# Measurement of muscle strength in haemodialysis patients by pinch and hand grip strength and comparison to lean body mass measured by multi-frequency bio-electrical impedance

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Abstract

Background

Muscle weakness is a risk factor for mortality in haemodialysis (HD) patients, We wished to determine whether measuring the composition of the arm with bioimpedance was associated with arm muscle strength.

Methods

We measured pinch strength (PS) and hand grip strength (HGS) in 250 adult haemodialysis (HD) patients with corresponding post dialysis multifrequency bio-electrical assessments (MFBIA) with segmental body analysis.

Results

Mean age 64.0 ± 15.6 years, 66% male and 45.6% diabetic. The maximum HGS in the dominant or non-fistula arm was 18.9 ±9.2 kg, and PS 4.09±1.96 kg respectively, with a correlation of $r=0.80$, $p<0.001$. HGS was associated with body cell mass (β 0.37, $p<0.001$, and PS with appendicular muscle mass (β 0.06, $p<0.001$). Both HGS and PS were independently associated with ratio of extracellular water (ECW) to total body water (TBW); β -139.5, $p=0.024$, β -44.8, $p<0.001$ in the arm. The presence of an arterio-venous fistula (AVF) increased the ECW/TBW ratio in the arm from 0.383±0.009 to 0.390±0.012, $p<0.05$.

Conclusion

Muscle strength measured by HGS and PS were associated with both markers of whole body and segmental body composition within the arm,

particularly ECW/TBW. Bioimpedance measurements and assessment of muscle strength should be measured in non-fistula arm.

## Introduction

Patients with progressive chronic kidney disease (CKD) have been recognised for many years to be at increased risk of both muscle weakness and loss of skeletal muscle mass (CKD) [1]. Muscle biopsies have generally shown nonspecific changes typically demonstrating type II muscle fibre atrophy, with biochemical analysis suggesting reduced energy potential, with reduced glycogen reserves and a mitochondrial energy deficit [2,3]. The causes of muscle weakness and muscle loss are complex and typically multifactorial, ranging from reduced dietary protein intake, and urinary protein losses to increased catabolism driven by the inflammatory milieu of CKD, vitamin D deficiency, insulin resistance, testosterone deficiency in men, anaemia, lack of physical activity, depression and protein losses associated with dialysis [1,3,4].

Both muscle weakness and muscle wasting have been reported to be associated with increased mortality risk for patients with chronic kidney disease treated by dialysis (CKD5d) [5-7]. Although some studies have reported a concordance between muscle wasting and muscle weakness, this has not been universal [7,8]. Whereas most studies have used hand grip strength as an assessment of muscle function [5,6], muscle mass has been variously estimated by clinical assessments using anthropomorphic measurements, dual energy X ray absorptiometry (DEXA), and bio-impedance techniques [7,9,10,11].

Haemodialysis patients gain weight between dialysis sessions, and as such hydration status varies during the course of the dialysis week [12]. Both DEXA and multi-frequency bioelectrical assessments (MFBIA) can be affected by hydration status over estimating muscle mass and under estimating body fat when patients are overhydrated [13], and this may account for the results of previous studies failing to demonstrate a strong association between muscle mass and muscle strength [8,9]. As such we wished to determine whether there was a correlation between muscle function, measured by both HGS and pinch strength (PS) [14] on one hand and muscle mass measured by MFBIA post-dialysis.

## Methods

We measured both HGS and PS using the grip-D strength dynamometer (Takei Scientific Instruments Co, Nigata, Japan) and a pinch gauge (Jamar digital plus, Lafayette Instrument, Lafayette, USA ). Patients were instructed and shown how to use the strength gauges, and measurements were made according to the manufacturer's recommendations with patients asked to make their maximal voluntary exertion. Three measurements were made for both arms, and we used the maximal value for each arm. In brief both measurements were made during dialysis treatments with patients sitting. PS was measured with the elbow flexed to 90°, and the wrist in the neutral position, and HGS with the arm dependent and the elbow at 180°.

MFBIA measurements were made with an 8 electrode multi-frequency segmental bioimpedance device (InBody 720, Seoul, South Korea) in CKD5d haemodialysis outpatients attending for their mid-week routine haemodialysis session in two free standing kidney dialysis centres [15]. Patients were asked to empty the bladder, and patients with amputations, pregnancy, and ascites were excluded [16]. Patients unable to stand for 2 minutes were also excluded. MFBIA measurements were made after the dialysis session had ended, needle venepuncture sites had stopped bleeding and dressed with a small plaster, and patients reweighed and time allowed for re-equilibration. MFBIA measured total body water (TBW), intracellular water (ICW), extracellular water (ECW) and body cell mass (BCM). Body composition determined by MFBIA divided the body into fat mass (FM) and fat free mass (FFM). Soft lean tissues were then obtained by subtracting osseus tissues from fat free mass, and appendicular skeletal muscle mass by adding skeletal muscle mass in all four limbs and skeletal muscle mass (SMM) as appendicular muscle mass and that of the trunk. To adjust for body size, FM and SMM were indexed to height squared.Patient co-morbidity was assessed using the Davies-Stoke co-morbidity scoring system [17]. Pre midweek blood samples were taken for measurement of urea, creatinine, haemoglobin, C reactive protein (CRP) and N terminal pro-brain natriuretic peptide (NT proBNP) [15].

This retrospective audit complied with the UK National Health Service (NHS) guidelines for clinical audit and service development, and was approved, and individual patient consent was waived by the Royal Free Hospital Research

and Development office as the audit complied with NHS guidelines (UK NHS guidelines for clinical audit and service development, available at http://www.hra.nhs.uk/documents/2013/09/defining-research.pdf, and http://www.gov.uk/government/publications/health-research-ethics-committees-governancearrangements.

## Statistical analysis

Data is presented as mean ± standard deviation, median (interquartile range), or as percentage. Standard statistical tests were used to analyse data, ( t test, Mann Whitney U test, anova, Chi square test) with appropriate corrections made for multiple testing, where appropriate. Correlation was by Pearson or Spearman analysis, depending upon whether variables were normally distributed. Non-parametric data was log transformed for multivariable backward linear analysis, using all variables with a $p<0.1$ correlation, and then variables were excluded if not significantly statistic, unless they improved the model fit. Models were checked for variable inflation factor and collinearity between variables. Area under the curve (ROC) analysis was performed using Janssen cut off for moderate loss of muscle mass [18].Statistical analysis used Prism 6.0 (Graph Pad, San Diego, USA) and SPSS 21, University Chicago, Chicago, USA). Statistical significance was taken as $p<0.05$.

## Results

PS and HGS were measured in 250 established haemodialysis (HD) patients attending for routine outpatient dialysis; 66% male, 45.6% diabetic, mean age 64.0 ± 15.6 years, median dialysis vintage 30.5 (13.7-64.4) months, median Davies co-morbidity score=1 (1-2). Haemodialysis was by central venous access catheter in 13.2%, right arm arterio-venous fistula or graft in 16.8%, and left arm arterio-venous fistula or graft in 69.2%. The maximum voluntary HGS in the dominant or non-fistula arm was 18.9 ±9.2 Kg, and the voluntary maximal PS recorded were 4.09±1.96 kg for the dominant or non-fistula hand, respectively.

As the HGS and PS were greater for men compared to women we divided the patients according to sex (table 1). Male patients were heavier, with more SMM , but lowerBF. There were no differences between the sexes in patient age, dialysis vintage, ethnicity, co-morbidity score or pre-dialysis haemoglobin, serum albumin, N-terminal brain natriuretic peptide or C reactive protein. More female patients dialysed with central venous access catheters (Chi square 14.9, p=0.001).

There was a positive correlation between the maximum voluntary HGS and PS in the dominant arms ($r=0.08$, $p<0.001$). In terms of body composition, the strongest associations with HGS and PS were for SMM and BCM (table 2,$r=0.43$, $p<0.001$ ). There was no association with body mass index for either HGS or PS.

Taking variables with a univariate association of <0.1 for the dominant arm, a series of step backward multiple regression models were constructed.

The maximum voluntary HGS was independently associated with male sex, BCM, and the ratio of ECW/TBW in the dominant arm, and negatively with age and the Davies co-morbidity score. PS was associated with male sex, appendicular muscle mass, and ratio of ECW/TBW in the dominant arm, and negatively with the Davies co-morbidity score (table 3).

Kidney dialysis patients differ from the general population by having arterio-venous fistula or arterio-grafts for dialysis access. We compared the effect of vascular access on body composition measurements and strength in the arms (table 4). Whereas there was no difference in the ratio of ECW/TBW between the arms of those patients dialysing with a central venous catheter, the arm with a fistula or graft had higher ECW/TBW. Fat mass did not differ between arms with vascular access, however the ratio of lean mass compared to an ideal for an age and sex matched control was greater in the fistula arm compared to the non-fistula arm, as was the lean mass in the fistula arm compared to the corresponding arm in those dialysing with a central venous catheter. HGS and PS were greater in the left arm for those dialysing with right arm vascular access, and conversely stronger in the right arm for those dialysing with left arm vascular access.

There have been a variety of cut off points suggested for muscle loss. We used the Janssen cut off for moderate muscle loss, at <10.75 kg/m$^2$ for men and <6.75 kg/m$^2$ for women [18]. Whereas 126 (76.4%) of men had moderate muscle wasting, only 3 (3.5%) of women had muscle wasting. ROC curves showed an area under the curve for HGS 0f 0.56, p=0.08, with a 90% sensitivity and specificity

at 8.6 kg and for PS, area under curve 0.59, p=0.01 with a 90% sensitivity and specificity at 2.1 kg.Discussion

Although muscle weakness has been repeatedly reported to be associated with increased mortality in dialysis patients [19,20], results of previous studies in dialysis patients have differed with regard to muscle wasting, with some reporting an association between muscle strength measured with HGS and body composition, whereas others found no association, or only a limited association with less than 10% of the variance in muscle strength explained by changed in muscle mass [21,22]. This could be due to changes in hydration status with dialysis [23], depending upon whether measurements are made prior to or post-dialysis, which could potentially influence anthropomorphic measurements, DEXA scans and bioimpedance assessments [13, 24]. Prior to dialysis most haemodialysis patients have gained fluid during the inter-dialytic interval and this fluid gain along with urea, other azotaemic osmolytes and sodium are removed. As such both DEXA and bioimpedance measurements will change pre and post dialysis [12]. DEXA and most bioimpedance devices use a 2 compartmental body composition model dividing the body into fat and fat free mass. As muscle contains more water than fat, this leads to an over estimation of lean body mass pre dialysis, with a reduction in lean body mass post dialysis [24]. More recently a 3 compartmental body composition model has been proposed, dividing the body into adipose tissues, normally hydrated lean tissue and excess water, but even this model still over estimates lean body mass pre-dialysis [25]. As such we measured bioimpedance post dialysis after allowing for

a redistribution of fluid, to overcome these effects on bioimpedance measurements.

Unless muscle is externally stimulated to ensure maximal force contraction [26,27], then measurements of muscle strength in most studies are voluntary, and therefore depend upon patient co-operation and motivation. Despite these caveats, besides the expected changes with age [28] and sex, we did find additional associations between voluntary arm strength and whole body composition, with positive associations with larger body size: including body cell mass, skeletal muscle mass, appendicular muscle mass and negative association withco-morbidity . As with other studies we found no association with body mass index [21].

Compared to previous studies, which have reported on whole body composition and muscle strength we measured muscle strength using both HGS and PS. Although these assessments use different muscle groups [6,29], we found a strong correlation between both methods. However a minimum strength is required for HGS, as the scale starts at 5 kg, whereas for PS much lower strength can be measured. We found that suggested cut off points for muscle wasting [18] may not be appropriate for dialysis patients.

In addition compared to earlier studies we also measured segmental bioimpedance to assess muscle and fat in the arms. There were positive univariate associations between both maximal voluntary HGS and PS in the dominant or non-fistula arm and the ratio of lean arm mass compared to that predicted by age and sex, and a negative associations with the ratio of

ECW/TBW. As dialysis patients may have arterio-venous fistulae or arterio-venous grafts placed in the arms we also compared arm strength according to dialysis vascular access. Patients with vascular access sited in the arm had a higher ECW/TBW and % lean arm mass in the fistula arm. Previous studies have reported that prior to dialysis more fluid is retained in the fistula arm than the contra-lateral arm [30], and even after dialysis the ECW/TBW remains greater in the fistula arm [31]. As right handed patients typically have left sided fistulae, then it was not surprising that both HGS and PS were greater in the dominant right hand. However the difference in strength between the arms was greater for those with a fistula compared to those dialysing with a central venous access catheters. We noted that the observed lean arm tissue was greater to that predicted in the fistula arm. Although the change in blood flow in the arm following arterio-venous fistula creation could have a trophic effect, it also increases fluid retention [32]. Fluid volumes change following dialysis, and this has been reported to lead to changes in muscle mass and fat content of the body measured by bio-impedance [24,32]. As such the observed difference in muscle between the arms could potentially be due to increased fluid retained in the arm, and as such this could account for some of the reported difference in muscle mass and muscle strength. As such it would be preferable to make measurements in the non-fistula arm to improve reliability.

We also noted univariate associations between co-morbidity score, diabetes, serum albumin, urea, creatinine, CRP and NT proBNP and measured muscle strength. Previous studies have also observed that co-morbidity, and

what has been termed "malnutrition-inflammation" is associated with both an increased risk of mortality and muscle weakness [33]. On multivariate analysis we found that the ratio of ECW/TBW in the dominant arm was independently negatively associated with both HGS and PS. An increased ratio of ECW to TBW can be due to either an increase in ECW or a reduction in ICW. Inflammation can cause an increased capillary leak and increased ECW, and inflammation can also lead to a reduction in cell mass, and therefore ICW [34]. As such our results are in keeping with other reports using single frequency bioimpedance demonstrating an association with over hydration and increased mortality [35], and others recording an association between an increased markers of inflammation and muscle weakness [33,36].

Bioimpedance devices differ, ranging from single frequency to multi-frequency devices and from whole body to segmental devices. Previous studies have reported that for body composition, multi-frequency devices provide greater reliability when measuring body composition [37]. Similarly equations derived from one population may not be readily applicable to a different population [38]. We used a multi-frequency device which had been validated against magnetic resonance measurement of muscle mass in a North London population [39]. Whereas other studies have estimated muscle mass from equations based on whole body bioimpedance we measured appendicular muscle mass using segmental bioimpedance [40].To exclude confounding by over hydration in kidney dialysis patients, we measured bioimpedance in a

standardised manner [41], post dialysis when patients were closest to their target weight [42].

We report that for haemodialysis patients HGS and PS are strongly correlated, and can be readily measured during a dialysis session. Both HGS and PS are independently associated with markers of whole body composition, but are also associated with arm composition, in particular the ratio of ECW/TBW in the arm. We also noted that the presence of an arterio-venous fistula was also associated with both functional and compositional changes in the arm, and as such this needs to be considered when comparing cohorts of haemodialysis patients, and measurements should preferably be made not only post dialysis but also in the non-fistula arm.

The authors have no conflict of interest
Author contribution : Yukie Omichi, Methavee Srivareerat, George HB Greenhall, Sanjana Gupta made HGS and PS measurements. Kwanpeemai Panorchan and Andrew Davenport collected MFBIA data. Andrew Davenport

analysed the data. All authors helped revise the manuscript and approved the final version

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Table 1. Patient cohort divided by sex. Values expressed as raw number, mean ±SD, median (interquartile range). As expected male patients were statistically significantly heavier, with greater muscle mass, and measurements of hand grip strength (HGS) and Pinch strength (PS), whereas women had greater percentage fat mass. Extra cellular water (ECW) total body water (TBW).

| | female | male |
|---|---|---|
| number | 85 | 165 |
| Age year | 63.4±15.9 | 64.4±15.5 |
| Diabetic % | 37.8 | 49.7 |
| Dialysis vintage (mo) | 38 (11.9-71.9) | 27.9(13.9-58.2) |
| Caucasoid | 29 | 62 |
| South Asian | 19 | 48 |
| African/Afro-Caribbean | 32 | 43 |
| East Asian | 5 | 11 |
| Central venous catheter | 21 | 12 |
| R arm fistula/graft | 12 | 31 |
| L arm fistula/graft | 52 | 122 |
| Post dialysis weight kg | 68.0±18.9 | 72.3±13.3 |
| Fat free mass kg | 41.2±7.4 | 51.5±9.9 |
| Fat free mass index kg/m$^2$ | 16.3±2.1 | 17.9+2.5 |
| Skeletal muscle mass kg | 22.1±4.5 | 28.2±5.8 |
| Skeletal muscle mass index kg/m$^2$ | 8.74±1.29 | 9.78±1.46 |
| Body fat mas kg | 26.7±5.3 | 21.0±10.3 |
| Body fat mass index kg/m$^2$ | 10.6±5.3 | 7.41±3.7 |
| % body fat | 37.1±11.1 | 28.3±10.4 |
| Lean R arm kg | 2.14±0.61 | 2.92±0.76 |
| Fat R arm kg | 2.28±1.77 | 1.58±1.10 |
| ECW/TBW R arm | 0.381±0.011 | 0.382±0.011 |
| Lean L arm kg | 2.26±0.76 | 3.01±0.75 |
| Fat L arm kg | 2.28±1.79 | 1.56±1.10 |
| ECW/TBW L arm | 0.393±0.013 | 0.385±0.117 |
| Maximum HGS dominant hand kg | 14.8±6.6 | 21.0±9.7 |
| Maximum PS dominant hand kg | 3.16±1.34 | 4.46±2.09 |
| Maximum R hand HGS kg | 14.5±6.3 | 20.1±9.6 |
| Maximum L hand PS kg | 3.13±1.32 | 4.32±2.16 |
| Maximum R hand HGS kg | 13.4±5.6 | 18.6±9.02 |
| Maximum L hand PS kg | 2.49±1.12 | 3.58±1.79 |
| Davies co-morbidity score | 1 (1-2) | 1 (0-2) |
| Haemoglobin g/L | 115.0±12.8 | 112.7±12.6 |
| Serum Albumin g/L | 39.1±3.7 | 39.7±4.0 |
| Serum C reactive protein mg/L | 6 (2-13) | 5 (2-12) |
| Serum N terminal BNP pmol/L | 458 (211-1032) | 322 (136-1071) |

Table 2. Variables associated with maximum voluntary pinch strength and hand grip strength statistically significant on univariate analysis ($p<0.05$). Measurements from dominant or non-fistula arm. Extracellular water (ECW), total body water (TBW) N terminal pro brain natriuretic peptide (NTproBNP).

| | Pinch | strength | Hand grip | strength |
|---|---|---|---|---|
| variable | r | p | r | p |
| Sex (male) | 0.31 | <0.001 | 0.32 | <0.001 |
| Total body water L | 0.36 | <0.001 | 0.37 | <0.001 |
| Body cell mass kg | 0.40 | <0.001 | 0.43 | <0.001 |
| Appendicular skeletal mass kg | 0.39 | <0.001 | 0.27 | <0.001 |
| Lean/ideal lean mass arm % | 0.36 | <0.001 | 0.36 | <0.001 |
| Skeletal muscle mass kg | 0.4 | <0.001 | 0.41 | <0.001 |
| Age years | -0.28 | <0.001 | -0.34 | <0.001 |
| ECW/TBW arm ratio | -0.27 | <0.001 | -0.27 | <0.001 |
| Davies score | -0.24 | <0.001 | -0.26 | <0.001 |
| Log serum creatinine umol/l | 0.30 | <0.001 | 0.29 | <0.001 |
| % body fat | -0.26 | <0.001 | -0.27 | <0.001 |
| Serum urea mmol/l | 0.17 | 0.008 | 0.18 | 0.005 |
| Log NTproBNP pmol/l | -0.21 | 0.001 | -0.19 | 0.003 |
| Serum albumin g/l | 0.16 | 0.01 | 0.21 | 0.008 |
| Diabetes mellitus | -0.20 | 0.002 | -0.16 | 0.011 |
| Fat mass arm kg | -0.15 | 0.024 | -0.14 | 0.044 |
| Body weight kg | 0.15 | 0.02 | 0.16 | 0.014 |

Table 3. Multivariable backward regression models for the maximum voluntary hand grip strength (HGS) and pinch strength (PS) from dominant or non-fistula access arm. Standard error (SE) of β coefficient, standardised β coefficient (st β), confidence limits (CL). Sex (male), Body cell mass (BCM), Extracellular water (ECW), total body water (TBW), C reactive protein (CRP). HGS model fit, r 0.50, $r^2$ 0.29, adjusted $r^2$ 0.27; PS model fit r 0.51, $r^2$ 0.27, adjusted $r^2$ 0.25.

| Variables | β | SE β | St β | t | 95% CL | p |
|---|---|---|---|---|---|---|
| Hand grip strength | | | | | | |
| Sex | 4.11 | 1.27 | 0.21 | 3.2 | 1.61 to 6.6 | <0.001 |
| BCM | 0.28 | 0.10 | 0.22 | 2.8 | 0.08 to 0.49 | 0.006 |
| ECW/TBWarm | -130 | 60 | -0.14 | -2.1 | -24.6 to – 9.7 | 0.034 |
| Davies score | -1.06 | 0.51 | -0.13 | -2.1 | -2.1 to -0.06 | 0.038 |
| Age | -0.08 | 0.04 | -0.14 | -2.1 | -0.16 to-0.01 | 0.039 |
| Pinch strength | | | | | | |
| Appendicular muscle mass | 0.06 | 0.01 | 0.28 | 4.3 | 0.32 to 0.09 | <0.001 |
| ECW/TBWarm | -44.2 | 12.2 | -0.22 | -3.6 | -68.2 to -20.2 | <0.001 |
| Sex | 0.79 | 0.27 | 0.19 | 2.9 | 0.27 to 1.32 | 0.004 |
| Davies score | -0.25 | 0.11- | -0.14 | -2.4 | -0.46 to -0.04 | 0.018 |
| BCM | 0.39 | 0.05 | 0.14 | 0.78 | -0.06 to 0.14 | 0.43 |
| Age | -0.01 | 0.01 | -0.09 | -1.4 | -0.03 to 0.01 | 0.16 |

Table 4..Patients divided according to vascular access site : central venous access catheter (no arm access), right sided arterio-venous fistula or graft (right arm access), or left sided arterio-venous fistula or graft (left arm access). Extracellular water (ECW), total body water (TBW), maximum voluntary hand grip strength (HGS), maximum voluntary pinch strength (PS). Data displayed as mean ±SD. **p<0.01 vs left arm access, *p<0.05 vs left arm access
$^{+}$ <0.05 vs R arm access.

| Variable. | no arm access | right arm access | left arm access |
|---|---|---|---|
| Right arm | | | |
| ECW/TBW | 0.382±0.002 | 0.390±0.012** | 0.383±0.009 |
| Lean mass kg | 2.42±0.73$^{+}$ | 2.92±0.88 | 2.64±0.75 |
| %lean/ideal mass | 116.4±21.1* | 118.1±32.7* | 103.9±21.4 |
| Fat mass kg | 1.7±1.1 | 1.8±1.8 | 1.8±1.3 |
| HGS kg | 16.7±9.8 | 14.9±8.1* | 18.8±8.9 |
| PS kg | 3.36±1.94 | 2.78±1.55** | 4.14±2.20 |
| Left arm | | | |
| ECW/TBW | 0.381±0.002 | 0.390±0.012* | 0.383±0.009 |
| Lean mass kg | 2.43±0.78* | 2.56±0.78 | 2.87±0.84 |
| %lean/ideal mass | 116.7±29.2 | 103.3±18.2* | 113.2±26.9 |
| Fat mass kg | 1.7±1.2 | 1.8±1.7 | 1.8±1.4 |
| HGS kg | 15.9±10.3 | 18.6±9.6 | 16.2±7.4 |
| PS kg | 2.96±1.93 | 3.53±1.91 | 3.11±1.45 |