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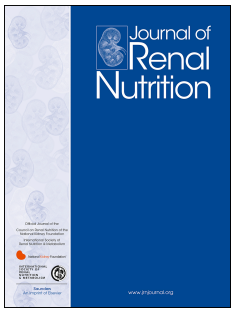

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Handgrip Strength Index: a Novel Parameter which quantifies clinical weakness in people on haemodialysis.

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Abstract: 282 words

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Short title: Handgrip strength in adults on haemodialysis

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Support and financial disclosure

Conflict of Interest Statement

Dr. Johansson has received speaker fees from Abbott.

Dr Ashby has nothing to disclose.

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Ayako Temple has nothing to disclose.

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Abstract

Objective: Muscle strength in people on haemodialysis is associated with nutritional status, quality of life, functional independence and survival. Handgrip Strength (HGS) is simple to measure, but clinical interpretation is limited by the lack of reference ranges for a haemodialysis population. This study aims to define a novel parameter, HGS index, which quantifies degree of clinical weakness specific to a haemodialysis population and to test if this predicts survival.

Methods: In a cross-sectional single centre study HGS was measured in stable participants on haemodialysis. HGS in the well-nourished subgroup, was used to develop a predictive equation for "expected" HGS according to demographic variables. This then was compared to observed HGS resulting in HGS index (%), an individualised parameter indicating weakness due to clinical variables whilst accounting for demographic ~~weakness~~ contributors to strength. The association between HGS index and survival was explored in all participants.

Results: Amongst 427 well-nourished individuals on haemodialysis, HGS was strongly associated with demographic variables and predicted in males by the equation: HGS(kg) = 0.38*height(cm) – 0.31*age(years) – 18, and in females by the equation: HGS(kg) = 0.25*height(cm) – 0.11*age(years) – 16. Amongst 547 participants (22% with protein energy wasting), lower HGS index was associated with diabetes (p=0.004), lower body mass index (p=0.005), lower albumin (p=0.033) and longer dialysis vintage (p=0.007). Over a mean observation period of 2.8 years, quintile of HGS index was strongly associated with survival (p=0.023), and in a Cox Proportional Hazards model, the independent predictors of mortality were age, albumin, body mass index and HGS index.

Conclusion: HGS index, defined as observed relative to expected HGS, is an individualised measure of clinical weakness. It is a novel parameter which independently predicts survival. HGS index improves the detection of clinically relevant muscle weakness in people on haemodialysis, opening up the possibility of earlier, individualised interventions and improving outcomes in this vulnerable group.

Keywords: handgrip; haemodialysis, equation, nutritional status, renal

Introduction

Despite gradual progress over the last decade, mortality in people on haemodialysis remains high, with many centres reporting median survival around 5 years for people in their 60's [1]. Protein energy wasting, noted in 28-54% of people on haemodialysis, could be a contributor to this as it is associated with decreased quality of life and increased hospitalization [2] . A key feature of the clinical diagnosis of protein energy wasting is the determination of muscle mass [3]. However, research has demonstrated that muscle strength is more strongly associated with the risk of mortality than muscle mass in people on haemodialysis [4,5]. Therefore muscle mass alone is not a proxy for strength and therefore muscle quality (ratio of strength to mass) may be better at describing the physiological changes in muscle that occur with aging [6].

Handgrip Strength (HGS) is a functional measure which has been linked to nutritional decline [7,8] and mortality in people on dialysis [9], and outside dialysis has been used to predict mortality [10] and old age disability [11]. Functional measures are often the earliest to exhibit change when the clinical condition deteriorates, and are closely linked to other important outcomes, such as ability to self-care and live independently [12]. HGS is cheap and easy to measure and may be useful for early detection of protein energy wasting, as well as a potential surrogate outcome measure for interventional studies. In addition, HGS is often used in evaluation of sarcopenia, in particular in older people on dialysis [13,14]. In these studies, a wide range of cut-offs and reference ranges are used to determine weakness that is beyond aging, exposing a gap in the determination of the presence sarcopenia and potentially frailty.

Abnormal HGS may be defined by deviation from reference ranges [15–17], often stratified by factors such as age, gender, height and ethnicity [18,19]. Additionally HGS

cut-off values have been used to identify clinically relevant (26 and 16kg) and mobility limiting (30 and 20kg) weakness in males and females over 65, respectively [20 21]. These reference ranges are problematic when applied to HGS values from people on haemodialysis as they have been derived from community dwelling populations and thereby generally reflect weakness of aging. As such, the values from people on haemodialysis fall predominantly within the weakest categories as the inherent clinical weakness and reduced function associated with being on haemodialysis is unaccounted for, thereby leading to a nonspecific tool with limited clinical applications. Haemodialysis specific HGS cut-offs have been used to help identify malnutrition [22] and predict mortality [5] e.g. 28.3kg for males and 23.4kgs for females [5]. However, they are based on crude gender categories without further demographic characterisation according to variables that are strong determinants of HGS e.g. age, height. It is challenging in a study of n=436 to produce reference ranges for all variables which is the approach undertaken in large population studies such as Spruit's UK biobank study with over 500,000 participants [17] which provides HGS ranges for several discrete demographic categories (age, height, sex). An alternative approach is to develop a predictive equation that determines "expected" HGS from demographic features, which can overcome the need to have thousands of participants for every subcategory. Currently, without haemodialysis-specific normative values, abnormal HGS is only obvious in the individual through repeated measures and noting a decline over time, which is how renal clinical guidelines recommend its clinical usage [23].

The lack of reference ranges highlights an important knowledge and clinical assessment gap to be addressed. The aims of this study are: (1) to determine the demographic variables that influence HGS in a well-nourished haemodialysis

population; (2) to determine a prediction equation to calculate an individual's "expected" HGS from these demographic variables; (3) to define a novel, demographically adjusted parameter, HGS index, as the observed HGS as a percentage of the expected HGS to determine degree of clinical weakness observed; and (4) to test if HGS index predicts survival in this group.

Methods

In this cross-sectional study, clinically stable adults were recruited from nine satellite haemodialysis units in an urban mixed-ethnicity renal centre in XXX. Adults (aged 18 years or older) were eligible if receiving dialysis for at least three months, without hospital admission in the previous month, able to consent, did not have a fistula in their dominant arm and able to stand for HGS measurement.

Data collection

HGS was measured once in each participant, immediately prior to a haemodialysis session, to avoid dialysis-associated fatigue [24] which leads to a weakening of maximal grip over the session [25,26]. HGS was measured in the dominant non-fistula hand, using a Jamar® Hand Dynamometer (Sammons Preston, Bolingbrook, Illnois, US). Measurements were undertaken under standard testing conditions: in the standing position, with elbow at full extension, and palm facing inwards, with people supporting themselves as necessary with their free arm. This standing position was selected as opposed to the sitting position as the chair available (e.g. with arms, without arms) is likely to vary between dialysis units. To allow participants to become familiar with the dynamometer, a training (warm up) measurement preceded the single recorded HGS measurement. This is thought to result in an increased grip

strength and could reflect a truly physiological maximum [27]. It has also been shown to be as reliable and instigate less pain than the best of (or mean of) two or three trials [28,29]. A unique assessment feature of this study was including a recording for pain. As this group are vulnerable to hand conditions such as carpal tunnel, pain was recorded on a 100mm visual analogue scale before and after measurements: those with pain scores above 20mm (value selected by researchers) were excluded, since pain confounds the measurement of maximal strength [30]. It was felt to be important by the authors to determine if significant pain was influencing an individual's maximal grip and to exclude these values.

Participants were divided into well and poorly nourished groups using the seven-point Subjective Global Assessment (SGA). SGA is a well validated global nutritional assessment tool used to determine if a person is well-nourished (score 6-7), mildly to moderately malnourished (score 3-5) or severely malnourished (score 1-2) [31]. Demographic and clinical data were also recorded.

Statistical analyses

~~This study was powered so that several groups (age > or ≤ 65 years, ethnic background of black, white and asian and gender) would be well represented. Enough dialysis shifts were targeted with the aim to recruit at least 500 people in total (anticipating at least 20% of this sample to have protein energy wasting).~~

This study size was determined so that the subgroups of age > or ≤ 65 years, ethnic background of Black, White and Asian; and gender would be well represented. A sample size of 30 is commonly considered sufficient (based loosely on the

convergence of normal and t-distributions) for representative parameter estimation in a predictive equation. The study sample size was designed by anticipating protein energy wasting in 20% of participants, a total sample size of 500 was therefore selected to achieve at least 30 well-nourished participants in each of the 12 planned subgroups.

Initial HGS analysis was restricted to well-nourished people (SGA 6 or 7) to define "expected" HGS in well-nourished, relatively stable, individuals on haemodialysis from demographics. Demographic variables associated with HGS were explored with ~~5-fold~~ k-fold cross-validation, which separates training and validation subgroups to ensure development of a generalisable model, but without loss of data [32,33]. The well-nourished group was first separated by gender and then randomly split into five subgroups: for each subgroup, linear regression was used to define predictors of HGS in the remaining well-nourished patients (with the subgroup removed), with prediction by the ~~final~~ resulting model tested and thereby validated in the subgroup (which did not contribute to model development). The mean of each coefficient averaged over ~~An average of~~ these five models was used to provide the coefficients for the prediction equation. Coefficient accuracy (number of significant figures) was selected so that increased accuracy would improve R^2 by less than 0.01. The aim of this stage was to define "expected" HGS in well-nourished dialysis patients, so only demographic predictors (such as age, gender, height and ethnicity) were assessed, and variables influenced by illness (such as comorbid conditions, weight and albumin) were not included.

Subsequently, a novel parameter, HGS index, was defined to quantify the degree of HGS clinical weakness, by comparison with the expected HGS for a stable, well-nourished individual of the same age, height and gender. HGS index was therefore defined as the ratio of observed to expected HGS, expressed as a percentage.

Simple HGS and HGS index were compared using multivariable linear regression in the whole group, in order to define the extent to which each overlaps with clinical and demographic predictors of weakness. Kaplan-Meier survival analysis was used to demonstrate the effect of HGS index on survival, and Cox Proportional Hazards models were used to compare HGS and HGS index as independent predictors of survival, alongside other risk factors.

There was minimal missing data (dialysis vintage was unknown for two participants and was coded as two years). SPSS v25.0 (IBM, New York) was used for survival and regression analyses.

Ethics

This study was approved by the XXX and was performed in accordance with the Declaration of Helsinki, with written informed consent from all participants.

Results

Between May 2010 and June 2015, HGS was measured in 547 participants (aged 18-92, 52% male), of whom 427 (78.1%) were considered to be well-nourished, with SGA score 6 or 7, the rest having mild/moderate (SGA 3-5, n=118, 21.6%) or severe protein energy wasting (SGA 1-2, n=2, 0.4%). Amongst males mean(+/-sd) age was

63.2(14.1) with height 172.6(7.3)cm, weight 76.2(17.1)kg, and BMI 25.5(5.2)kg/m^2, whereas amongst females mean(+/-sd) age was 61.9(15.1), with height 159.7(8.0)cm, weight 70.0(17.2)kg, and BMI 26.2(6.4)kg/m^2. One-hundred and three patients (18.8%) had a BMI over 30kg/m^2 (categorised as obese). A diagram illustrating an overview of patient flow through each stage of the study can be found in supplementary information (Figure S1). Other characteristics of the whole group, well-nourished and poorly nourished subgroups, are provided in Table 1. This sample was drawn from a total population of 1350 people on haemodialysis (in flux over time with new people starting dialysis and some discontinuing due to withdrawal or death or having a transplant). Aside from the participants that were not eligible due to being unable to consent or unable to stand (wheelchair or bedbound), only 5.9% declined to take part in the study.

Amongst the 427 well-nourished participants (aged 18-92, 54% male) mean(+/-sd) HGS was 28.1(10.6)kg with a right-skewed distribution in males and 17.3(6.5)kg in females (Figure 1A). This distribution is however very different from a healthy, non-dialysis population: using large population studies from healthy individuals stratified by age and gender [19] or age, gender and height [17], HGS values in our study are seen to cluster predominantly below the 10th percentile (Figure S2 in supplementary information).

Demographic variables associated with HGS were explored separately in males and females with 5-fold cross-validation and showed strong associations with age and height ~~and gender~~, and ~~a weaker~~ no consistent association with ethnic background (Table 2).

Averages across the five models were used to derive coefficients for ~~a~~ male and female prediction equations:

Predicted HGS(kg) = 0.38*height(cm) – 0.31*age(years) – 18 (males)

= 0.25*height(cm) – 0.11*age(years) – 16 (females)

HGS index was then defined as the observed HGS relative to this prediction as a percentage:

HGS index (%) = 100 x [observed HGS / expected HGS]

HGS index in the whole group (N=547, including well and poorly nourished participants) was normally distributed with mean(+/-sd) 98.5(33.9)%. Mean(+/-sd) HGS index in well-nourished patients was 100.4(32.5)% and in malnourished patients was 91.7(37.6)%. The distribution of HGS index was similar in males and females (Figure 1B). As an example, where the observed HGS matches the expected HGS derived from the predictive equation based on demographics of well-nourished individuals on haemodialysis, the HGS index would be 100%. Where the observed is lower than the expected, the HGS index would be less than 100%.

In linear regression models, simple HGS is associated strongly with demographic variables (age, gender and height) and with the addition of clinical data (dialysis vintage, diabetes status, albumin, BMI) much of the variation ~~in HGS~~ can be explained (R^2=0.430) as is shown in Table 3. In contrast HGS index is most closely associated with illness variables (dialysis vintage, diabetes status and BMI), however these variables only mildly influence it (R^2=0.039, Table 3). In addition, as is

expected, HGS index is not associated with demographic variables as these are included in the prediction equation when calculating expected HGS. Therefore, unlike simple HGS measurement which overlaps substantially with the clinical and demographic data, HGS index adds new information reflecting muscle weakness beyond aging and being on haemodialysis.

Over a mean follow-up duration of 2.8 years (1,530 patient-years total), there were 138 deaths (25.2% of the group). Dividing participants into quintiles of HGS index (with quintile cut-offs at 72, 91, 107 and 126%), higher HGS index quintile at baseline predicted longer survival (p=0.023, Figure 2).

In Cox Proportional Hazards models, HGS index quintile performed at least as well as simple HGS quintile, as being an independent predictor of survival after adjustment for age, albumin and body mass index (p=0.049, Table 4). Being two quintiles weaker (e.g. being in the lowest vs middle quintile of HGS index) was associated with a 26% increased mortality hazard, equivalent on average to an additional mortality of 2.7%, and equal to the mortality disadvantage of being 4 years older, having 3.2 g/L lower albumin, or 7.5 kg/m^2 lower body mass index.

Discussion

This study of 547 participants describes the distribution of HGS in people on haemodialysis and develops a predictive equations for males and females to determine expected HGS values based on people who are well-nourished. Defining HGS index as the ratio of observed to expected HGS as a method to determine degree of weakness, was found to be a strong independent predictor of survival. By defining what is 'normal for haemodialysis' and having a parameter that represents

individualised as opposed to generic weakness, HGS index facilitates early and rapid detection of muscle weakness through a single as opposed to serial measurements, paving the way for potential targeted and timely interventions.

This study confirms the near universal presence of muscle weakness in people on haemodialysis when compared with similar aged individuals without kidney disease. For example, in a study of 3700 healthy volunteers (mean age 63, range 52 – 82 years) from the English Longitudinal Study of Ageing [34], investigators reported a mean HGS of 42.9 and 26.0kg in males and females respectively, which by comparison with these data suggests that HGS is reduced by approximately 30% even in well-nourished people on haemodialysis, regardless of gender. The ~~comparative distribution illustrated in~~ supplementary information demonstrates the limited utility of assessing weakness in people on haemodialysis compared to a healthy reference range since the vast majority of individuals would be defined as weak. A method specific to people on haemodialysis that more accurately determines degree of weakness, which might respond to targeted intervention, is certainly of value in clinical practice.

In other studies of people on haemodialysis, similar demographic predictors of HGS have been observed: in 156 participants from Brazil, Pinto found both height (R=0.57) and age (R=-0.35) to be closely correlated with HGS, suggesting that these predictive relationships are reproducible in different haemodialysis populations. In healthy populations, height is also an important predictor of HGS. With such a strong contribution from a continuous variable, one approach, for example adopted by Spruit in a study of over 500 000 participants [17], is to provide reference ranges

stratified by height. We adopt the alternative strategy, more suited to a smaller population, of defining the expected HGS predicted by demographic variables including height and describing observed HGS as a percentage of this prediction (HGS index). This approach is well-established in other areas of clinical nutrition and physiology: target energy requirements, for example, are calculated using equations which include age, weight, and ethnicity. Similarly, lung function tests are commonly reported as a percentage of the expected value, predicted by height amongst other variables. The concept of HGS index therefore has reasonable precedent in clinical practice.

HGS index is (mostly) not predicted by demographic variables as one component of the index (expected HGS) is already adjusted for age, height and sex. ~~Demographic variables are mostly not predictive of HGS index since expected HGS is already adjusted for these variables. This independence from demographic variables makes HGS index a more meaningful measure of weakness, since simple HGS may be appropriately low due to older age or shorter stature, in the absence of any reduction in strength due to clinical reasons. As expected,~~ Illness variables, such as diabetes status and BMI, however, remain associated with HGS index. HGS index was also found to reduce by 1% for each additional year on haemodialysis (dialysis vintage). HGS declines more rapidly than HGS index over time in people on haemodialysis as it is influenced by aging as well as clinical variables. In Kaysen's paper, males on haemodialysis lost a mean of 3.9% of their HGS over 12 months [35].

A similar relationship between HGS and haemodialysis mortality has been observed previously: for example, Matos reported baseline handgrip in 443 adults and subsequent mortality over a median follow-up of 34 months, finding 17% increased mortality in those with low HGS compared to those with high HGS [5]. The association has been confirmed also in a meta-analysis in which low HGS was predictive of mortality [36], and the relationship between reduced muscle mass and poor survival has been observed in a number of settings [37–39]. Muscle strength rather than muscle mass is thought to be the dominant factor, so it is not surprising that HGS would be associated with increased mortality [9,10]. But since there is much co-linearity between HGS and other clinical parameters as well as aging [10,22] it can be difficult to be clear that HGS is indicating something beyond older age and kidney failure.

~~HGS index however indicates weakness beyond that to be expected from having end stage renal disease on treatment.~~ Since HGS index performs as well as simple HGS as an independent predictor of survival, it can be seen that HGS index captures the value of HGS yet enhances this further by accounting for individual demographic values e.g. height, age, as well as quantifying degree of weakness. This makes HGS index a more useful clinical tool than simple HGS and allows a single measurement to be clinically meaningful.

Being a single centre study enables accurate outcome data and consistency of treatment practices but the external validity is less clear, and it is possible that some of the conclusions are centre specific. In addition, HGS was measured at a single timepoint, with a limited set of other variables available. One challenge in comparing studies is lack of consistency in the method of HGS measurement. Hwang's meta-

349 analysis describes variability in dynamometer type and calibration, arm side
350 (dominant vs non-fistula) and position, duplicate measurement and statistical
351 handling of repeated measures. A recent study determined a standardised method
352 of HGS assessment, which does differ from our study, which was completed
353 previously [40]. Our study was however large and broadly inclusive, with reasonable
354 duration of post-measurement observation, so it is likely that findings are broadly
355 generalisable.
356
357 In conclusion, the reduced HGS of people on haemodialysis is influenced by
358 demographic and clinical variables. HGS index, already demographically adjusted,
359 reflects mostly clinical weakness and is a strong independent predictor of mortality.
360 HGS index therefore detects the degree of muscle weakness in people on
361 haemodialysis, allowing for potential earlier intervention and detection of responses
362 to therapy. Further research demonstrating the clinical utility of this novel parameter
363 is anticipated.
364

Practical applications

This study illustrates the need for haemodialysis specific reference ranges and discusses a novel and demographically adjusted index to interpret handgrip strength developed for people on haemodialysis and predictive of survival.

Handgrip strength has the potential to be implemented routinely in clinical practice providing objective and individualised data on muscle weakness derived from a reference group of well-nourished people on haemodialysis. Our method enables a single (versus ongoing) handgrip strength measurement to provide valuable clinical information, which has not been available to date.

Authors' contributions

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Table 1. Patient characteristics and Handgrip Strength in the well-nourished, poorly nourished and whole group.

	Well-nourished (N=427)		Poorly nourished (N=120)		Whole group (N=547)	
	Med(IQR) / N(%)	**HGS(kg)**	**Med(IQR) / N(%)**	**HGS(kg)**	**Med(IQR) / N(%)**	**HGS(kg)**
All patients		22 (16.5-28)		18.5 (12-25)		21 (15.5-28)
Age (years)	63 (52-75)		65 (53-74)		64 (53-75)	
< 65	227 (53.2)	24 (18-32)	58 (48.3)	19 (13.5-29)	285 (52.1)	23 (18-30)
> 65	200 (46.8)	19 (15-25)	62 (51.7)	18 (11-23)	262 (47.9)	19 (14-25)
Gender						
Male	232 (54.3)	27.5 (21-33)	50 (41.7)	23.5 (17-30)	282 (51.6)	26.5 (20-32)
Female	195 (45.7)	18 (13-21)	70 (58.3)	15 (10-20)	265 (48.4)	18 (12-21)
Ethnicity						
Black	119 (27.9)	24 (18-32)	26 (21.7)	19 (12-28)	145 (26.5)	22 (17-30)
White	143 (33.5)	23 (18-29.5)	41 (34.2)	20 (13-27.5)	184 (33.5)	22 (16.5-29)
Asian/other	165 (38.6)	20 (16-26)	53 (44.2)	16 (11-24)	218 (39.9)	19 (14-26)
Height (cm)	1.68 (1.60-1.73)		1.65 (1.57-1.73)		1.68 (1.59-1.73)	
< 170	248 (58.1)	18 (14-23)	78 (65.0)	16 (11-21)	326 (59.6)	18 (14-22)
> 170	179 (41.9)	28 (22-34)	42 (35.0)	25 (17-31.5)	221 (40.4)	28 (21-33)
BMI (kg/m^2)	25.9 (22.6-29.6)		21.8 (19.7-24.4)		24.8 (21.7-28.9)	
< 25	184 (43.1)	22 (17-28)	94 (78.3)	18 (12-24)	278 (50.8)	20 (15-28)
> 25	243 (56.9)	21 (16-28.5)	26 (21.7)	20 (11-28)	269 (49.2)	21 (16-28)
Vintage (years)	2.1 (1.0-4.3)		2.5 (1.0-6.2)		2.1 (0.9-4.6)	
< 2	212 (49.6)	23 (16-30)	53 (44.2)	17 (13-23)	265 (48.4)	21 (15-29)
> 2	215 (50.4)	21 (17-28)	67 (55.8)	19.5 (11-26)	282 (51.6)	20.5 (16-28)
Comorbidity						
Diabetes	193 (45.2)	20 (16-26)	39 (32.5)	16 (11-23)	232 (42.4)	20 (15-26)
Vascular	103 (24.1)	20 (14.5-26)	32 (26.7)	17 (13.5-21)	135 (24.7)	20 (14-25.5)
Albumin (g/L)	35.0 (32.0-38.5)		33.5 (31.0-37.0)		35.0 (32.0-38.0)	
< 35	196 (45.9)	21 (16-27)	69 (57.5)	19 (13.24)	265 (48.4)	20 (14-27)
> 35	231 (54.1)	22 (18-30)	51 (42.5)	18 (12-27)	282 (51.6)	21 (16-30)

Characteristics are given as N(%) or median(IQR)
HGS: Handgrip Strength (kg)

Table 2. Prediction of HGS by demographic ~~(non-illness)~~ variables, confirmed by cross-validation in 5 subgroups of well-nourished group (N=427), separated by gender.

	Group 1		Group 2		Group 3		Group 4		Group 5		Final model*	
Males	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	SE
Height (cm)	.453	.000	.433	.000	.326	.000	.374	.000	.330	.001	0.38	.080
Age (years)	-.310	.000	-.253	.000	-.353	.000	-.303	.000	-.345	.000	-0.31	.043
Model fit	R^2	p value	R^2	p value	R^2	p value	R^2	p value	R^2	p value	R^2	SEE
Training set	.316	.000	.291	.000	.301	.000	.267	.000	.290	.000		
Validation set	.185	.004	.285	.000	.233	.001	.434	.000	.291	.000	.290	8.94
Females	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	SE
Height (cm)	.263	.000	.247	.000	.193	.001	.307	.000	.235	.000	0.25	.052
Age (years)	-.086	.009	-.090	.013	-.146	.000	-.093	.004	-.118	.000	-0.11	.029
Model fit	R^2	p value	R^2	p value	R^2	p value	R^2	p value	R^2	p value	R^2	SEE
Training set	.164	.000	.144	.000	.204	.000	.196	.000	.163	.000		
Validation set	.209	.004	.332	.001	.064	.087	.088	.050	.191	.007	.168	5.89

~~Validation group characteristics are given as mean sd or N %, as appropriate.~~
~~HSG: handgrip strength~~
SE: standard error of the coefficient
SEE: standard error of the estimate
*Final model validated in the complete data set

Table 3. Demographic and clinical predictors of Handgrip Strength and Handgrip Strength Index in the whole group (N=547)

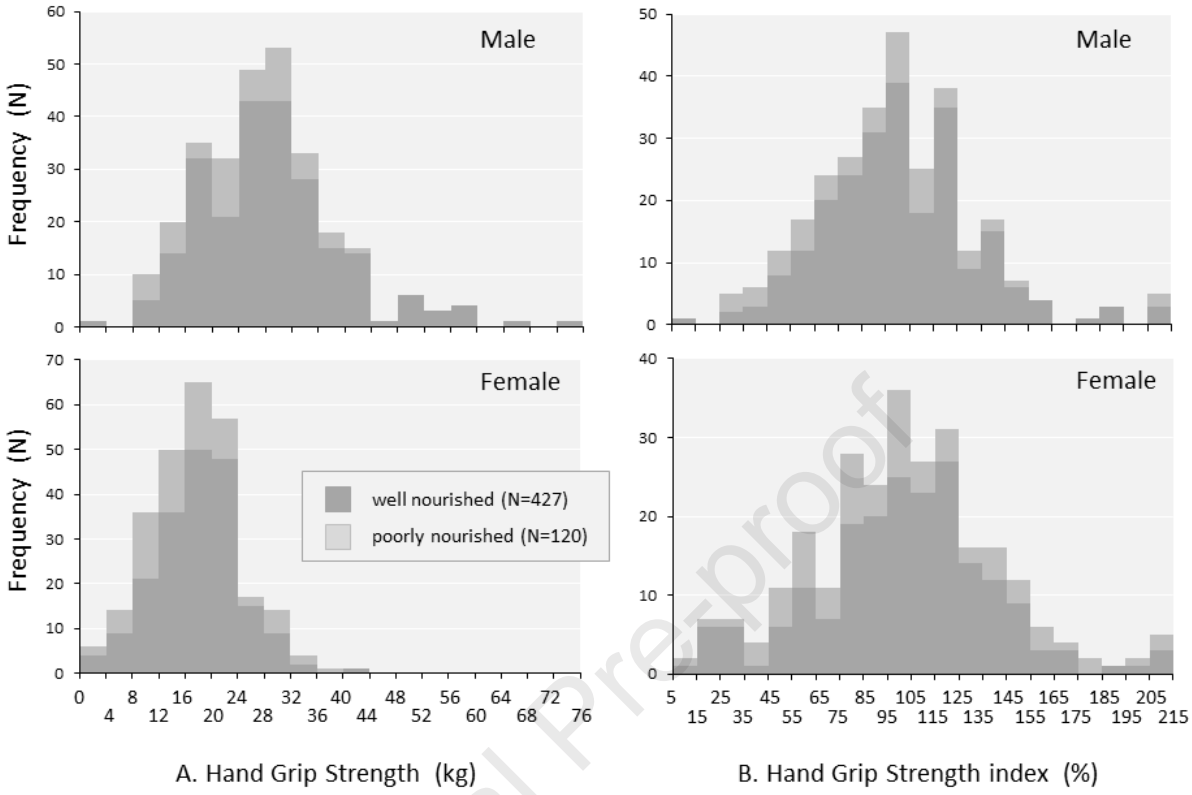
	Handgrip Strength (kg)				Handgrip Strength Index (%)			
	Univariable		Multivariable[a]		Univariable		Multivariable[b]	
	R	p value	B	p value	R	p value	B	p value
Age (year)	-0.277	.000	-0.169	.000	0.037	.390		.083
Gender (Female)	-0.504	.000	-6.637	.000	0.019	.649		.881
Ethnicity (Black)	0.129	.003		.294	0.061	.153		.305
Height (cm)	0.537	.000	0.322	.000	-0.019	.655		.662
BMI (kg/m^2)	0.040	.345	0.186	.002	0.107	.012	0.122	.005
Vintage (year)	-0.097	.024	-0.243	.007	-0.105	.014	-0.118	.007
Diabetes	-0.119	.005	-2.370	.001	-0.086	.045	-0.128	.004
Vascular	-0.107	.013		.219	-0.103	.016		.130
Albumin (g/l)	0.138	.001	0.169	.008	0.111	.010	0.090	.033

[a]adjusted R^2 = 0.430 for the final model
[b]adjusted R^2 = 0.039 for the final model
Beta missing for terms excluded from the final model

Table 4. Predictors of survival by Cox Proportional Hazards model in the whole group (N = 547)

		Univariable			Multivariable With HGS			Multivariable With HGS index		
		HR	**(95% CI)**	**p value**	**HR**	**(95% CI)**	**p value**	**HR**	**(95% CI)**	**p value**
Age	(year)	1.06	(1.05-1.08)	.000	1.06	(1.05-1.08)	.000	1.06	(1.05-1.08)	.000
Albumin	(g/L)	0.92	(0.89-0.96)	.000	0.92	(0.89-0.96)	.000	0.93	(0.89-0.97)	.000
BMI	(kg/m^2)	0.96	(0.93-0.99)	.009	0.96	(0.93-0.99)	.014	0.97	(0.94-0.99)	.029
HGS	(quintile)	0.74	(0.65-0.84)	.000			.053			
HGS index	(quintile)	0.87	(0.77-0.98)	.023				0.89	(0.78-0.99)	.049
Ethnicity	(Black)	0.49	(0.30-0.79)	.004			.250			.303
Vascular		1.49	(1.04-2.12)	.028			.296			.394
Vintage	(year)	1.02	(0.98-1.06)	.290			.382			.467
Gender	(Female)	0.84	(0.60-1.18)	.309			.734			.689
Diabetes		1.20	(0.85-1.68)	.289			.899			.962

Survival censored for moving out of area or at study end, not censored at transplantation
HGS: Handgrip strength
HR: hazard ratio
CI: confidence interval



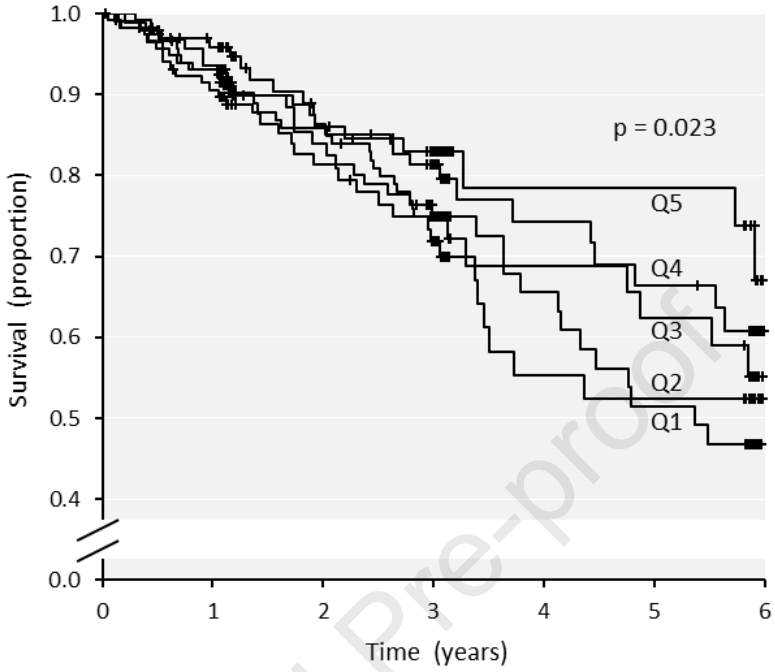


Figure 1. Distribution of Handgrip Strength and Handgrip Strength index. (A) Left panels: Handgrip Strength (simple, without any adjustment) in well-nourished and poorly nourished participants (B) Right panels: Handgrip Strength index (percentage of HGS expected derived from a well-nourished haemodialysis population, adjusted for age, gender and height) in well-nourished and poorly nourished participants. Upper panels: males. Lower panels: females.

Figure 2. Patient survival by Handgrip Strength index. Patients were separated by baseline Handgrip Strength Index into quintiles (Q1-Q5) with quintile cutoffs at 72, 91, 107 and 126%. Survival was censored at the end of observation, or at transplantation or transfer to another centre.

Credit Author Statement

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