed voiding urine collection (without ultrasound or bladder catheterization) as a component of a single injection $^{99m}$Tc-DTPA mGFR method. The performance of the eGFR equations was considerably poorer when
UV/P $^{99m}$Tc-DTPA method was used as a reference for mGFR than when the plasma $^{99m}$Tc-DTPA method was used. Because the eGFR measurements were the same and plasma samples similar for both sets of comparisons, the source of error was likely the urine collections. We therefore conclude that if scrupulous urine collection methods cannot be employed, then plasma-only methods for measuring GFR should be used, such as the 1-compartment, 2-sample plasma $^{99m}$Tc-DTPA method. It should be noted that if long continuous infusion techniques are employed with extended intervals of urine and/or plasma collection, plasma clearance methods should equal urinary clearance. However, this would require a substantially greater investment of time and effort in performing these studies than the methods performed herein.

At the time of preparation of the current report, we are aware of several other publications evaluating the performance of improved equations for estimated GFR (eGFR) in patients with hepatic cirrhosis. In each of these reports, different reference methods were used to establish mGFR. One small study of 14 subjects (Adachi et al) utilized inulin clearance, presumably with urine and plasma collections, but did not include comparisons with the MDRD formula nor was there a discussion of methods employed to insure complete urine collection (13). Another report (Krones et al) utilized Sinistrin clearance for mGFR, based on 12 blood samples obtained over 4 hours. Sinestrin is not Food and Drug Administration (FDA) approved or available in the U.S. (14). A report by Mindikoglu et al utilized iohexol (non-radioactive iothalamate iodinated contrast media), which requires high performance liquid chromatography (HPLC) (15).
Another study (Omar et al) employed a camera based $^{99m}$Tc-DTPA method for measuring GFR. Although the camera based method can be useful in following patients over time, we as well as others have shown to correlation poorly with more traditional reference methods for measuring GFR (12). An additional study (Torre et al) utilized urinary excretion of $^{99m}$Tc-DTPA, but did not include details regarding methods to insure complete urine collections (11).

There are similarities and differences between the results of the current study and those of the other publications that evaluate the performance of the MDRD and EKD-EPI estimating equations in measuring GFR in patients with hepatic cirrhosis. In all of the reports, including ours, the CKD-EPI (CysC+SCr) equation, which incorporates both serum creatinine and cystatin C, outperformed the other estimating equations based on serum creatinine or cystatin C alone. All the referenced publications, including the current, show a moderately good positive correlation between the mGFR and each of the eGFR estimating equations. However, this value can be misleading if it considered in isolation, as it does not provide an assessment of either the precision, bias or accuracy of the tests.

A parameter that is commonly used in the literature to describe accuracy of the estimating GFR equations is the percent of patients in whom the eGFR varies by $<$30% from the mGFR (p30). This cutoff value has been criticized as insufficiently rigorous. More discriminating targets of accuracy (p20, p10) are more clinically justifiable but less frequently reported. In the current study, using the plasma $^{99m}$Tc-DTPA method for
mGFR, the estimating equations show better performance in terms of accuracy than most of the published reports, with a p30 of 88.89% for MDRD and 85.19% for CKD-EPI (CysC+SCr). The p30 for CKD-EPI (CysC+SCr) was reported as 60.4% for the Torre report (11), 64.3% for the Adlachi report (13), and 76.39% for the Mindikoglu report (15). These values are to the performance of the eGFR’s in comparison to the UV/P plasma $^{99m}$Tc-DTPA mGFR in the current report (p30 55.56% to 61.11%). This further places into suspicious the rigor of the reference methods for mGFR in these prior reports. There were no major differences identified in the overall renal function between the subjects examined in these reports from the current study. In one published report, the Krones article (11), accuracy of CKD-EPI (CysC+Cr) resulted in a p30 of 84% and a p10 of 49%, which are similar our results with plasma $^{99m}$Tc-DTPA mGFR. The Krones study utilized a very conscientious methodology for establishing mGFR, Sinistrin (Inutest®) clearance. This is laborious, with 12 serially drawn blood samples obtained over 4½ hours post-injection. Sinestrin is not FDA approved for use in the US. The plasma $^{99m}$Tc-DTPA method used in the current report is simpler, involving 2 blood samples and gives similar results as a reference for eGFR performance.

Absolute bias, percent bias and precision are less consistently reported in the literature in evaluating the performance of estimating equations for measuring GFR in patients with hepatic cirrhosis. As was true for measurements regarding accuracy, bias and precision were better in the current study, as well as in the literature when reported, for CKD-EPI (CysC+Cr) than for the other estimating equations. Precision for CKD-EPI
(CysC+Cr) for the current study was 14.18 ml/min when compared to plasma $^{99m}$Tc-DTPA mGFR. This was slightly better than in values reported in other articles, which ranged from 17.9 to 23.49 ($^{11,13,15}$). Measurements of bias of eGFR values vary somewhat in the literature, but are generally fairly small, both as a raw value and as a percent of the mGFR. For the current study, bias of eGFR values, when compared to plasma $^{99m}$Tc-DTPA mGFR ranged from approximately -2.69 to 1.54 ml/min, and was lower for CKD-EPI (CysC+Cr) than the other estimating equations. It should be noted that inaccurate eGFR values that are similarly distributed both above and below the mGFR could result in a small mean bias. Therefore, bias should be carefully considered in conjunction with the other measures of test performance.

There are a number of potential limitations of the current study that should be acknowledged. Although the bias was low for the plasma $^{99m}$Tc-DTPA mGFR method, when compared to the estimating equation eGFR methods, there is the theoretical potential that the plasma method could overestimate GFR in patients with hepatic cirrhosis. The volume of distribution and elimination of radiometal-DTPA varies as a function of extracellular fluid volume ($^{26}$). In the case of cirrhosis, a third space/compartment is created by ascites as well as edema due to decreased serum albumin/protein. $^{99m}$Tc-DTPA could diffuse into this fluid space, artifactually appearing as enhanced renal clearance from the blood. This could result in an overestimation of GFR by plasma $^{99m}$Tc-DTPA clearance methods in patients with cirrhosis. In this study, very few patients had more than trace ascites and a distinction was not made between the
patients with, and those without ascites. Nonetheless, in patients with significant ascites, consideration for measurement of GFR by a more rigorous method that employs a constant infusion and both plasma and urine sampling should be considered.

In the past, $^{99m}$Tc-DTPA showed variable degrees of protein binding. We have traditionally performed plasma $^{99m}$Tc-DTPA clearance methods using ultrafiltered plasma samples to eliminate protein binding as a variable in GFR measurements (21). However, current $^{99m}$Tc-DTPA formulations are quite stable and there is no current evidence that filtration of plasma samples is any longer required.

In the study design of the current report, the timing of the plasma samples for the single injection, 1-compartment, 2-sample $^{99m}$Tc-DTPA plasma clearance method for measuring GFR was at 60 and 180 minutes post injection, which is consistent with our previously reported methodology (21). However, more recent recommendations support that longer intervals from injection to plasma sampling, for example at either 90 or 120 minutes, and again at 240 minutes, may be preferable (16,27). It is possible that sampling of plasma at later intervals could further improve performance of the $^{99m}$Tc-DTPA plasma clearance mGFR, and of comparisons with the eGFR derived from estimating equations.

Glomerular filtration rate values are often indexed (normalized) to a standard BSA, typically 1.73 m$^2$. This allows a comparison to be made between the GFR of different patients. It has long been recognized that there is not a constant relationship between BSA, weight and height (28). There is considerable controversy regarding the
necessity or preferable methodology for indexing GFR by BSA (29, review). Scaling GFR to BSA may be fraught with inaccuracy in children, obese and very thin patients. This is especially true when using BSA calculations based on height and weight. In the current report, mGFR and eGFR values are reported as ml/min (not BSA corrected). However, this could slightly affect direct comparisons eGFR performance between the current and previous published reports.

**Conclusion**

In this report, the CKD-EPI (CysC+Cr) showed the best overall performance of the various estimating equations for GFR. The performance of all of the equations was generally better in the current report than to the reported performance in the most of published comparisons. The published reports have utilized inconsistent reference methods for mGFR determination. We believe that inaccuracies inherent in many of the reference methods, particularly those that utilize camera-based or urinary excretion, may have contributed to the less favorable performance of the estimating equations in many of the other reports. The single injection, 1-compartment, 2-sample ultra-filtered plasma $^{99m}$Tc-DTPA clearance, which is widely used as an accurate method for measuring GFR in the U.S. and Europe, avoids many of the sources of inaccuracy. Despite these improved results, and using the best performing eGFR formula (CKD-EPI [CysC+SCr]), 14% of subjects in the current study demonstrated and eGFR > 30% of the mGFR, 24% demonstrated eGFR > 20% of the mGFR and approximately 57% had an eGFR > 10% of the mGFR. These results support that the estimating equations, particularly CKD-EPI
(CysC+SCr) may be adequate in following renal function under routine circumstances. However, when highly accurate assessments of renal function are required for management of patients with hepatic cirrhosis, or when significant ascites is present, more rigorous procedures should be considered. Methods for measuring GFR that utilized voluntary timed voiding urine collections following a single injection of $^{99m}$Tc-DTPA should be regarded as potentially inaccurate and are not recommended unless conscientious measures can be taken to insure completeness of the urine collections, continuous infusion techniques are employed, and more extended intervals of sample collection can be observed.

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References:


FIGURE 1. Scatter plots of mGFR vs eGFR values for MDRD and CKD-EPI (Scr), CKD-EPI (CysC) and CKD-EPI (CysC+Scr). The graphs in the left-hand column use the UV/P $^{99m}$Tc-DTPA method for mGFR as a reference. The corresponding graphs in the right
hand column use the plasma $^{99m}$Tc-DTPA method. The line of identity (dashed line),
linear line fit (solid line) and 95% confidence intervals (thin dotted lines) are shown for
each set of comparisons.
FIGURE 2. Scatter plots of mGFR vs eGFR values for CKD-EPI (CysC) and CKD-EPI (CysC+SCr). The graphs in the left-hand column use the UV/P $^{99m}$Tc-DTPA method for mGFR as a reference. The corresponding graphs in the right hand column use the
plasma $^{99m}$Tc-DTPA method. The line of identity (dashed line), linear line fit (solid line) and 95% confidence intervals (thin dotted lines) are shown for each set of comparisons.
TABLE 1. Descriptive statistics for $^{99m}$Tc-DTPA methods for measured GFR (mGFR) and 4 equations for estimated GFR (eGFR) in 54 patients with hepatic cirrhosis.

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<thead>
<tr>
<th>GFR METHOD</th>
<th>MEAN (ml/min)</th>
<th>STANDARD DEVIATION</th>
<th>RANGE</th>
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<tbody>
<tr>
<td>Plasma DTPA mGFR</td>
<td>96.40</td>
<td>31.89</td>
<td>52.45 – 189.78</td>
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<tr>
<td>UV/P DTPA mGFR</td>
<td>88.63</td>
<td>43.33</td>
<td>34.95 – 262.60</td>
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<td>94.86</td>
<td>23.95</td>
<td>47.42 – 169.56</td>
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<td>99.09</td>
<td>20.86</td>
<td>51.35 – 138.38</td>
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<tr>
<td>CKD-EPI (CysC)</td>
<td>95.24</td>
<td>27.49</td>
<td>42.97 – 165.04</td>
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<tr>
<td>CKD-EPI (CysC+Scr)</td>
<td>97.25</td>
<td>22.82</td>
<td>45.96 – 154.79</td>
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<td>ESTIMATING EQUATION</td>
<td>PARAMETER</td>
<td>REFERENCE GFR METHOD</td>
<td>UV/P DTPA mGFR</td>
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<td><strong>MDRD</strong></td>
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<tr>
<td></td>
<td>Accuracy p20</td>
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<td>Precision</td>
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<td>Mean bias (95% CI)</td>
<td>-6.23 (-14.70 to 2.23)</td>
<td>1.54 (-4.73 to 7.86)</td>
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<tr>
<td></td>
<td>Mean percent bias</td>
<td>19.32%</td>
<td>2.53%</td>
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<td>Correlation (95% CI)</td>
<td>0.72 (0.56 to 0.83)</td>
<td>0.69 (0.52 to 0.81)</td>
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<tr>
<td><strong>CKD-EPI (SCr)</strong></td>
<td>Accuracy p10</td>
<td>20.37%</td>
<td>35.19%</td>
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<td></td>
<td>Accuracy p20</td>
<td>38.89%</td>
<td>64.81%</td>
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<td>Accuracy p30</td>
<td>55.56%</td>
<td>83.33%</td>
</tr>
<tr>
<td></td>
<td>Precision</td>
<td>17.28</td>
<td>15.06</td>
</tr>
<tr>
<td></td>
<td>Mean bias (95% CI)</td>
<td>-10.46 (-20.22 to -0.70)</td>
<td>-2.69 (-8.93 to 3.55)</td>
</tr>
<tr>
<td></td>
<td>Mean percent bias</td>
<td>26.03%</td>
<td>17.90%</td>
</tr>
<tr>
<td></td>
<td>Correlation (95% CI)</td>
<td>0.57 (0.36 to 0.73)</td>
<td>0.70 (0.53 to 0.81)</td>
</tr>
<tr>
<td><strong>CKD-EPI (CysC)</strong></td>
<td>Accuracy p10</td>
<td>22.22%</td>
<td>31.48%</td>
</tr>
<tr>
<td></td>
<td>Accuracy p20</td>
<td>44.44%</td>
<td>61.11%</td>
</tr>
<tr>
<td></td>
<td>Accuracy p30</td>
<td>59.26%</td>
<td>77.78%</td>
</tr>
<tr>
<td></td>
<td>Precision</td>
<td>25.55</td>
<td>19.59</td>
</tr>
<tr>
<td></td>
<td>Mean bias (95% CI)</td>
<td>-6.61 (-16.73 to 3.50)</td>
<td>1.16 (-5.13 to 7.44)</td>
</tr>
<tr>
<td></td>
<td>Mean percent bias</td>
<td>34.84%</td>
<td>19.51%</td>
</tr>
<tr>
<td></td>
<td>Correlation (95% CI)</td>
<td>0.53 (0.30 to 0.70)</td>
<td>0.71 (0.54 to 0.82)</td>
</tr>
<tr>
<td><strong>CKD-EPI (CysC+SCr)</strong></td>
<td>Accuracy p10</td>
<td>16.67%</td>
<td>42.59%</td>
</tr>
<tr>
<td></td>
<td>Accuracy p20</td>
<td>50.00%</td>
<td>75.93%</td>
</tr>
<tr>
<td></td>
<td>Accuracy p30</td>
<td>61.11%</td>
<td>85.19%</td>
</tr>
<tr>
<td></td>
<td>Precision</td>
<td>18.13</td>
<td>14.18</td>
</tr>
<tr>
<td></td>
<td>Mean bias (95% CI)</td>
<td>-8.63 (-17.99 to 0.74)</td>
<td>-0.85 (-6.25 to 4.54)</td>
</tr>
<tr>
<td></td>
<td>Mean percent bias</td>
<td>23.21%</td>
<td>15.04%</td>
</tr>
<tr>
<td></td>
<td>Correlation (95% CI)</td>
<td>0.62 (0.42 to 0.76)</td>
<td>0.79 (0.66 to 0.87)</td>
</tr>
</tbody>
</table>