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Applicability of the Japanese equation for estimating glomerular filtration rate in patients with advanced-stage thoracic cancer

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ABSTRACT

Background: The 24-h creatinine clearance (24-h Ccr) and the Cockcroft-Gault equation (CG) are commonly used as markers of renal function in clinical practice. However, the utility of the Japanese equation for estimating glomerular filtration rate (eGFR) in cancer patients has not yet been evaluated. The aim of this cross-sectional study was to investigate the extent and correlating factors for differences between eGFR and both 24-h Ccr and CG in advanced-stage thoracic cancer patients.
Methods: eGFR, 24-h Ccr, and CG were calculated in 90 patients with thoracic malignancies. We evaluated how these three parameters are affected by clinical factors, including age, body surface area, serum creatinine concentration, and body mass index.
Results: eGFR and CG were significantly correlated with 24-h Ccr ($r=0.64$, $p<0.001$ and; $r=0.67$, $p<0.001$, respectively). However, the median value derived from eGFR was higher than the median 24-h Ccr and the CG value (74.0, 65.2, and 63.9 mL/min, respectively). Age had a significant positive correlation with the differences between eGFR and both 24-h Ccr and CG value ($r=0.30$, $p=0.005$ and; $r=0.47$, $p<0.001$, respectively). The differences between eGFR and the other two parameters were significantly higher in older patients (age ≥ 70 years) than in younger patients (age <70 years) ($p=0.023$, $p<0.001$, respectively).
Conclusions: eGFR is likely to overestimate the renal function of elderly cancer patients. A modified equation for evaluating the renal function of Japanese older patients might be needed.

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1. Introduction

Platinum-based chemotherapy plays a pivotal role in the treatment of advanced-stage lung cancer and other thoracic malignant tumors [1–3]. Considering that the majority of the thoracic cancer patient population consists of elderly people with deteriorating organ function, the correct assessment of renal function in thoracic cancer patient is necessary for determining the appropriate drug dose for treatment. For example, with regard to carboplatin, the dose is derived by using the following Calvert formula: dose (mg) = target area under the curve (AUC) × (glomerular filtration rate [GFR]+25) [4].

Although GFR can be accurately determined by measuring the clearance of an ideal filtration marker such as inulin [5], measurement of inulin levels is expensive and time-consuming [6]. As a result, other indexes such as creatinine clearance (Ccr) and the Cockcroft-Gault equation (CG) are adopted [7]. However, these two indexes have some limitations. Due to tubular creatinine secretion, use of the Ccr tends to overestimate true GFR by 10–40% [8,9]. Estimation of 24-h Ccr (24-h Ccr) requires measurement of creatinine in a 24-h urine specimen, and incomplete 24-hour urine collection often hampers precise measurement of urine creatinine levels for determining 24-h Ccr. On the other hand, the CG equation was derived from data collected in a primarily Caucasian patient population and may not be generalizable to other nationalities or races.

To address this issue in the Japanese population, Matsuo et al. formulated the Japanese equation for estimating GFR from the data of 413 Japanese subjects with relatively stable kidney function [10]. The Japanese Society of Nephrology promoted the use of this equation for GFR evaluation in their guideline for the treatment of chronic kidney disease [11]. Since this equation is based on data from participants with a mean age of 51.4 years, it remains unknown whether or not the GFR estimated from the Japanese equation (eGFR) is appropriate for evaluating renal function in elderly patients for determining drug dose. A previous study in cancer patients showed that eGFR predicted inulin clearance without bias, whereas 24-h Ccr and CG overestimated inulin clearance [12]. However, the factors that potentially contribute to differences in these values in cancer patients have not yet been investigated.

The present study was designed to evaluate the extent of differences between eGFR and both 24-h Ccr and CG values, and to analyze the relative influence of the various factors that are used to derive these equations, on differences in their derivative values in patients with advanced-stage thoracic cancer.

2. Patients and methods

2.1. Patients

We retrospectively reviewed the clinical records of patients with stage III or IV lung cancer or malignant mesothelioma, who underwent platinum-based chemotherapy at Wakayama Medical University Hospital between January and December of 2013. This study protocol was reviewed and approved by the ethics committee of Wakayama Medical University (Wakayama, Japan; approval number, 1651; approval date, September 17, 2015).

2.2. Renal function parameters

We evaluated eGFR, 24-h Ccr and CG values as renal function parameters. All of the parameters were measured within 7 days before initiating chemotherapy. Serum and 24-h urine samples were obtained, and the creatinine concentration of both samples and 24-h urine volume were measured. Creatinine concentration was measured by an autoanalyzer using the enzymatic method (TBA-c16000, Toshiba Medical Systems, Tochigi, Japan). eGFR, 24-h Ccr and CG values were calculated according to the following equations, where Scr and Ucr indicate serum and urine creatinine concentrations (mg/dL), respectively: eGFR (mL/min/1.73 m^2) = $194 \times \mathrm{Scr}^{-1.094} \times \mathrm{age}^{-0.287}$ (× 0.739 if female) [10]; 24-h Ccr (mL/min) = Ucr × 24-h urine volume (mL)/(Scr × 1440); CG value (mL/min) = (140 − age) × body weight/(Scr × 72) (× 0.85 if female) [7]. eGFR was corrected for the body surface area (BSA) of the patients according to the following equation: eGFR (mL/min) = eGFR (mL/min/1.73 m^2) × BSA/1.73. As described above, Ccr is generally known to be greater than GFR. Therefore, to derive GFR values from these equations, the 24-h Ccr and CG values were multiplied to 0.715 and 0.789, respectively, as correction coefficients [10].

2.3. Statistical analysis

All data are expressed as median with ranges. To evaluate the difference between eGFR and both 24-hCcr and CG values, we subtracted the 24-h Ccr from the eGFR (24-h Ccr gap), and the CG value from the eGFR (CG gap). A linear regression analysis was performed by using the least-squares method. Significance was analyzed by the Spearman rank test. The Mann-Whitney test was used for single comparisons. Probability values of less than 0.05 ($p < 0.05$) were considered significant. GraphPad Prism 5 (GraphPad Software, Inc., San Diego, CA) was used for all the analyses.

Abbreviations: AUC, area under the curve; BMI, body mass index; BSA, body surface area; Ccr, creatinine clearance; CG, Cockcroft-Gault equation; eGFR, glomerular filtration rate estimated from the Japanese equation; GFR, glomerular filtration rate; Scr, serum creatinine concentrations; Ucr, urine creatinine concentrations

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