association between HGS, inspiratory muscle strength an EC, an to assess the reliability of the HGS in hemo ialysis patients.

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This cross-sectional stu y was con ucte between May 2013 an January 2015 in the hemo ialysis unit of the Santa Casa e Cari a e e Diamantina Hospital an the Car iovascular Rehabilitation Laboratory (LABCAR) of the Universi a e Fe eral os Vales Jequitinhonha e Mucuri (Diamantina-Minas Gerais state, Brazil). The research was carrie out in accor ance with the eclaration of Helsinki (2013) an was approve by ethics committee of the Universi a e Fe eral os Vales o Jequitinhonha e Mucuri (protocol 088/12). All the patients gave their written informe consent before participating in the stu y.

ESRD patients ol er than 18 years who were receiving hemo ialysis treatment three times a week for at least six months an ha an arteriovenous fistula for hemo ialysis access were inclu e in the stu y. Exclusion criteria were contrain ications or inability to perform the exercise tests. The sample size was calculate a priori, consi ering a correlation coefficient of 0.76 between MIP an HGS [18], statistical power of 99% an alpha error of 1%. The sample size was estimate in 19 volunteers.

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The selecte patients un erwent clinical evaluation by nephrologists following anthropometrics measurements [weight, height, bo y mass in ex (BMI) an waist circumference] an evaluation of HGS, inspiratory muscle strength an EC. All evaluations were performe uring a week on ialysis ays, always on the same ay shift, in the following sequence: imme iately before first weekly hemo ialysis session – anamnesis an anthropometric measurements; imme iately after secon weekly hemo ialysis session – inspiratory muscle strength; imme iately before thir weekly hemo ialysis session – HGS an EC. Prior to all evaluations the volunteers remaine seate for 10 minutes. The investigators were blin e to test results, an all volunteers ha previously been traine to perform the functional tests. After 6-to 8-week (trial 2) patients performe the secon HGS [20]. The interval forms part of a control perio in a clinical trial. Pre- an post- ata were use to reliability analysis.

H (HG)

The HGS was obtaine using Jamar® mechanical ynamometer with a precision of 0.5 kg (Sammons Preston, Masan, Korea), in the arm without arteriovenous fistula [14,16,21]. The volunteers remaine seate with the arm an forearm in neutral position an 90° at elbow flexion. Three measurements were performe with intervals of about 60 s between each run an the highest score was recor e in kilograms. HGS values less than the 10th percentile of a Brazilian-base reference stu y were consi ere low HGS [22].

I y

Respiratory muscle strength was etermine using a previously calibrate aneroi vacuum manometer (MV-150/300, Ger-Ar, São Paulo, Brazil) equippe with a 2 mm iameter hole in the nozzle to compensate for the pressure change in uce by the oropharynx muscles, following recommen ations of American Thoracic Society/ Europen Respiratory Society [23]. MIP was evaluate base on resi ual volume while the volunteers were seate , an the highest value of three vali measurements was retaine [23]. The measurements were consi ere acceptable if the variance between them was less than 10%. Respiratory measurements are shown as absolute an relative values base on the percentage achieve compare to the maximum pre icte by age an sex [24]. IMW was efine as MIP less than 70% of the pre icte value [23].

E C y (EC)

EC was evaluate by the Incremental Shuttle Walk Test (ISWT) [25]. Volunteers were instructe to walk or run [26] in a 10 m corri or an the minimum spee was etermine by an au io signal. The ISWT has 12 progressive intensity levels, an the test is complete when the volunteer either completes the 12 levels of intensity or fails to reach the minimum spee require on a given level two consecutive times [11,27,28]. The istance walke was recor e , an the pre icte values were estimate [29]. Prior to ata collection, the test-retest reliability of the ISWT was evaluate in twenty-two hemo ialysis patients [age, 55.0 years (95% CI 49.4–60.7)] an showe an intra-class correlation coefficient of 0.90 (95% CI 0.77-0.95).

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After 6-to 8-week anthropometric measurements were re-evaluate an patients performe the secon HGS (trial 2). Patients were instructe to maintain their habitual lifestyle uring interval an all were weekly monitore . The same researcher applie all the tests an the HGS followe exactly the same protocol in both trials. Test–retest was use to etermine the relative reliability. Stan ar error of measurement (SEM) an minimal etectable change (MDC) scores were calculate to etermine the absolute reliability of the HGS.

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Date analysis was performe using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). The normal istribution an homosce asticity was assesse by Shapiro Wilk test an Levene test, respectively. Categorical variables are presente as absolute an relative frequencies, an continuous variables are presente as the mean (95% CI). Correlation analysis was carrie out using the Pearson or Spearman tests (continuous variables), as appropriate. We consi ere a mo erate to goo correlation when "r"=0.50 to 0.75 an values above 0.75 were consi ere to represent a strong or excellent correlation [30]. The associations between HGS an MIP an EC were assesse by univariate regression analysis, followe by stepwise multivariate linear regression analysis, with a justment for age, sex an BMI. The comparisons of the HGS between groups stratifie by MIP (with or without IMW) were performe by unpaire two-taile t-tests. Data from the ISWT (istance walke) was ivi e into tertiles. The tertiles were efine by stratifying the sample into three ifferent EC levels to verify the effectiveness of the HGS in i entifying ifferent functional status (low, mo erate an high) [31,32]. The comparison of the HGS results among groups ivi e by EC levels was performe by the one-way analysis of variance with a post hoc analysis by Bonferroni test. To assess the accuracy of using HGS to iscriminate between those who ha low inspiratory muscle weakness an low EC, a receiver operating characteristic (ROC) curve was constructe . The area un er the curve was calculate to represent the accuracy of the test at iscriminating those with inspiratory muscle weakness an low EC. An area un er the curve of 1.0 correspon s to perfect iscrimination. The ROC curve constructe was also use to etermine the sensitivity an specificity of ifferent cut-off values of the HGS for the pre iction of inspiratory muscle weakness an low EC. The optimal cut-off value was efine by the value with the best combination of sensitivity an specificity. The test-retest reliability of ata for all repeate tests was assesse with the intra-class correlation coefficient (ICC), mo el alpha, 2-way ran om effects mo el. We consi ere an ICC ≥ 0.90 as "excellent" [33]. The absolute reliability was evaluate by stan ar error of measurement (SEM) for repeate measures an minimal etectable change (MDC) scores following formulas previously [34] escribe . SEM was calculate by following equations: SEM=SD * √ (1-r), where r=ICC for the participant group. The MDC at in ivi ual an group levels were calculate at 90% CI (MDC90). The MDC90 was calculate as: MDCin iv=SEM * 1.65 * √2, where the 1.65 represents the z-score at the 90%CI. The √2 represent the account for errors associate with repeate measures. Differences between trials 1 an 2 were evaluates by Wilcoxon test an agreement by Blan –Altman plot. The significance level set at 0.05 in all analyses.

Forty-one ESRD patients were selecte an 36 volunteers were enrolle in the stu y (one i not provi e consent, one ha angina an three were unable to perform all the steps of the evaluation protocol). The baseline characteristics are shown in Table 1. The volunteers were pre ominantly male (66.7%) an with overweight. Systemic arterial hypertension was the most prevalent etiology of ESRD (50.0%) an kt/v in exes of 1.6 (95% CI 1.5–1.7) emonstrate the efficiency of hemo ialysis treatment. All volunteers were taking vitamin C an B complex, an 31 (86.1%) were using erythropoietin.

Figure 1: Graph of inspiratory weakness.

Figure 2: Graph showing sensitivity values.

possible to verify the agreement between trials 1 an 2, with a bias of 0.5 kg, representing a ifference lower than 1.5% between then (see S1 Table Original ata from HGS).

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To the best of our knowle ge, this is the first stu y to emonstrate that the re uctions of the peripheral muscle strength are associate with the inspiratory muscle strength an EC in hemo ialysis patients. In a ition, the HGS is able to i entify patients with IMW an low EC. The main fin ings of the present stu y were: (1) the association between HGS an MIP an between HGS an EC; (2) HGS cut-off values to i entify patients with IMW an with low EC; (3) the high reliability of the HGS. These results have important clinical meaning, as HGS is an easy-to-perform metho with known prognostic values an important for the nutritional evaluation of this population [14]. Moreover, can also be use on a large scale for screening, risk stratification an functional assessment in the hemo ialysis units.

As previously reporte , changes in the characteristic of muscle structure an function of people with ESRD may a versely affect muscle strength an en urance [35]. Re uction of the oxi ative capacity, increase of protein epletion, vitamin D eficiency an chronic inflammation are cause of worse of muscular function [36]. Thus, the re uction of muscular strength in these patients may also be manifeste by the weakness of the respiratory muscles. The strongest association between MIP an HGS suggests a worse of global muscular function in affecte patients, a common consequence of ESRD [3].

It is known that the strengthening of the upper trunk portion is ecisive for increasing the strength of the upper limbs, as well as the MIP [37]. Correlations between upper limb strength an respiratory muscle strength have been emonstrate in populations with a functional impairment [18,19,38,39], similar results to those observe in the present stu y. In a ition, we observe that HGS was ifferent between in ivi uals with an without IMW, which emonstrates the ability of the HGS, as a measure of muscle function capable of i entifying

Base on SEM showe in Table 3 (1.3 kg), there is a 68% probability that a repeate measure of the test will be within 1 SEM an there is a 96% probability that a repeate test will be within 2 SEM (2.6 kg). This information is extremely useful in clinical practice.

We also calculate the MDC90, a score use to ifferentiate a true change from an in ivi ual variation in the test. Clinically is use to etermine whether a single patient has ma e a real improvement. The value of the MDC90 showe for HGS (3.1 kg) was close to 3.4 kg foun in a previously stu y [46]. Segura-Ortí an Martínez-Olmos (2011) evaluate the highest HGS value in both ominant an non ominan arms in ol er patients an we evaluate the highest value in the arm without arteriovenous fistula in younger in ivi uals. In a ition the time frame of the test–retest assessment was longer in our stu y (6-8 weeks). Despite the ifferences pointe out in the HGS assessment protocols an in the sample characteristics between our stu y an the previous stu y, excellent reliability was presente in both. This emonstrates the high reliability of the HGS in this population.

Some limitations nee e to be a resse . The sample of the present stu y was compose of younger in ivi uals with less morbi ity than those observe in other stu ies. One possible explanation is that this stu y was con ucte in a region with a low human evelopment in ex, where car iovascular iseases, such as hypertension an iabetes are early manifeste . In a ition, in this region, specialize health services (nephrology) are ifficult to reach the population, elaying the iagnosis an clinical management of renal isease. Many in ivi uals, especially the el erly, ie before starting ialysis. The HGS values of the present stu y sample were close to those observe by other authors who stu ie in ivi uals with similar age [16]. However, we believe that the characteristics of our sample may limit external vali ation. Finally, the criteria use for EC classification was base on tertiles of the ISWT. Because the ISWT is a functional test with a high correlation with the car iopulmonary exercise test an that in ivi uals can achieve values of peak oxygen uptake similar to those obtaine in the maximal exercise test at ISWT, we believe that this limitation i not influence the results.

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Base on these results, we can conclu e that HGS is a reliable outcome measures an is irectly relate to the inspiratory muscle strength an EC of hemo ialysis patients. Being a simples an easy to perform test, the HGS can be applie in large scale in the hemo ialysis units. In this context, the HGS measurement becomes a useful tool for functional evaluation an monitoring of this population. Consequently, allowing early etection of functional impairment an contributing to the planning of therapeutic strategies for the rehabilitation.

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