Overestimation of glomerular filtration rate calculated from serum creatinine as compared with cystatin C in patients with subclinical hypercortisolism: Hyogo Adrenal Metabolic Registry

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Abstract. The skeletal muscle mass are decreased in the patients with hypercortisolism. Glomerular filtration rate (eGFR) is not accurately evaluated by calculation from serum creatinine (eGFRcre) in these patients. However, it is not known whether it applies to patients with subclinical hypercortisolism. We investigated the dissociation between eGFRcre and eGFR calculated from cystatin C (eGFRcys) in patients with subclinical hypercortisolism and its association with the skeletal muscle mass. This cross-sectional study includes 23 patients with overt Cushing’s syndrome (CS), 84 patients with possible autonomous cortisol secretion (pACS) and 232 patients with non-functioning adenomas (NFA). eGFRcre, eGFRcys, the ratio of eGFRcre to eGFRcys (eGFRcre/eGFRcys) were calculated. Skeletal muscle index (SMI) was measured by a direct segmental multi-frequency bioelectrical impedance body composition analyzer. eGFRcre/eGFRcys was significantly higher (p < 0.01) in pACS (mean ± standard error: 1.15 ± 0.02) than NFA (1.06 ± 0.01). In multiple linear regression analysis, the presence of pACS (β = 0.162, p < 0.01), and post 1 mg-DST cortisol levels (β = 0.190, p < 0.01) were significantly associated with eGFRcre/eGFRcys independent of age, gender, BMI and diabetes. eGFRcre/eGFRcys was significantly and inversely associated with SMI (r = –0.164, p = 0.02). Furthermore, post 1 mg-DST cortisol levels was significantly associated with SMI in simple (r = –0.177, p = 0.01) and multiple (β = –0.089, p = 0.01) regression analyses. In conclusion, dissociation between eGFRcre and eGFRcys was observed in patients with subclinical hypercortisolism at least partly explained by muscle mass. Our findings raise an important clinical point that eGFRcre value should be carefully evaluated even in the phase of subclinical hypercortisolism.

Key words: Hypercortisolism, Glomerular filtration rate, Skeletal muscle index, Hyogo Adrenal Metabolic Registry

RENAL DYSFUNCTION is now recognized as an essential predictor for cardiovascular disease (CVD) [1, 2]. Therefore, it is important to accurately evaluate the renal function for prevention the occurrence of CVD in patients with atherosclerotic risk factors. Glomerular filtration rate (eGFR) estimated from serum creatinine (eGFRcre) is a universal marker of renal function [3]. This marker is affected by whole skeletal muscle mass because creatinine is a metabolite of muscle [4]. Therefore, serum creatinine levels is lower in the patients with decreased muscle mass, such as muscle atrophy and sarcopenia. In contrast, cystatin C is a cysteine proteinase inhibitor expressed in all nucleated cells, and it is not affected by the skeletal muscle mass [5]. Thus, evaluation of renal function with eGFR from serum cystatin C (eGFRcys) may be a useful alternative method in patients with decreased muscle mass.

Hypercortisolism has been shown as a risk factor for atherosclerosis and CVD [6-9]. Endogenous hypercortisolism, such as possible autonomous cortisol secretion (pACS) and Cushing syndrome (CS), is caused by an adrenal cortisol-secreting tumor. Most cases of hypercortisolism are diagnosed by the low-dose dexamethasone suppression tests (DST) [10]. Hypercortisolism also causes Cushingoid appearance, including moon facies, truncal obesity, purpura, and especially the limbs muscle atrophy. The skeletal muscle mass are shown to be
decreased in patients with hypercortisolism than those with normal cortisol level [11, 12]. Indeed, renal function is reported to be overestimated in patients with Cushing syndrome [12] when it is evaluated by eGFRcre, since serum creatinine is markedly affected by muscle mass. However, it is not known whether renal function estimated by eGFRcre is already affected in patients with subclinical hypercortisolism.

In the present study, we investigated dissociation between eGFRcre and eGFRcys in patients with adrenal tumor as classified by degree of cortisol secretion. We also examined the impact of body muscle mass on the dissociation.

Subjects and Methods

Study design and participants
Ongoing Hyogo Adrenal Metabolic Registry was conducted from October 2010, and this study retrospectively analyzed 459 patients who were registered in the cohort until November 2018. All agreed to participate by providing written informed consent, and the study was approved by the Ethics Committee of Hyogo College of Medicine (approval No. 2891). Patients with adrenal tumor being followed at the Division of Diabetes, Endocrinology and Metabolism of Hyogo Medical College Hospital (Hyogo, Japan) were registered. Among 459 subjects, 339 completed evaluations of both cortisol secretion and eGFR estimation. A random set of 194 among 339 patients received measurements of body skeletal muscle mass.

Assessment of clinical backgrounds
We obtained the medical history of each subject, and measured height and body weight. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m²). Smoking status was based on self-reported history of cigarette smoking. We defined a previous myocardial infarction, coronary intervention, and stroke as history of cardiovascular diseases. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or treatment for hypertension. Dyslipidemia was defined as the presence of low density lipoprotein cholesterol (≥140 mg/dL), high density lipoprotein cholesterol (≤40 mg/dL), elevated triglyceride level (≥150 mg/dL), or treatment for dyslipidemia [13]. Type 2 diabetes was diagnosed by fasting plasma glucose ≥126 mg/dL, casual plasma glucose ≥200 mg/dL, or 2-hour plasma glucose ≥200 mg/dL during a 75-g oral glucose tolerance test, or previous therapy for diabetes [14]. eGFRcre and eGFRcys in each patient were calculated using an equation for Japanese subjects, as follows: eGFRcre (mL/min/1.73 m²) = 194 × age^{-0.287} × Crea^{-1.043} (if female, ×0.739), eGFRcys (mL/min/1.73 m²) = 104 × 0.996^{80} × Cys^{-1.019} (if female, ×0.929) – 8 [3]. The dissociation between eGFRcre and eGFRcys was defined as the ratio of eGFRcre to eGFRcys (eGFRcre/eGFRcys).

Assessment of autonomous cortisol secretion
To investigate the levels of autonomous cortisol secretion, 1 mg overnight dexamethasone suppression test (1 mg-DST) was performed according to the 2016 European Society of Endocrinology guidelines [10]. Morning plasma cortisol levels following night 1 mg-DST (post 1 mg-DST cortisol) between 1.8 and 5 μg/mL were considered as possible autonomous cortisol secretion (pACS), and the greater than 5 μg/mL as Cushing’s syndrome (CS). 1 mg-DST cortisol levels below 1.8 μg/mL were considered as non-functioning adenoma (NFA). These patients were not diagnosed as primary aldosteronism.

Assessment of body skeletal muscle mass
Body composition was measured using a direct segmental multi-frequency bioelectrical impedance body composition analyzer (Inbody720® , Inbody Japan Inc., Tokyo, Japan), as previously described [15]. Skeletal muscle mass analyzed with this method is shown to be correlated with that measured by dual energy X-ray analysis (DEXA) method [16, 17]. The skeletal muscle index (SMI) was defined as limbs skeletal muscle mass in kilograms divided by height in meter squared, as previously described [18]. SMI has been used as a marker of whole body muscle mass [19].

Statistical analysis
To compare baseline variables among groups, ANOVA or Kruskal-Wallis test for continuous variables, and chi-square test (for categorical variables) were utilized. Pearson’s correlation coefficient and multiple linear regression analyses were performed to explore independent relationships among variables. For analyses, 1 mg-DST cortisol levels were natural logarithm-transformed (ln) to normalize the skewed distribution. All statistical analyses were performed using the Statistical Package for the Social Sciences software (PASW Statistics version 18.0). All reported p values are 2-tailed and were considered to be statistically significant at the <0.05 level.

Results
The clinical characteristics of the subjects are shown in Table 1. They were divided into NFA (n = 232), pACS (n = 84) and CS (n = 23) according to the 1 mg-DST cortisol levels. pACS group exhibited higher age, whereas, CS group showed significantly lower age than NFA...
group. As compared with NFA, CS group had significantly lower percentage of males, lower dyslipidemia, and lower BUN, creatinine, and cystatin C levels. Both pACS and CS groups had lower ACTH value as compared to the NFA group. Although urinary cortisol level was significantly higher in CS than NFA group, its level was not significantly different between pACS and NFA groups. The median of post 1 mg-DST cortisol levels were 1.1 (0.9–1.3), 2.4 (2.0–3.5) and 10.7 (8.0–16.2) in NFA, pACS and CS groups, respectively. BMI, the percentage of current smoking and past history of CVD, hypertension, dyslipidemia and diabetes mellitus were not significantly among three groups.

Fig. 1 presents comparisons of eGFRcre and eGFRcys, as well as the ratio of eGFRcre to eGFRcys (eGFRcre/eGFRcys) among three groups. eGFRcre was in similar levels in NFA (81.6 ± 1.2 mL/min/1.73 m²) and pACS (82.2 ± 2.2 mL/min/1.73 m²), whereas eGFRcys was significantly lower in pACS (72.0 ± 1.8 mL/min/1.73 m²) than NFA (77.9 ± 1.1 mL/min/1.73 m²). Accordingly, eGFRcre/eGFRcys was significantly higher in pACS (1.15 ± 0.02) than NFA (1.06 ± 0.01). CS patients exhibited significantly higher eGFRcre and eGFRcys than NFA possibly due to much younger age. eGFRcre/eGFRcys was not statistically significantly different between CS and NFA, however, there was a tendency to be also higher in CS than NFA.

Table 2 shows Pearson’s correlation coefficients to examine associations of the factors with eGFRcre/eGFRcys. In simple regression analyses, age, diabetes mellitus, pACS (r = 0.200, p < 0.01) or pACS + CS (r = 0.189, p < 0.01), and post 1 mg-DST cortisol levels (r = 0.186, p < 0.01) still remained significantly associated with eGFRcre/eGFRcys. In multiple linear regression analyses, which were fully adjusted for age, gender, BMI, smoking habits, history of CVD, hypertension, dyslipidemia and diabetes mellitus, the presence of pACS (β = 0.162, p < 0.01), pACS + CS (β = 0.173, p < 0.01), or post 1 mg-DST cortisol levels (β = 0.190, p < 0.01) still remained significantly associated with eGFRcre/eGFRcys.

### Table 1 Comparisons of clinical characteristics of subjects (n = 339) among NFA, pACS and CS groups classified with 1 mg-DST

| Variables               | NFA     | pACS    | CS      | p      |
|-------------------------|---------|---------|---------|--------|
| Number                  | 232     | 84      | 23      |        |
| Age, years              | 58.9 ± 0.8 | 64.1 ± 1.2* | 49.8 ± 3.2* | <0.01  |
| Male gender, n (%)      | 110 (47.4%) | 42 (50.0%) | 4 (17.4%) | 0.01   |
| Body mass index, kg/m²  | 25.3 ± 0.3 | 24.6 ± 0.4 | 23.0 ± 1.0 | 0.11   |
| Current smoking, n (%)  | 56 (24.1%) | 23 (27.4%) | 9 (39.1%) | 0.27   |
| Past history of CVD, n (%) | 22 (9.5%) | 8 (9.5%) | 0 (0.0%) | 0.30   |
| Hypertension, n (%)     | 162 (69.8%) | 67 (79.8%) | 15 (65.2%) | 0.16   |
| Dyslipidemia, n (%)     | 123 (53.0%) | 51 (60.7%) | 7 (30.4%)* | 0.03   |
| Diabetes mellitus, n (%)| 56 (24.2%) | 28 (33.3%) | 3 (13.0%) | 0.09   |
| BUN, mg/dL              | 14.6 ± 0.2 | 13.8 ± 0.4 | 11.8 ± 0.6* | 0.01   |
| Creatinine, mg/dL       | 0.70 ± 0.01 | 0.68 ± 0.02 | 0.57 ± 0.03** | 0.01   |
| Cystatin C, mg/L        | 0.95 ± 0.01 | 1.00 ± 0.02 | 0.87 ± 0.04* | 0.01   |
| UA, mg/dL               | 5.7 ± 0.1 | 5.5 ± 0.1 | 5.3 ± 0.3 | 0.35   |
| TSH, μU/mL              | 3.04 ± 0.43 | 3.24 ± 0.28 | 1.85 ± 0.30 | 0.54   |
| Free T4, ng/mL          | 1.20 ± 0.01 | 1.20 ± 0.01 | 1.15 ± 0.03 | 0.40   |
| Plasma ACTH, pg/mL      | 28.7 ± 1.2 | 22.8 ± 2.0* | 10.4 ± 2.8** | 0.01   |
| Plasma cortisol, μg/mL  | 13.8 ± 0.3 | 15.2 ± 0.5 | 14.3 ± 1.3 | 0.18   |
| Urinary cortisol, μg/day| 40.0 ± 1.4 | 39.7 ± 2.8 | 103.4 ± 25.2** | <0.01  |
| Post 1 mg-DST plasma cortisol, μg/mL | 1.1 (0.9–1.3) | 2.4 (2.0–3.5)* | 10.7 (8.0–16.2)** | <0.01  |

Data are presented as the mean ± standard error or median (25th–75th percentile) for continuous variables, and n (%) for dichotomous variables. P values show comparisons of means (ANOVA) and median (Kruskal-Wallis test), or percentages (Chi-square test) of 3 groups. DST, dexamethasone cortisol suppression test; NFA, non-functioning adenomas; pACS, possible autonomous cortisol secretion; CS, Cushing syndrome; CVD, cardiovascular disease; BUN, blood urea nitrogen; UA, uric acid; TSH, thyroid-stimulating hormone.

* p < 0.05, ** p < 0.01 (post-hoc analysis, Tukey-Kramer test for ANOVA, Steel-Dwass test for Kruskal-Wallis test, Chi-square test, vs. NFA).
versely, among patients excluding CS, eGFRcre/eGFRcys was significantly associated with the presence of pACS ($\beta = 0.174$, $p < 0.01$), even after adjusted for age, gender, BMI, smoking habits, history of CVD, hypertension, dyslipidemia and diabetes mellitus. These results suggest that dissociation between eGFRcre and eGFRcys may be useful to predict subclinical hypercortisolism in patients with adrenal tumor.

We next examined the impact of muscle mass on the association of post 1 mg-DST cortisol levels with

**Fig. 1** Hypercortisolism is associated with the dissociation between eGFRcre and eGFRcys

Comparisons of eGFRcre (A), eGFRcys (B) and eGFRcre/eGFRcys (C) among NFA ($n = 232$), pACS ($n = 84$) and CS ($n = 23$). Each column represents mean ± standard error. Yellow column: NFA; red column: pACS and blue column: CS. Overall $p$ values for 3-group comparison of means were calculated by ANOVA F-test, and post hoc test for multiple comparisons used Tukey-Kramer test. GFR denotes estimated glomerular filtration rate; eGFRcre, eGFR calculated from serum creatinine; eGFRcys, eGFR from serum cystatin C; NFA non-functioning adenomas; pACS, possible autonomous cortisol secretion; CS, Cushing syndrome. * $p < 0.05$, ** $p < 0.01$.

**Table 2** Simple and multiple linear regression analyses of the factors associated with eGFRcre/eGFRcys

| Variables                              | $r$ | $r^2$ | Model 1 $\beta$ | Model 2 $\beta$ | Model 3 $\beta$ |
|----------------------------------------|-----|-------|-----------------|-----------------|-----------------|
| Age                                    | 0.215** | —     | 0.241**         | 0.242**         | 0.255**         |
| Gender (male = 1, female = 0)          | −0.034 | —     | −0.103          | −0.100          | −0.093          |
| Body mass index                        | 0.051 | —     | 0.160**         | 0.138*          | 0.156**         |
| Current smoking (yes = 1, no = 0)      | 0.087 | —     | 0.081           | 0.096           | 0.090           |
| Past history of CVD (yes = 1, no = 0)  | 0.046 | —     | 0.038           | 0.037           | 0.034           |
| Presence of hypertension (yes = 1, no = 0) | 0.002 | —     | −0.103          | −0.094          | −0.095          |
| Presence of dyslipidemia (yes = 1, no = 0) | 0.072 | —     | −0.013          | −0.011          | −0.006          |
| Presence of diabetes mellitus (yes = 1, no = 0) | 0.190** | —     | 0.134*          | 0.129*          | 0.123*          |
| NFA vs. pACS (pACS = 1, NFA = 0)       | 0.200** | —     | 0.162*          | —               | —               |
| NFA vs. pACS + CS (pACS + CS = 1, NFA = 0) | 0.189** | —     | —               | 0.173**         | —               |
| Logarithm of post 1 mg-DST cortisol     | 0.186** | —     | —               | —               | 0.190**         |
| $R^2$                                  | —   | —     | 0.106**         | 0.104**         | 0.109**         |

Simple and multiple linear regression analyses were performed. GFR, glomerular filtration rate; eGFRcre, eGFR calculated from serum creatinine; eGFRcys, eGFR from serum cystatin C; eGFRcre/eGFRcys, the ratio of eGFRcre to eGFRcys; CVD, cardiovascular disease; NFA, non-functioning adenomas; pACS, possible autonomous cortisol secretion; CS, Cushing syndrome; DST, dexamethasone cortisol suppression test. Post 1 mg-DST cortisol was natural logarithm-transformed to achieve a normal distribution. * $p < 0.05$, ** $p < 0.01$.

$r$: Pearson’s correlation coefficients, $\beta$: standard regression coefficients.
increased eGFRcre/eGFRcys, SMI levels tended to decrease in proportion to the severity of hypercortisolemia (6.8 ± 0.1, 6.6 ± 0.1, and 6.2 ± 0.2 for NFA, pACS and CS groups, respectively, \( p = 0.177 \) ANOVA). In all subjects, SMI was negatively and significantly associated with eGFRcre/eGFRcys \( (r = -0.164, p = 0.02) \) (Fig. 2). Even when CS patients were excluded from the analysis, inverse association of SMI with eGFRcre/eGFRcys was still at borderline significance \( (r = -0.130, p = 0.08) \). As shown in Table 3, SMI was strongly and positively associated with male gender, BMI and current smoking, and inversely with age and post 1 mg DST cortisol \( (r = -0.177, p = 0.01) \) in simple regression analyses. Even after adjustment for these confounders, post 1 mg-DST cortisol levels remained significantly associated with SMI \( (\hat{\beta} = -0.089, p = 0.01) \). Whereas, urinary cortisol levels were not significantly associated with SMI (data not shown).

Finally, we examined changes in eGFRcre/eGFRcys following adrenalectomy in patients with hypercortisolism \( (n = 19) \). Both eGFRcre (pre; 94.0 ± 4.7, post; 81.7 ± 3.7, \( p < 0.01 \)) and eGFRcre/eGFRcys (pre; 1.09 ± 0.04, post; 0.95 ± 0.05, \( p < 0.01 \)) levels were significantly decreased after adrenalectomy (Fig. 3).

### Discussion

This study was conducted to examine whether autonomous cortisol secretion even without Cushing syndrome, may affect eGFR estimation by serum creatinine. We first showed that, even in the phase of pACS, the dissociation between eGFRcre and eGFRcys were increased in hypercortisolism as the compared with NFA. Of note, the dissociation could be attributable to low skeletal muscle mass potentially due to the subclinical hypercortisolism.

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**Fig. 2** Simple regression analyses between SMI and eGFRcre/eGFRcys

SMI was negatively and significantly associated with eGFRcre/eGFRcys in all subjects \( (r = -0.164, p = 0.02, n = 194) \), and those without CS \( (r = -0.130, p = 0.08, n = 181) \). Yellow circle, NFA; red circle, pACS; blue circle, CS. GFR, glomerular filtration rate; eGFRcre, eGFR calculated from serum creatinine; eGFRcys, eGFR from serum cystatin C; SMI, skeletal mass index. \( r \): Pearson’s correlation coefficient.

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**Table 3** Simple and multiple linear regression analyses of the factors associated with SMI

| Variables                      | \( r \)   | \( \hat{\beta} \) |
|--------------------------------|-----------|------------------|
| Age                            | -0.195**  | -0.105*          |
| Gender (male = 1, female = 0)  | 0.607**   | 0.562**          |
| Body mass index                | 0.630**   | 0.580**          |
| Current smoking (yes = 1, no = 0) | 0.277**   | 0.108*           |
| Past history of CVD (yes = 1, no = 0) | -0.019    | -0.046           |
| Presence of hypertension (yes = 1, no = 0) | 0.180*    | 0.006            |
| Presence of dyslipidemia (yes = 1, no = 0) | 0.067    | -0.093*          |
| Presence of diabetes mellitus (yes = 1, no = 0) | 0.224**   | -0.008           |
| Logarithm of post 1 mg-DST cortisol | -0.177*  | -0.089*          |
| \( R^2 \)                      |   —       | 0.755**          |

Simple and multiple linear regression analyses were performed. Post 1 mg-DST cortisol was natural logarithm-transformed to achieve a normal distribution. SMI, skeletal mass index; CVD, cardiovascular disease; DST, dexamethasone cortisol suppression test.

* \( p < 0.05 \), ** \( p < 0.01 \).

\( r \): Pearson’s correlation coefficients, \( \hat{\beta} \): standard regression coefficients.
Conversely, our results also suggest that this dissociation may be clinically useful to predict subclinical hypercortisolism in patients with adrenal tumor.

Serum creatinine levels are well known to be lower in the patients with decreased muscle mass, such as muscle atrophy and sarcopenia [4]. It is also well established that skeletal muscle mass is decreased in patients with Cushing syndrome than those with normal cortisol levels, the underlying mechanisms of which include decreased protein synthesis [20] via blunting the anabolic effect of insulin [21] and increased rate of proteolysis [22]. Therefore, eGFR measured by serum creatinine can be overestimated in patients with hypercortisolism. In a recent study showing association between hypercortisolism and cardiac function [23], serum creatinine levels were not significantly different among NFA with pACS, however, this report did not compare eGFR estimated by multiple parameters including serum creatinine and cystatin. The present study is the first to address this important issue, and found that eGFRcre is overestimated even in the pACS patients without Cushing syndrome. In preliminary analyses, both eGFRcre and eGFRcre/eGFRcys levels significantly decreased after adrenalectomy, further supporting the effect of hypercortisolism on eGFRcre. Our data also highlighted the possibility of subclinical decrease in muscle mass could be attributable.

Multiple clinical factors including aging and diabetes mellitus were shown to be established risks for sarcopenia [24, 25]. In the present study, patients with pACS exhibited higher age and a higher prevalence of diabetes mellitus than NFA, where both of the factors were significantly and independently associated with the dissociation of eGFRcre and eGFRcys in multiple linear regression analyses. BMI also strongly and positively associated with muscle mass, which could be an important confounder of the effect of hypercortisolism [12]. Of importance, association of hypercortisolism remained independently associated with dissociation between eGFRcre and eGFRcys even after adjustment for these confounders. Therefore, our study indicated that even subclinical autonomous cortisol excess is an important factor to be paid attention for evaluating renal function.

Generally, cystatin C is freely filtered by the glomerulus. It is not secreted, but is reabsorbed by tubular epithelial cells and catabolized so that it does not return to the blood flow [26]. Therefore, cystatin C may be an endogenous marker dependent of filtration in glomerular. Cortisol is suggested to increase filtration in glomerulus, however, its biological effect on cystatin C kinetics is not yet clearly understood. A past study showed that methylprednisolone decreased serum cystatin C levels after 1 week therapy in asthmatic patients [27]. Another study showed that using steroids was not associated with serum cystatin C in the patients with various renal disease [28]. In the present study, CS group had lower serum cystatin C levels than NFA and pACS. Thus, the dissociation between eGFRcre and eGFRcys in the present study might be affected by the biological function of cortisol on glomerular filtration and cystatin C metabolism, besides its effect on muscle metabolism. In addition, serum cystatin C levels are also known to be affected by various disease, such as liver cirrhosis, rheumatoid arthritis, chemotherapy or dialysis [29]. Recently, thyroid function is shown to be associated with the serum cystatin C levels [30]. In the present study, the patients with liver cirrhosis, rheumatoid arthritis, chemotherapy or dialysis were not included. There were not significant differences in thyroid function among the three groups.

Our study has some limitations. There were inequalities in regard to the numbers and distribution of characteristics, such as age and gender, between NFA and pACS. Because of the nature of the study design, although SMI is related to the important results of the study, only a random set of the participants received this measurement. We found a trend of inverse association of SMI with severity of hypercortisolism, without reaching statistical significance possibly due to small numbers of SMI data. In our hands, post levels of 1 mg DST were significantly associated with SMI. However, urinary cortisol levels, which may be a more suitable marker for

**Fig. 3** Changes in eGFRcre and eGFRcre/eGFRcys following adrenalectomy

Changes in eGFRcre (A) and eGFRcre/eGFRcys (B) were shown before and after adrenalectomy in patients with hypercortisolism (n = 19). Green circle, before; purple circle, after adrenalectomy. p values for the comparison of means were calculated by paired t-test. eGFR: estimated glomerular filtration rate; eGFRcre: eGFR calculated from serum creatinine; eGFRcys: eGFR from serum cystatin C. * p < 0.01.
chronic hypercortisolemia, were not significantly associated with SMI. Since urinary cortisol level was identical between NFA and pACS, it may not be sensitive enough to discriminate subtle changes in cortisol secretion. Further, information regarding duration of hypercortisolemia, another potential predictor of SMI, was not obtained from our clinical charts. Nevertheless, our results definitely provide important messages regarding significant association of subclinical hypercortisolism with dissociation between eGFRcre and eGFRcys.

In conclusion, even in the phase without Cushing syndrome, hypercortisolism is associated with overestimation of eGFR measured by serum creatinine, potentially due to lower muscle mass. Our findings raise an important clinical point that renal function evaluated by eGFRcre should be carefully interpreted even in the phase of subclinical hypercortisolism.

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Disclosure

None of the authors have any potential conflicts of interest associated with this research.

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