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# Validity of computed tomography defined body composition as a prognostic factor for functional outcome after kidney transplantation

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## Abstract

**Background** The prevalence of sarcopenia is markedly higher in kidney transplant candidates than in the general population. It is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength, which increases the risk of adverse postoperative outcomes.

**Methods** We studied the impact of computed tomography defined preoperative sarcopenia, defined as a skeletal muscle index below age and gender specific cut-off values, on postoperative physical functional outcomes (grip strength, 4-m walking test, timed up and go, and sit to stand) at 6 months follow up.

**Results** A total of 107 patients transplanted between 2015 and 2019 were included in this single-centre study. Mean age was 60.3 (±13.1), and 68.2% of patients were male. Ten patients (9.4%) were identified as sarcopenic. Sarcopenic patients were younger (55.6 (±15.1) vs. 60.8 (±12.9) years), more likely to be female (60.0% vs. 28.9%), and had an increased dialysis vintage (19 [2.5–32.8] vs. 9 [0.0–21.0] months) in comparison with their non-sarcopenic counterparts. In univariate analysis, they had a significantly lower body mass index and skeletal muscle area ( $P \le 0.001$ ). In multivariate regression analysis, skeletal muscle index was significantly associated with grip strength ( $\beta = 0.690$ ,  $R^2 = 0.232$ ) and timed up and go performance ( $\beta = -0.070$ ,  $R^2 = 0.154$ ).

**Conclusions** We identified a significant association between sarcopenia existing pre-transplantation and poorer 6 months post-transplantation physical functioning with respect to hand grip strength and timed up and go tests in kidney transplant recipients. These results could be used to preoperatively identify patients with an increased risk of poor postoperative physical functional outcome, allowing for preoperative interventions to mitigate these risks.

Keywords Computed tomography; Kidney transplantation; Physical functioning; Sarcopenia

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## Introduction

Kidney transplantation is the preferred treatment option for patients with end-stage kidney disease, as it is associated with a better quality of life compared with dialysis.<sup>1</sup> Among kidney transplant recipients, metabolic complications, dialysis and the associated sedentary lifestyle contribute to the development of sarcopenia in these patients.<sup>2</sup> Consequentially, the incidence of sarcopenia is far greater in patients with end stage kidney disease and kidney transplantation candidates than in the general population (15-21% vs. 3-6%).<sup>3</sup>

Sarcopenia has been defined by the European Working Group on Sarcopenia in Older People as a syndrome characterized by progressive and generalized loss of skeletal muscle

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mass and strength with a risk of adverse outcomes.<sup>4</sup> Studies conducted in various other surgical populations have demonstrated that sarcopenia is associated with greater rates of postoperative complications, intensive care unit admittance, increased duration of hospital stay and overall increased economic burden.<sup>5–9</sup> Therefore, illustrating the importance of quantifying a patient's muscle mass and diagnosing sarcopenia preoperatively. Recent studies have shown that computed tomography (CT) scan analysis is a valid and reliable tool for determining the presence and severity of sarcopenia.<sup>10</sup>

Within our centre, we utilize an in-house developed artificial intelligence assisted analysis software, enabling rapid, autonomous and objective quantification of a patient's muscle mass.

To date, the vast majority of published evidence on the impacts of sarcopenia on postoperative outcomes have primarily focused on clinical outcomes. Therefore, there is a lack of empirical evidence regarding its impact on functional outcomes, which illustrate a patient's physical functioning postoperatively.

Utilizing CT scan analysis as an objective method to diagnose sarcopenia, we aim to investigate the impact of preoperative sarcopenia on functional outcomes at 6 months post-kidney transplantation.

## **Materials and methods**

#### Study design

This retrospective study is part of a larger research line investigating the impact of sarcopenia and frailty on postoperative outcomes in kidney transplant recipients. The study population consisted of patients who underwent a kidney transplantation at the University Medical Center Groningen (UMCG) between 2015 and 2019. To be eligible for inclusion, patients needed to have undergone an abdominal CT scan within the 12 months before their transplantation and have available functional outcome measurements. The CT scans were performed in accordance with our centre's pre-transplant screening protocol, which involved selecting patients based on criteria such as age (>50 years), comorbidities (diabetes mellitus and peripheral artery disease), and dialysis vintage (>2 years), or at the surgeon's discretion. Patients who either were under 18 years old at the time of transplantation, who objected to the use of their medical imaging for research, had an interval of more than 12 months between CT and transplantation, or those with unsuitable CT imaging for sarcopenia analysis were not eligible for inclusion in the study. This study was approved by the institutional review board of the UMCG (METc 2018/050) and performed in line with the Declaration of Helsinki and the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

### Data collection

Baseline data were retrospectively collected from the UMCG kidney transplant database (NITRA) and supplemented where necessary using the patients' digital medical records (Epic Systems, Wisconsin, USA). Collected data included age (years), height (cm), weight (kg), sex (male/female), type of dialysis prior to transplantation [haemodialysis (HD), peritoneal dialysis (PD), pre-emptive (no dialysis)], duration of dialysis (months), comorbidities, acute rejection (biopsy proven), postoperative complications and hospital readmissions within 30 days of discharge. Patients' comorbidities were assessed using the Charlson Comorbidity Index,<sup>11</sup> which grades pre-existing comorbidities based on their severity. Postoperative complications were additionally graded in accordance with their severity using the Clavien-Dindo classification, and quantified using the Comprehensive Complication Index.<sup>12,13</sup> For this study, the Charlson Comorbitdy Index and the Comprehensive Complication Index were used to numerically quantify patients' comorbidities and complications allowing for a more efficient statistical analysis. Postoperative measures of physical functioning [grip strength, 4 m walking test, timed up and go (TUG), and sit to stand] were extracted from the TransplantLines database, a prospective single-centre study among solid organ transplant recipients and living organ donors (NCT03272841). The study has been described in detail previously.<sup>14</sup> Physical functioning parameters are measured in transplant recipients at 6 months follow up post transplantation.

## Computed tomography quantification of sarcopenia

CT imaging was performed on a Siemens SOMATOM Definition (AS, Edge, Flash), Force or Sensation (Siemens Medical, Erlangen, Germany) scanner. A cross-sectional area of skeletal muscle, derived from an axial CT slice at the level of the third lumbar vertebrae (L3), was analysed using an in-house developed artificial intelligence-assisted analysis software (SarcoMeas, version 0.54, UMCG, Groningen), supervised (and where necessary corrected) by two experienced radiologists (M. Z. and A. V.). These slices were exported and anonymized from the picture archiving and communication system in native Digital Imaging and Communications in Medicine format for further processing.

Within the drawn muscle outlines, voxels of muscle tissue and intramuscular fat were defined based on radiodensity [in Hounsfield Units (HU)]. The HU range for skeletal muscle has been determined by previous studies to be -29 to +150HU.<sup>15</sup> Fat was defined as voxels with a density ranging from -190 to -30 HU. The following skeletal muscles were included: rectus abdominis, obliquus externus/internus abdominis, transversus abdominus, erector spinae, quadratus

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lumborum and psoas major. The skeletal muscle area (SMA,  $cm^2$ ) was corrected for the patient's height by dividing the area by the squared patient length, resulting in the skeletal muscle index (SMI,  $cm^2/m^2$ ). Age- and gender-specific SMI cut-off values for the classification of sarcopenia are presented in Table 1.

### Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (IBM SPSS Statistics, version 28.0., Armonk, NY, USA). Data distribution was assessed through means of Kolmogorov–Smirnov and Wilk–Shapiro analyses. Baseline characteristics are presented as mean  $\pm$  SD for normally distributed continuous variables, median and interquartile range for abnormally distributed variables and as frequency (%) for categorical variables. Baseline patient characteristics were compared between non-sarcopenic (NS) and sarcopenic (S) patients using unpaired *t*-tests and Mann–Whitney *U* tests for continuous variables and chi-square tests for categorical variables.

A multivariable linear regression analysis was performed for the variables that had an independent association with one of the functional outcomes in the univariable analysis or were associated with functional outcomes in pre-existing literature. The covariates included in the multivariable model [age, gender, body mass index (BMI), Charlson Comorbidity Index, dialysis vintage and SMI] were selected in accordance with known determinants of functional outcomes in the literature and subject matter knowledge. Tests were considered significant with a *P*-value <0.05.

### Results

A total of 107 kidney transplant recipients transplanted between 2015 and 2019 within the UMCG with a preoperative CT < 1 year of transplant were included. Baseline characteristics are presented in Table 2. Mean age of patients was  $60.3 \pm 13.1$ ; of which, 73 (68.2%) were male. The mean BMI equated to 26.8  $\pm$  4.1. Sixty-eight patients (63.6%) were

| Table 1 | Age | and | gender | specific | cut-off | values | for | SMI | (cm <sup>2</sup> | /m² | ) |
|---------|-----|-----|--------|----------|---------|--------|-----|-----|------------------|-----|---|
|---------|-----|-----|--------|----------|---------|--------|-----|-----|------------------|-----|---|

| Age   | Male | Female |
|-------|------|--------|
| 20–29 | 38.8 | 37.5   |
| 30–39 | 39.2 | 35.5   |
| 40–49 | 39.9 | 32.8   |
| 50–59 | 39.0 | 33.2   |
| 60–69 | 37.0 | 31.3   |
| 70–79 | 36.8 | 31.5   |

dialysis dependent at the time of transplantation with almost twice as many patients undergoing haemodialysis (HD) as peritoneal dialysis (PD) [HD: 46 (43.0%) vs. PD: 22 (20.6%)]. The vast majority (70.1%) of patients received grafts from living donors. Patients had a median comorbidity index of 20.9 [0.0–29.6] and postoperative hospital admission duration of 9 [8.0–12.0].

### Univariable analysis

Patients were stratified into a sarcopenic and non-sarcopenic group, in accordance with the aforementioned SMI age and gender specific cut-off values. The characteristics of both groups are presented in Table 2. Ten patients were classified as sarcopenic (9.4%). Sarcopenic patients had a significantly lower BMI (27.4  $\pm$  3.8 vs. 20.92  $\pm$  2.7, P  $\leq$  0.001), SMA (142.9  $\pm$  30.5 vs. 98.3  $\pm$  18.1,  $P \le$  0.001), and SMI (45.9  $\pm$  8 vs. 31.5  $\pm$  3.6,  $P \leq$  0.001). Although not statistically significant, sarcopenic patients were younger (55.6 ± 15.1 vs. 60.8 ± 12.9), more likely to be female (60% vs. 28.9%), and more likely to be on dialysis (90% vs. 60.8%) with an increased dialysis vintage (9 [0.0-21.0] vs. 19.0 [2.5-32.8]). No statistically significant difference was observed in number or severity of surgical complications, acute rejection episodes or hospital readmissions between non-sarcopenic and sarcopenic patients. However, a statistically significant difference in functional outcomes was determined for hand grip strength (P = 0.004).

### Multivariate analysis

In the multivariable linear regression analyses, the functional outcomes (grip strength, 4 m walking test, sit to stand, and TUG) are presented as the dependent variable. The results of these analyses are presented in Table 3. SMI was significantly associated with grip strength ( $\beta = 0.690$ ;  $R^2 = 0.232$ ; 0.446 to 0.933;  $P \leq$  0.001) and TUG outcomes. In the case of grip strength this significant association remained with adjustment for BMI ( $\beta$  = 0.740;  $R^2$  = 0.004; 0.462 to 1.019;  $P \le 0.001$ ), gender ( $\beta = 0.395$ ;  $R^2 = 0.392$ ; 0.111 to 0.679; P = 0.007), and age ( $\beta = 0.270$ ;  $R^2 = 0.495$ ; 0.005 to 0.535; P = 0.046). This association lost significance after adjustment for comorbidity index ( $\beta$  = 0.239;  $R^2$  = 0.510; -0.026 to 0.504; P = 0.077). In the case of TUG, the association was highly significant, maintaining a P-value <0.001 after adjustment for all confounders (Model 6:  $\beta = -0.092$ ;  $R^2 = 0.390$ ; -0.137to -0.048;  $P \le 0.001$ ). However, there was no significant association between SMI and the physical outcomes of 4 m walking test and sit to stand test in the crude model (Model 1: P = 0.263 and 0.298).

| Table 2         Patient characteristics for the total | population and stratified b | y patient sarcopenia status |
|---|-----------------------------|-----------------------------|
|---|-----------------------------|-----------------------------|

|  | Total population ( $N = 107$ ) | Non-sarcopenic (NS) ( $N = 97$ ) | Sarcopenic (S) ( $N = 10$ ) | P value |
|--|--------------------------------|----------------------------------|-----------------------------|---------|
| Age (years)                            | 60.32 ± 13.14                  | 60.8 ± 12.9                      | 55.6 ± 15.1                 | 0.234   |
| Gender                                 |                                |                                  |                             | 0.044   |
| Male                                   | 73 (68.2%)                     | 69 (71.1%)                       | 4 (40%)                     |         |
| Female                                 | 34 (31.8%)                     | 28 (28.9%)                       | 6 (60%)                     |         |
| BMI <sup>a</sup>                       | 26.80 ± 4.13                   | 27.4 ± 3.8                       | 20.9 ± 2.7                  | < 0.001 |
| Donor type                             |                                |                                  |                             | 0.149   |
| Postmortal                             | 32 (29.9%)                     | 31 (31.9%)                       | 1 (10%)                     |         |
| Living                                 | 75 (70.1%)                     | 66 (68.1%)                       | 9 (90%)                     |         |
| Dialysis                               |                                |                                  |                             | 0.188   |
| PD                                     | 22 (20.6%)                     | 19 (19.6%)                       | 3 (30%)                     |         |
| HD                                     | 46 (43.0%)                     | 40 (41.2%)                       | 6 (60%)                     |         |
| Pre-emptive                            | 39 (36.4%)                     | 38 (39.2%)                       | 1 (10%)                     |         |
| Dialysis vintage (months)              | 9 [0.0–21.0]                   | 9 [0.0–21.0]                     | 19.0 [2.5–32.8]             | 0.114   |
| Diabetes                               |                                |                                  |                             | 0.101   |
| Yes                                    | 21 (19.6%)                     | 21 (21.6%)                       | 0 (0%)                      |         |
| No                                     | 86 (80.4%)                     | 76 (78.4%)                       | 10 (100%)                   |         |
| Comorbidities <sup>b</sup>             | 5 [4.0-7.0]                    | 5 [3.5–7.0]                      | 5 [3.75–7.50]               | 0.820   |
| Previous abdominal intervention        |                                |                                  |                             | 0.233   |
| Yes                                    | 67 (62.6%)                     | 59 (60.8%)                       | 8 (80%)                     |         |
| No                                     | 40 (37.4%)                     | 38 (39.2%)                       | 2 (20%)                     |         |
| Operation duration (min)               | 179 [155.0–212.0]              | 179 [155.0-212.5]                | 175 [148.5–212.5]           | 0.979   |
| Acute rejection <sup>f</sup>           |                                |                                  |                             | 0.693   |
| Yes                                    | 14 (12.8%)                     | 12 (12.4%)                       | 2 (20%)                     |         |
| No                                     | 90 (82.6%)                     | 82 (84.5%)                       | 8 (80%)                     |         |
| Borderline                             | 3 (2.8%)                       | 3 (3.1%)                         | 0 (0%)                      |         |
| Severe postoperative                   |                                |                                  |                             | 0.701   |
| Complication <sup>g</sup>              |                                |                                  |                             |         |
| Yes                                    | 15 (13.8%)                     | 14 (14.4%)                       | 1 (10%)                     |         |
| No                                     | 92 (84.4%)                     | 83 (85.6%)                       | 9 (90%)                     |         |
| Comprehensive Complication Index (CCI) | 20.9 [0.0–29.6]                | 20.9 [4.4–29.3]                  | 11.9 [0.0–33.3]             | 0.867   |
| Duration of admission (days)           | 9 [8.0–12.0]                   | 9 [8.0–12.0]                     | 9 [8.0–13.5]                | 0.562   |
| ICU admission                          |                                |                                  |                             | 0.273   |
| Yes                                    | 4 (3.7%)                       | 3 (3.1%)                         | 1 (10%)                     |         |
| No                                     | 103 (96.3%)                    | 94 (96.9%)                       | 9 (90%)                     |         |
| Hospital readmission within 30 days    |                                |                                  |                             | 0.114   |
| Yes                                    | 8 (7.3%)                       | 6 (6.2%)                         | 2 (20%)                     |         |
| No                                     | 99 (90,8%)                     | 91 (93.8%)                       | 8 (80%)                     |         |
| CT – TX interval (months) <sup>c</sup> | 6.05 + 3.25                    | 6.2 + 3.2                        | $4.8 \pm 4.0$               | 0.102   |
| SMA <sup>d</sup>                       | 138.75 + 32.24                 | 142.9 + 30.5                     | 98.3 + 18.1                 | < 0.001 |
| SMI <sup>e</sup>                       | 44.58 + 8.76                   | 45.9 + 8.0                       | 31.5 + 3.6                  | < 0.001 |
| Grin strength (kg)                     | 36.45 + 12.55                  | $37.6 \pm 12.3$                  | 257 + 98                    | 0.004   |
| 4 m walking test (m/s)                 | $1.28 \pm 0.24$                | $1.3 \pm 0.3$                    | $1.3 \pm 0.2$               | 0.790   |
| Sit to stand (s)                       | 13.05 + 3.60                   | 13.0 + 3.6                       | 13.4 + 3.4                  | 0.816   |
| Timed up and go (s)                    | 7.64 + 1.59                    | $7.6 \pm 1.6$                    | 7.8 + 1.6                   | 0.808   |
|  | , io i = 1155                  | , io = 110                       | ,.0 = 1.0                   | 0.000   |

<sup>a</sup>Body mass index.

 $^{\mathrm{b}}$ According to the Charlson Comorbidity Index, a weighted index that predicts the 1 year mortality by measuring the burden of comorbidities (range from 0 to 19.).

<sup>c</sup>Interval between date of computed tomography and transplantation.

<sup>d</sup>Skeletal muscle area (cm<sup>2</sup>). <sup>e</sup>Skeletal muscle index (cm<sup>2</sup>/m<sup>2</sup>).

<sup>f</sup>Biopsy proven acute rejection.

<sup>9</sup>Complications above grade 2 in the Clavien–Dindo classification.<sup>12</sup> P values  $\leq 0.05$  were considered statistically significant.

### Discussion

This study shows that sarcopenia, as defined through artificial intelligence CT scan analysis, is strongly associated with poorer performance in physical functional tests at 6 months follow up.

Performance in these tests can be seen as a surrogate measure for a patient's overall physical functioning. Our findings illustrate the detrimental impact of preoperative sarcopenia on postoperative functional outcomes after kidney transplantation.

The prevalence of sarcopenia in our cohort was higher (9.4%) compared with the general population, but lower than reported among kidney transplant recipients and end-stage renal disease patients.<sup>10</sup> Sarcopenia used to be seen as a condition affecting only older individuals, but new insights recognize its development at earlier stages of life due to various factors beyond aging.<sup>16</sup> Sedentary lifestyle, malnutrition, and dialysis are major contributors to sarcopenia in patients awaiting kidney transplantation.<sup>17</sup> In chronic kidney disease patients, sarcopenia is more prevalent, develops earlier, and progresses more rapidly compared with age-matched

|         | Unstandardized β-coefficient | R <sup>2</sup> | Change R <sup>2</sup> | 95% CI           | P-value |
|---------|------------------------------|----------------|-----------------------|------------------|---------|
|         |                              | Grip strengt   | th (kg)               |                  |         |
| Model 1 | 0.690                        | 0.232          | 0.232                 | 0.446 to 0.933   | <0.001  |
| Model 2 | 0.740                        | 0.236          | 0.004                 | 0.462 to 1.019   | <0.001  |
| Model 3 | 0.395                        | 0.392          | 0.155                 | 0.111 to 0.679   | 0.007   |
| Model 4 | 0.270                        | 0.495          | 0.104                 | 0.005 to 0.535   | 0.046   |
| Model 5 | 0.239                        | 0.510          | 0.015                 | -0.026 to 0.504  | 0.077   |
| Model 6 | 0.214                        | 0.540          | 0.030                 | -0.045 to 0.473  | 0.104   |
|         |                              | 4 m walking t  | est (m/s)             |                  |         |
| Model 1 | 0.007                        | 0.051          | 0.051                 | -0.002 to 0.015  | 0.110   |
| Model 2 | 0.007                        | 0.053          | 0.001                 | -0.003 to 0.017  | 0.154   |
| Model 3 | 0.011                        | 0.072          | 0.019                 | -0.002 to 0.023  | 0.086   |
| Model 4 | 0.008                        | 0.112          | 0.040                 | -0.005 to 0.021  | 0.216   |
| Model 5 | 0.008                        | 0.113          | 0.001                 | -0.006 to 0.021  | 0.263   |
| Model 6 | 0.007                        | 0.193          | 0.080                 | -0.006 to 0.020  | 0.256   |
|         |                              | Timed up and   | d go (s)              |                  |         |
| Model 1 | -0.070                       | 0.154          | 0.154                 | -0.107 to -0.033 | <0.001  |
| Model 2 | -0.093                       | 0.206          | 0.052                 | -0.134 to -0.051 | <0.001  |
| Model 3 | -0.115                       | 0.245          | 0.039                 | -0.161 to -0.068 | <0.001  |
| Model 4 | -0.098                       | 0.359          | 0.114                 | -0.142 to -0.054 | <0.001  |
| Model 5 | -0.091                       | 0.386          | 0.026                 | -0.135 to -0.046 | <0.001  |
| Model 6 | -0.092                       | 0.390          | 0.004                 | -0.137 to -0.048 | <0.001  |
|         |                              | Sit to stan    | id (s)                |                  |         |
| Model 1 | -0.017                       | 0.002          | 0.002                 | -0.108 to 0.074  | 0.711   |
| Model 2 | -0.066                       | 0.051          | 0.049                 | -0.168 to 0.036  | 0.204   |
| Model 3 | -0.099                       | 0.070          | 0.019                 | -0.214 to 0.016  | 0.089   |
| Model 4 | -0.071                       | 0.134          | 0.064                 | -0.185 to 0.043  | 0.220   |
| Model 5 | -0.061                       | 0.143          | 0.009                 | -0.178 to 0.055  | 0.298   |
| Model 6 | -0.065                       | 0.150          | 0.007                 | -0.183 to 0.052  | 0.270   |

Table 3 Multivariable linear regression with SMI, BMI, gender, age and CCI as independent variables and physical functional outcome as the dependent variable

Model 1: Crude (Skeletal Muscle Index (SMI)). Model 2: Adjusted for Body Mass Index (BMI). Model 3: Adjusted for model 2 + patient gender. Model 4: Adjusted for model 3 + patient age. Model 5: Adjusted for model 4 + Charlson comorbidty index. Model 6: Adjusted for model 5 + dialysis vintage.

BMI, body mass index; CI, confidence interval; CCI, Comprehensive Complication Index; SMI, skeletal muscle index.

peers.<sup>18</sup> The best method to assess muscle mass has been a hotly debated topic during the last decade.<sup>19</sup> Recent advancements in artificial intelligence have aided the accurate and rapid guantification of skeletal muscle mass on cross sectional CT imaging. CT scan analysis has the major advantage of providing quantitative tissue measurements in a highly reproducible way that reflect not only the muscle mass but also the muscle quality, better reflecting the patient's overall health condition.<sup>20</sup> Significant correlations have been found between muscle mass measured axially at the level of the third lumbar vertebrae (L3) and whole-body muscle mass. Consequently, this imaging technique has proven valuable in identifying low muscle mass, even in individuals with normal or high body weights. Furthermore, numerous studies across diverse patient populations have utilized and validated this method, establishing it as the recognized gold standard for non-invasive measurement of skeletal muscle by the European Working Group on Sarcopenia in Older People.<sup>16</sup>

Our results found sarcopenia to be associated with a significant decrease in hand grip strength and TUG performance. In the case of grip strength this significant association remained in the multivariate model until adjustment for the Charlson Comorbidity Index. Our results do suggest that sarcopenia is strongly associated with poorer performance in the TUG test with the association remaining strongly significant ( $P \le 0.001$ )

even after adjustment for important confounders. Surprisingly, a low SMI was not associated with a poorer outcome in all the functional parameters studied. After multivariable analysis no significant association between sarcopenia and increased time for the 4 m walking test or sit to stand test was found. This is surprising as both walking and sit to stand tests are often used to determine sarcopenia and physical frailty preoperatively.<sup>21,22</sup> Although the outcomes of these tests can be influenced by a multitude of factors in the postoperative period, further investigation is required to determine whether these tests are indeed a valid surrogate metric for objectively defined muscle mass.

There is limited pre-existing literature reporting the impact of preoperative sarcopenia on postoperative physical functioning outcomes. There is however a large repertoire of published evidence reporting on the association between diminished physical functioning and disability and subsequent mortality. Our results show a significant association between preoperative CT defined sarcopenia and poor performance in the TUG. Donogue et al. published the results of a large prospective cohort study conducted in 1664 community dwelling adults aged 65 and older.<sup>23</sup> In this study, the TUG test was found to be highly predictive of disability in activities of daily living (ADL) and subsequent loss of independence. A separate cohort study (n = 598) published by Millan et al concluded that loss of independence in ADL was strongly associated with an increase in morbidity and mortality among elderly patients.<sup>24</sup> Additionally, our results illustrate a significant association between CT defined sarcopenia and diminished grip strength. The Concord Health and Ageing in Men project, a cohort study of 1705 men found that diminished grip strength was associated with physical disability in basic activities of daily living.<sup>25</sup> Therefore, this study highlights the importance of determining sarcopenia preoperatively due to its predictive capacity for postoperative ADL disability and associated morbidity and mortality. Our results could be used to identify patients who have an increased risk of postoperative disability and subsequent increased morbidity and mortality, allowing for the application of preoperative interventions such as prehabilitation to increase their muscle mass, making them more fit for surgery and thus improving kidney transplant outcomes.<sup>26</sup>

In our opinion, it is important to consider that what constitutes an operative success differs between the clinician and the patient. While a clinician may focus on outcomes such as number/severity of postoperative complications and duration of hospital stay, the patient is far more concerned about return to independence in daily activities. Value based healthcare and shared decision making are being increasingly promoted. During shared decision making, it is essential that information on patient relevant outcomes is discussed among patients and healthcare professionals, thus that any intervention will yield an outcome that is as closely aligned to the patients' expectations and preferences.<sup>27,28</sup> Although survival outcome data and biomarkers are frequently collected in the context of kidney transplantation, parameters related to a patient's quality of life such as physical functioning are rarely recorded.<sup>29,30</sup> In an online survey conducted in 2017 by the International Consortium of Health Outcomes Measurement among 358 chronic kidney disease patients and kidney transplant recipients' quality of life domains were ranked as the most important outcomes, with over 80% considering return to daily activities and physical functioning an essential outcome.<sup>31</sup>

This study has limitations that need to be addressed. First, the lack of baseline physical functioning data in the analysis which, due to the retrospective study design, was unavailable. However, despite this limitation, our analysis of a single time point at 6 months postoperatively remains relevant and yields clinically significant findings. These results underscore the need for further investigation into the impact of sarcopenia on post-transplantation physical functioning. Second, the prevalence of sarcopenia in our population was lower than previously published literature,<sup>26</sup> likely due to our study population consisting mostly of patients receiving a kidney graft from a living donor who generally have a shorter dialysis vintage or undergo pre-emptive transplantation. Third, only patients with a preoperative CT scan within 1 year pretransplant were included, introducing selection bias. Although within our centre preoperative CT imaging has become more common in recent years, it remains bound by certain criteria (age >50 years, presence of diabetes, history of heavy smoking, previous cardiovascular events or surgery, and dialvsis vintage >2 years). However, the criteria for performing a preoperative CT scan have become more liberal, making the patients included more representative of the general kidney transplant population. Fourth, the lack of a set time frame for preoperative imaging means that the CT scans used for skeletal muscle measurement could range in age, leading to potential over- or underestimation of skeletal muscle mass at the time of transplantation, which is particularly significant in dialysis patients given the significant correlation between dialysis vintage and development of sarcopenia.<sup>17</sup> Fifth, there is a lack of consensus on cut-off values for CT skeletal muscle mass measurements, with variation in reported values due to differences in populations studied and the failure to account for age, sex, and BMI as potential confounders.<sup>32–35</sup> Our group has emphasized the need for consensus on cut-off values. In this study, we utilized age and gender specific cut-off values for SMI determined in a large cohort of living kidney donors.<sup>36</sup> Sixth, there is a lack of consensus on normative values and cut-offs for physical functioning tests due to variations in study design.<sup>37-40</sup> Resulting in our analyses being conducted with physical functioning outcomes as continuous variables, instead stratified into groups of normal and impaired physical functioning due to the absence of cut-off values in literature. Lastly, due to the retrospective study design, certain variables that could have an impact on physical functioning at 6 months post-transplant, such as type of immunosuppression and steroid treatments after rejection episodes, could not be included.

In conclusion, this study identified a significant association between sarcopenia and poorer physical functioning at 6 months post kidney transplantation. The results of this study are the first to our knowledge to provide insight into the impact of preoperative CT defined sarcopenia on postoperative physical functioning within the context of kidney transplantation. The findings of this study could be used to preoperatively identify sarcopenic patients with an increased risk of poor postoperative physical functional outcome, allowing for preoperative interventions to be applied to mitigate these risks.

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The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.<sup>41</sup>

## **Conflict of interest**

All authors declare that they have no conflict of interest.

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