

Research Article

Evaluation of the accuracy and precision of glomerular filtration rate based equations for the detection of kidney disease in Egyptian patient with hepatitis C virus-related liver cirrhosis

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Abstracts

Introduction: Chronic liver disease is associated with primary and secondary kidney disease and impacts markedly on survival (Slack et al., 2010). **Aim of The work:** The study aimed to compared the accuracy of different glomerular filtration rate equations based on creatinine, cystatin C and both valuable tools in the detection of kidney disease in hepatitis C virus (HCV)-cirrhosis Egyptian patients. **Patients and Methods: Study Participants:** The study was reviewed and approved by the local ethics committee and was conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all participants. **Results:** A total of 60 patients with hepatitis C virus (HCV) – related liver cirrhosis who met the inclusion criteria and 30 healthy volunteers as a control group were included in this observational hospital-based, cohort study. **Patients and Methods: Study Participants:** The study was reviewed and approved by the local ethics committee and was conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all participants. **Conclusion:** Our study concluded that the most predicting model is CKD-EPI Creatinine - Cystatin C ($R^2=0.785$).

Key words: filtration rate, hepatitis C, liver cirrhosis

Introduction

Chronic liver disease is associated with primary and secondary kidney disease and impacts markedly on survival (Slack et al., 2010). The evaluation of kidney function and injury relies on the measurement of the concentration of serum creatinine, which is affected by the degree of liver disease (Takabatake et al., 1988) and the analytical method employed (Slack et al., 2009).

The integral role of creatinine concentration in the different classifications of acute kidney injury (AKI), chronic kidney disease and the survival predictive score, MELD, for chronic liver disease, confers large inaccuracies across this population, but currently offers the most cost-effective measure available. Use of exogenous measures of kidney function and biomarkers, like Cystatin C and the Cystatin C-based equation for estimated GFR, more frequently, as these have been shown to be superior to creatinine⁽¹⁾.

Cystatin C is a 122 amino acid protein with a molecular mass of 13 kDa⁽²⁾. Cystatin C has been thought of produced at a content rate by a

"housekeeping" gene expressed in all nucleated cells. Cystatin C is freely filtered at the glomerulus. After filtration, approximately 99 % of the filtered cystatin C is reabsorbed and catabolized by the proximal tubular cells⁽³⁾. Levels of serum cystatin C have shown no correlation to any pathophysiological state other than GFR⁽⁴⁾. Reductions in estimated glomerular filtration rate (eGFR) have been associated with reductions in concentrations of serum cystatin C⁽⁵⁾. The concentration of serum cystatin C has also been shown to be unaltered in certain inflammatory conditions or other disorders of metabolism⁽⁶⁾. Furthermore, it has been suggested that because of the independence of cystatin C from many factors that affect serum creatinine, including age, sex, race, and muscle mass, an equation based on cystatin C may be more useful in detecting kidney disease in children, the elderly, and individuals with conditions affecting muscle composition⁽⁷⁾.

Aim of the work

The study aimed to compared the accuracy of different glomerular filtration rate equations based on creatinine, cystatin C and both

valuable tools in the detection of kidney disease in hepatitis C virus (HCV)-cirrhosis Egyptian patients.

Patients and Methods

Study Participants

The study was reviewed and approved by the local ethics committee and was conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all participants. This study was an observational hospital – based, cohort study to compare the accuracy of different glomerular filtration rate equations based on creatinine, cystatin C and both as valuable tools in the detection of kidney disease in liver cirrhosis related to HCV with Egyptian patients; with the participants recruited from the Internal Medicine Department of **Minia University hospital**, in the period from May 2014 to September 2016.

The study enrolled sixty (60) patients with hepatitis C virus (HCV)-related liver cirrhosis; as well as thirty (30) age- and sex-matched healthy controls. The diagnosis of cirrhosis was based on a combination of physical examination, laboratory tests, and abdominal ultrasonography. The *inclusion criterion* was HCV-related liver cirrhosis in adult patients > 18 years old of both genders. The exclusion criteria for patients and healthy controls were acute viral, bacterial infection, primary renal disease or hepatorenal syndrome (HRS), chronic obstructive pulmonary disease (COPD), diabetes mellitus, thyroid dysfunction, active GIT bleeding or gastrointestinal bleeding during the month before enrollment, hepatocellular carcinoma, congestive heart failure (CHF), , amputation of whole or part-limb, medications use including corticosteroids, antiviral drugs, angiotensin-II receptor blockers, angiotensin-converting enzyme inhibitors, aminoglycosides, nonsteroidal anti-inflammatory drugs (NSAIDs) and L-ornithine-L-aspartate.

Primary Outcome Measures:

Percentage of estimated Glomerular Filtration Rate values within 30% of 'true' measured glomerular filtration Rate. The accuracy of Glomerular Filtration Rate (GFR) estimating equations is commonly expressed as the P30 value, the percentage of estimated GFR values within 30% of 'true' GFR. The study will estimate and compare the accuracy and precision of GFR-estimating equations based on Cockcroft-Gault formula, the Modification of Diet in Renal Disease (MDRD) equation and three Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations using either creatinine or cystatin C or a combination of both in patients with liver cirrhosis related to HCV expressed as the P30 value.

Every participant was educated on proper techniques for 24-hour urine collection and provided with a detailed patient education pamphlet. One day prior to visit 2, each subject completed a 24-hour urine collection for timed urine creatinine clearance using the formula urine creatinine/serum creatinine multiplied by 24-h urine volume (UCr/PCr) x V. This was divided by 1440 to get the value in ml/min.

Results

A total of 60 patients with hepatitis C virus (HCV) – related liver cirrhosis who met the inclusion criteria and 30 healthy volunteers as a control group were included in this observational hospital-based, cohort study.

The baseline characteristics of the cohort are presented in table 1. Both groups are age- and sex-matched (58.05±5.91 years vs. 56.43.1±7.75 years; $p = 0.274$). There were 31 females and 29 male patients. The weight (81.5±7.31 vs. 79.53±7.65; $p = 0.239$) height (164.65±6.51 vs. 164.2±6.38; $p = 0.756$), body surface area (1.92±0.09 vs. 1.9±0.1; $p = 0.141$) and BMI (30.91±3.49 vs. 29.59±3.35; $p = 0.435$) showed no statistically significant difference between the two groups

Table 1: Patients demographic data:

	HCV group (n=60)	Control Group (n=30)	P value
Age (yr)			
Range	(45-68)	(42-72)	
Mean ± SD	58.05±5.91	56.43.1±7.75	0.274
Sex (frequency)			
Male	29(48.3%)	15(50%)	
Female	31(51.7%)	15(50%)	0.881
Weight (Kg)			
Range	(67-98)	(65-95)	
Mean ± SD	81.5±7.31	79.53±7.65	0.239
Height (cm)			
Range	(154-180)	(155-175)	
Mean ± SD	164.65±6.51	164.2±6.38	0.756
Body surface area (m²)			
Range	1.92 ±0.09	1.9 ±0.1	
Mean ± SD	(1.69-2.09)	(1.73-2.1)	0.141
BMI			
Range	(22.84-38.05)	(24.45-35.3)	
Mean ± SD	30.19±3.49	29.59±3.35	0.435

Independent sample t test for parametric quantitative data between the two groups

Chi square test for qualitative data between the two groups

*: Significant difference at p value < 0.05

Discussion

A total of 60 patients with hepatitis C virus (HCV) – related liver cirrhosis who met the inclusion criteria and 30 healthy volunteers as a control group were included in this observational hospital-based, cohort study.

Both groups are age- and sex-matched (58.05±5.91 years vs. 56.43.1±7.75 years; $p = 0.274$). There were 31 females and 29 male patients. The weight (81.5±7.31 vs. 79.53±7.65; $p = 0.239$) height (164.65±6.51 vs. 164.2±6.38; $p = 0.756$), body surface area (1.92±0.09 vs. 1.9±0.1; $p = 0.141$) and BMI (30.91±3.49 vs. 29.59±3.35; $p = 0.435$) showed no statistically significant difference between the two groups

Our study aimed to compare the accuracy of different glomerular filtration rate equations based on creatinine, cystatin C and both as valuable tools in the detection of kidney disease in hepatitis C virus (HCV)-cirrhosis Egyptian patients.

There is an urgent need for early and precise detection of impaired GFR in cirrhotic patients, especially in those suffering from acute on

chronic liver failure (ACLF) and being evaluated for liver transplantation.

We, therefore, prospectively evaluated GFR in 60 patients with cirrhosis and 30 healthy controls by measuring the renal function using creatinine clearance (mGFR) and comparing its value with estimated (e)GFR using creatinine (Cr)- and Cystatin (Cys) C-based equations. We found that Cr- and CysC-based equations were inaccurate for the assessment of renal function in cirrhotic patients.

Patients with known renal disease, diabetes or nephrotoxic drugs were excluded in order to exclusively study patients with impaired renal function most likely due to their liver disease. Only by the use of the combined CKD-EPI equation (CKD-EPI-Cr-CysC) we could obtain results comparable to those measured by creatinine clearance. This represents the first prospective study with direct comparison of several equations for estimating GFR with the determination of GFR by measurement of creatinine clearance using the collecting 24 hours urine.

Due to various limitations (e.g. malnutrition, muscle atrophy) the commonly used Cr-based equations for estimating renal function in cirrhosis are unreliable. Although having been considered a more sensitive indicator of renal function in cirrhosis, CysC is influenced by factors independent of GFR which are frequently present in patients with cirrhosis such as elevated CRP or low serum albumin levels.

Conclusion

Our study concluded that the most predicting model is CKD-EPI Creatinine - Cystatin C ($R^2=0.785$).

References

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