ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Correlation of physical function and physical activity with muscle mass measured with computed tomography in adult hemodialysis patients

Estudio de correlación de la funcionalidad física y la actividad física con la masa muscular medida con tomografía computarizada en pacientes adultos en hemodiálisis

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Abstract

Background: muscle mass (MM) plays an important role in the physical function of hemodialysis patients; however, muscle mass measurement can be unreliable and expensive. In contrast, the measurement of physical function (PF) is simple and inexpensive and may serve as an alternative. The aim of this study was to correlate the measurement of MM by computed tomography (CT) with physical function measurements and physical activity (PA) levels in HD patients.

Methods: this was a cross-sectional study that included 38 HD patients from a single HD clinic. Each participant had a CT scan to measure mid-thigh muscle mass. Physical function tests were assessed using the six-minute walk test (SMWT), handgrip strength (HGS) test, 5 x sit-to-stand test (STS5), timed up and go test (TUGT) and Short Physical Performance Battery (SPPB), while physical activity levels were measured using the Godin-Shephard leisure-time physical activity questionnaire. Correlation analysis was used to examine the relationship between variables.

Results: handgrip strength was strongly positively correlated with thigh muscle area (r = 0.656, p ≤ 0.001) and weakly correlated with arm muscle area (r = 0.396, *p* = 0.002), SMWT (r = 0.373, *p* = 0.004), SPPB (r = 0.269, *p* = 0.041) and physical activity (r = 0.323, *p* = 0.013). There was also a trend for an inverse correlation between handgrip strenght and TUGT (r = -0.235, *p* = 0.076). Positive correlations were found between the thigh muscle area and the SPPB (r = 0.339, *p* = 0.009) and PA (r = 0.293, *p* = 0.025), while there was a trend for an inverse correlation between thigh muscle area and STS5 (r = -0.256, *p* = 0.052).

Conclusion: several measures of PF and strenght were correlated with objectives measurements of MM, thus provide options for low-cost measurements related to muscle mass.

Keywords:

Hemodialysis. Muscle mass. Handgrip strength. Physical function. Computed tomography.

Received: 07/12/2023 • Accepted: 21/04/2024

Acknowledgements: we are grateful to the nursing staff in the dialysis unit at Hospital General de México.

Funding: the National Council of Science and Technology (CONACYT) (CVU: 708803) and the Clinical Research Program of the International Society of Nephrology provided a grant for the first author and corresponding author.

Author contributions: GMA and RVO designed the study. GMA was the main author of the manuscript, assessed nutritional status, collected, and analyzed the data. RVO and KRW supervised the project and gave final approval to publish the manuscript. MPN supervised the collection of data and statistical analysis. KRW and PB assisted the methodology of the clinical trial, interpretation of the results, revised the content of the manuscript, writing the manuscript and discussion of results and gave final approval to publish the manuscript. MRC, RH and MOB assisted in the interpretation of the results and writing the manuscript.

Conflicts of interest: the authors declare no conflicts of interest.

Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Martín-Alemañy G, Pérez-Navarro M, Wilund KR, Hernández R, Bennett PN, Oseguera-Brizuela M, Reyes-Calderas MÁ, Valdez-Ortiz R. Correlation of physical function and physical activity with muscle mass measured with computed tomography in adult hemodialysis patients. Nutr Hosp 2024;41(5):1010-1016
DOI: http://dx.doi.org/10.20960/nh.05069

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Resumen

Antecedentes: la masa muscular (MM) juega un papel importante en la funcionalidad física de los pacientes en hemodiálisis; sin embargo, la medición de la masa muscular en esta población de pacientes puede ser poco confiable y costosa. Por el contrario, la medición de la función física (FF) es simple, económica y puede servir como alternativa. El objetivo de este estudio fue correlacionar la medición de la MM mediante tomografía computarizada (TC) con la funcionalidad física y los niveles de actividad física (AF) en pacientes en HD.

Métodos: se realizó un estudio transversal que incluyó a 38 pacientes en HD de una clínica de hemodiálisis. Se utilizó la TC para medir la masa muscular del muslo medio de cada participante. Se midió la funcionalidad física con la prueba de la caminata de seis minutos (SMWT), la dinamometría de mano (HGS), la prueba de sentarse y levantarse cinco veces (STS5), la prueba de levantarse y caminar (TUGT) y la Batería de Desempeño Físico Corto (SPPB), mientras que los niveles de actividad física se midieron utilizando el cuestionario de actividad física de Godin-Shephard "Leisure-Time Physical Activity Questionnaire". Se utilizó un análisis de correlación para examinar la relación entre las variables.

Resultados: la dinamometría de mano se correlacionó positiva y fuertemente con el área muscular del muslo (r = 0,656, $p \leq 0{,}001$) y débilmente con el área muscular del brazo (r = 0,396, $p = 0{,}002$), SMWT (r = 0,373, $p = 0{,}004$), SPPB (r = 0,269, $p = 0{,}041$) y actividad física (r = 0,323, $p = 0{,}013$). También se encontró una correlación inversa no significativa entre la dinamometría de mano y el TUGT (r = -0,235, $p = 0{,}076$). Se encontró una correlación positiva entre el área muscular del muslo y el SPPB (r = 0,339, $p = 0{,}009$) y la AF (r = 0,293, $p = 0{,}025$), mientras que se encontró una correlación inversa no significativa entre el área muscular del muslo y STS5 (r = -0,256, $p = 0{,}052$).

Conclusión: varias medidas de la función física y la fuerza se correlacionaron con mediciones objetivas de la masa muscular, proporcionando así opciones para mediciones de bajo costo relacionadas con la masa muscular.

Palabras clave:

Hemodiálisis. Masa muscular. Dinamometría de mano. Funcionalidad física. Tomografía computarizada.

INTRODUCTION

Skeletal muscle tissue is one of the major tissues affected by chronic kidney disease (CKD) (1). It is well known that individuals undergoing hemodialysis (HD) experience loss of muscle mass (MM) due to many factors, including the dialysis procedure *per se*, which induces a catabolic state, as well as insufficient food intake; multiple endocrine disorders; persistent inflammation; metabolic acidosis; and physical inactivity, among other fractors (2).

The loss of muscle mass also reduces physical function (PF) (3), and reductions in MM and PF are directly associated with premature death, poor quality of life, frailty, disability and hospitalizations (1,4-8).

Low level of physical activity (PA) are a common feature in dialysis patients (9) and this may be either a cause or consequence of the reduced MM in this population (10).

The measurement of MM can be complicated, as a patient´s hydration status can impact assessment techniques such as anthropometry and bioelectrical impedance. While there are accurate methods for determining MM that are not influenced as much by hydration status, including computed tomography (CT) and magnetic resonance imaging (11), these techniques are relatively costly, so have limited clinical application.

The measurement of PF and handgrip strength (HGS), which can be an indirect measurement of MM functionality, is low cost and easy to perform. PF can be evaluated by different clinical methods, such as the six-minute walk test (SMWT), HGS, 5 x sit-to-stand test (STS5), timed up and go test (TUGT), or Short Physical Performance Battery (SPPB). The relevance of measuring PF in HD patients has been described in some studies. Isomaya et al. (4). showed that low MM alone was not associated with an increased risk of mortality, but low muscle function (muscle strength) irrespective of the appropriate muscle stores increased the risk of mortality by 98 %. They concluded that muscle atrophy does not explain the alterations in muscle function (4) and that MM and PF are two domains of skeletal muscle tissue that can be affected by different factors (12). In similar studies, younger HD patients with greater mid-thigh muscle area had poorer PF measured with the six-minute walk test than elderly subjects with smaller muscle area who were not on dialysis. This was not explained by the size of the muscle mass or comorbid conditions (3).

Given this background, our primary aim was to determine the correlation between the measurement of MM by CT and simple and low-cost PF tests and PA assessments. As a secondary analysis, we explored the correlation between the measurements of anthropometrics with CT, PF and PA as well as the correlation between muscle strength measured with HGS and anthropometrics, CT muscle mass and PA.

MATERIALS AND METHODS

STUDY DESIGN AND PATIENTS

This was a cross-sectional study that was conducted in accordance with the ethical standards described in the1964 Declaration of Helsinki. This study was approved by the ethics committees with the registration number DI/18/105-B/04/021. Informed consent was obtained from all subjects involved in the study. The inclusion criteria were as follows: regular HD two or three times a week, age > 18 years and ability to perform physical function tests. Patients with amputation, hospitalization in the last 3 months, unsatisfactory attendance at HD sessions, pregnancy, severe dyspnea, femoral fistula and orthopedic or neurological compromises or cognitive alterations affecting their participation in the study were excluded.

PHYSICAL FUNCTION TESTS

PF was assessed using the five repetitions of the sit-to-stand test (STS5), which measures the muscle strength of lower limbs, and the Short Physical Performance Battery (SPPB) (13), which measures the global function of patients. These PF tests were chosen because both provide information about lower extremity function, which we want to compare with the MM of the mid-thigh muscle. The STS5 measures the time taken to complete 5 repetitions of the sit-to-stand test. To conduct this test, we used a chair with a height of 42 cm that was placed next to a wall, and we asked patients to fold their arms across their chest and stand up and sit down five times as quickly as possible. We record time from the initial sitting position to the final standing position. The SPPB is a well-validated test and measures three different dimensions of PF: 4-meter gait speed, chair stand (STS5), and standing in three different positions for assessment of balance. Each of these tasks are assigned a score ranging from 0 to 4, with 4 indicating the highest level of performance. The scores from each tasked are summed, providing a final score with a range of 0 to 12, where the highest scores indicated better PF (13).

Other measurements for PF were the SMWT and TUGT. The SMWT involved walking back and forth along a 22 m course (two 10-m straight lines connected by two 1-m curves) in a corridor for 6 min. We used the protocol of the American Thoracic Society. Subjects were allowed to rest in case of fatigue or pain. For the TUGT, we asked the patient to rise from a standard armchair, walk 3 meters, turn around, and return and sit down again, with time to complete the task measured in seconds.

HANDGRIP STRENGTH

Although the measurement of MM was performed in the mid-thigh muscle, we also measured handgrip strength using a hand dynamometry (Smedley III; Takei Scientific Instruments, Niigata City, Japan). Patients were seated in a relaxed position with shoulders adducted with neutral rotation, elbow in a 180° extension, forearm and wrist in a neutral position and they were asked to squeeze the dynamometer as hard as they could for 5 seconds (14). The measurement was taken 3 times, and the average of the 3 measurements was recorded as the handgrip strength. We used the European Working Group on Sarcopenia in Older People II (EWGSOP II) criteria to evaluate the muscle strength (15).

For patients who had a fistula, the measurement was performed with the hand opposite to the fistula; for patients with a catheter, the measurement was performed using the dominant hand.

PHYSICAL ACTIVITY

To assess PA, we used the physical activity questionnaire of the University of Laval, which has been shown to be sensitive and reproducible in our population (16). This questionnaire lists nine different types of activities, assigns each of them a caloric expenditure, and measures the kilocalories from PA in 24 hours. We measured PA on a different day of the weekend or the HD session.

MUSCLE MASS ASSESSMENT AND NUTRITIONAL STATUS

Acquisition of images was performed twice using 2 identical CT scanners (Siemens Somatom 128 slices, 2011) without the use of iodinated contrast. Measurements of the muscle tissue were performed at workstations (Carestream Vue PACS) at half of the femur in each patient. The protocol used was a 0.8 mm slice thickness with a 3 mm reconstruction in a soft tissue window. The CT scanner tube voltage was on average between 100 and 120 kV, exposure varied from 50 to 200 mAs, and a soft tissue kernel was used.

A freehand ROI tool was used to draw the margins of the muscle tissue and aponeurosis to calculate the thigh muscle area (quantity of muscle mass) and intramuscular lipid content via attenuation (density values), expressed in Hounsfield units (17). Any increment would express the substitution of fat tissue for muscle in the measured area (Fig. 1).

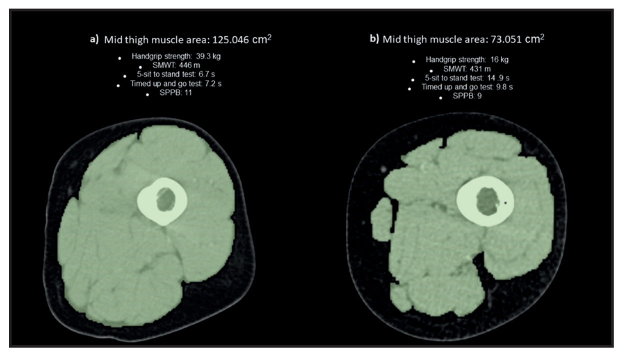

Figure 1.

Representative computed tomography images of the mid-thigh muscle area and physical function tests of two hemodialysis patients.

Anthropometric measurements were taken with a Lange skinfold caliper by a trained dietitian (G.M.A.) to estimate mid-arm muscle circumference and arm muscle area; these measurements were performed before the HD sessions when the patients were close to their dry weight. According to Heymsfield et al., we decided to use the bone-free arm muscle area and the arm muscle circumference formulas to evaluate and classify the muscle mass, also the midarm circumference was measured midway between the tip of the acromion and olecranon process (18). The following formulas were used to estimate mid-arm muscle circumference and bone-free arm muscle area (16):

- Mid-arm muscle circumference: Mid arm circumference – (π x triceps skinfold thickness)
- Bone-free arm muscle area:
  - Males = $[(\text{midarm circumference (cm)} - \pi \times \text{triceps (cm)}]^2 / 4\pi) - 10$
  - Females = $[(\text{midarm circumference (cm)} - \pi \times \text{triceps (cm)}]^2 / 4\pi) - 6.5$

Nutritional status was evaluated using the malnutrition inflammation score (MIS). This is a validated tool frequently used to assess the malnutrition status of patients. A higher score reflects a more severe degree of malnutrition and inflammation (19).

STATISTICAL ANALYSIS

To evaluate the distribution of each quantitative variable, we used the Kolmogorov-Smirnov test, and according to the data distribution, we report the data as the means with standard deviations or medians with interquartile ranges. Categorical variables are presented as absolute numbers and proportions. To evaluate the direction and strength of the association between the muscle mass measured with the CT and the PF tests, we used Pearson's correlation coefficient, and a *p*-value < 0.05 was considered statistically significant. SPSS version 21.0 was used to analyze the data.

RESULTS

BASELINE CHARACTERISTICS

We analyzed 38 patients with a mean age of 33 ± 10.8 years, 52.6 % (*n* = 20) of the patients were male, and the etiology of kidney failure was unknown in most cases (71.1 %). Baseline scores for all PF tests are shown in table I.

CORRELATION BETWEEN THIGH MUSCLE AREA, PHYSICAL ACTIVITY, AND PHYSICAL FUNCTION TESTS

Positive correlations were found between mid-thigh muscle area and SPPB (r = 0.339, *p* = 0.009) (Fig. 2) and physical activity (r = 0.293, *p* = 0.025) (Fig. 3). An inversely correlation was also found between mid-thigh muscle area and STS5 (r = -0.256, *p* = 0.052) (Fig. 4). No significant correlations were found between the thigh muscle area and the six-minute walk test nor the TUGT.

CORRELATION BETWEEN ARM MUSCLE AREA AND MID-ARM CIRCUMFERENCE AND PHYSICAL FUNCTION TESTS AND PHYSICAL ACTIVITY

Arm muscle area was significantly correlated with physical activity (r = 0.323, *p* = 0.013), and no statistical correlations were found with the PF tests. Mid-arm muscle circumference was positively correlated with physical activity, but this correlation was not statistically significant (r = 0.249, *p* = 0.059). No correlations were found with the PF tests.

CORRELATION OF HANDGRIP STRENGTH WITH ANTHROPOMETRICS, CT AND PA

Handgrip strength was positively correlated with arm muscle area measured with anthropometrics (r = 0.396, *p* = 0.002),

Table I. Demographics, body composition, laboratory and physical function characteristics of the study population

Patient characteristics	Total (*n* = 38)
Age (years)	33 ± 10.8
Sex	
Male, *n* (%)	20 (52.6)
Etiology, n (%)	
Unknow	27 (71.1)
Diabetes mellitus	3 (7.9)
Glomerulopathy	1 (2.6)
Hypertension	4 (10.5)
Other	3 (7.9)
Frequency of dialysis (n/%)	
2 times per week	32 (84.2)
3 times per week	6 (15.8)
Dialysis vintage (years)	2 (1, 3.2)
Uresis (ml/24 h)	85 ± 26
Comorbidities, n (%)	
Diabetes	2 (7.9)
Hypertension	38 (100)
Vascular access, n (%)	
Catheter	16 (42.1)
Arteriovenous fistula	22 (57.9)
Weight (kg)	56.6 ± 8.2
Body mass index (kg/m^2)	21.9 ± 2.9
Anthropometrics	
Arm muscle circumference (mm)	246.30 ± 64.7
Arm muscle area (cm^2)	35 ± 14.65
Computed tomography	
Mid-thigh muscle area (cm^2)	100 ± 20
Muscle attenuation (HU)	53 ± 4
MIS (score)	5.1 ± 2.7
Physical function tests	
Six-minute walk (m)	408 ± 64.1
Time up and go (s)	8.2 ± 1.5
5t-sit to stand (s)	9.4 ± 2.7
Short Physical Performance Battery (score)	10.8 ± 1.3
Handgrip strength (kg)	24.7 ± 9.3
Physical activity (kcal from PAQ)	2398 ± 725
Hemoglobin (g/dl)	10.19 ± 2.1
Creatinine (mg/dl)	13 ± 4.1
Albumin (g/dL)	4.2 ± 0.43
Phosphorus (mg/dl)	5.7 ± 2.3
Potassium (mmol/L)	5.4 ± 0.99
CRP (mg/L)	11.7 ± 20.6

Data are indicated as absolute number (percentage), mean ± standard deviation. Fat mass is presented as a percentage of body weight from anthropometry. HU: Hounsfield units; CRP: C-reactive protein; MIS: malnutrition inflammation score.

mid-thigh muscle area measured with CT (r = 0.656, $p = 0.000$) (Fig. 5), SMWT (r = 0.373, $p = 0.004$), SPPB (r = 0.269, $p = 0.041$) and physical activity (r = 0.323, $p = 0.013$) and was negatively correlated with the TUGT (r = -0.235, $p = 0.076$).

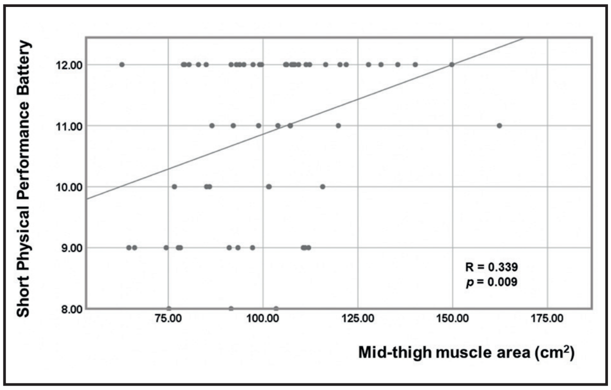

Figure 2.

Correlation between the mid-thigh muscle area measured with computed tomography and the Short Physical Performance Battery.

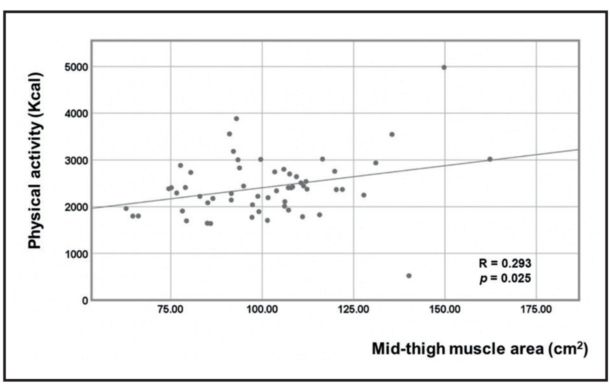

Figure 3.

Correlation between the mid-thigh muscle area measured with computed tomography and physical activity.

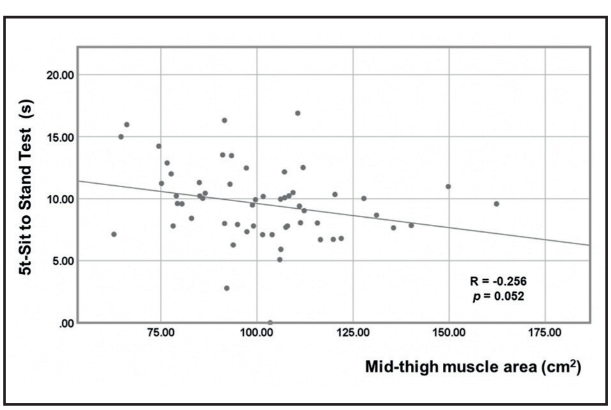

Figure 4.

Correlation between the mid-thigh muscle area measured with computed tomography and the 5 x sit-to-stand test.

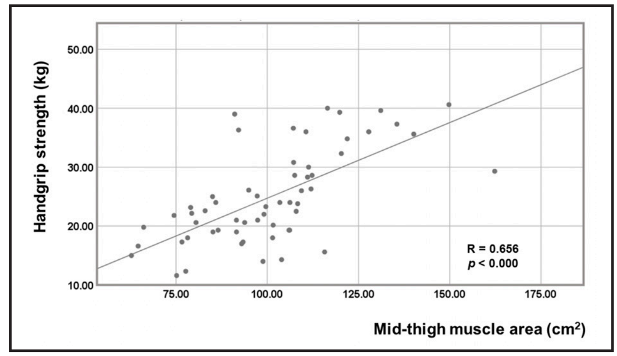

Figure 5.

Correlation between the mid-thigh muscle area measured with computed tomography and handgrip strength.

CORRELATION OF ARM MUSCLE AREA AND MID-ARM MUSCLE CIRCUMFERENCE WITH THIGH MUSCLE AREA

The mid-thigh muscle area was significantly correlated with the arm muscle area (r = 0.431, $p = 0.001$) and arm muscle circumference ($p = 0.357$, $p = 0.006$).

DISCUSSION

The primary finding in this study was that handgrip strength was strongly and significantly correlated with mid-thigh muscle area and with arm muscle area, it was also correlated with different PF tests, such as SMWT, SPPB, and TUGT, and a positive correlation with physical activity was also found. In addition, significant correlations were found between the mid-thigh muscle area and PF measurements obtained with the SPPB and STS5, and physical activity.

It is sometimes difficult to measure muscle mass in HD patients, in part because typical measurement techniques such as bioelectrical impedance analysis can be affected by patient´s hydration status. By contrast, other techniques such as dual-energy X-ray absorptiometry, magnetic resonance imaging and computed tomography are considered to be the "gold standard" reference methods for muscle mass evaluation, but their use is mainly confined to research purposes because they are either too expensive or inaccessible (20). As a result, physical function tests are often used as a proxy to assess muscle function, but few studies have examined how well these functional tests correlate with muscle mass measurements in this patient population (11).

Reduction in muscle mass and function are directly associated with premature death, poor quality of life, frailty, disability and hospitalizations (1,4-8). According to Roshanvaran et al., poor physical function measured with the six-minute walk test, TUGT, gait speed and handgrip strength are associated with an increase in all-cause mortality (5).

Improvement of both domains of muscle mass (muscle size and muscle quality) is important for dialysis patients because both are strong predictors of mortality; low muscle mass increased the risk of mortality by 98 % (HR: 1.98, 95 % CI: 1.01 to 3.87), and low muscle strength increased the risk of mortality by 23 % (HR: 1.23, 95 % CI: 0.56 to 2.67). Skeletal muscle dysfunction leads to mobility limitation and loss of functional independence, which can be translated to poor quality of life (4,3,21). Johansen et al. reported that dialysis patients were weaker and less active and walked more slowly than sedentary controls, although the quantity of muscle mass was not significantly different between the two groups (10). In this study, dialysis subjects had less contractile tissue and a poorer quality of muscle mass due to increased intramuscular fat infiltration (10). Other similar studies showed that younger dialysis patients (49.2 ± 15.8 years) with a greater mid-thigh muscle area (106.2 ± 26.8 cm^2) had poorer physical function than non-hemodialysis elderly subjects (75.3 ± 7.1 years) with a smaller muscle area (96.1 ± 2.1 cm^2), and this difference was not explained by muscle mass or comorbid conditions (3).

Taken together, our study adds to the literature suggesting that these low-cost functional measurements can provide valuable information related to the muscle mass of HD patients.

One of the interesting findings of this study was that HGS strongly correlated with the mid-thigh muscle area measured with CT and with different PF tests, but in other studies, this measurement was associated with the risk of malnutrition and inflammation (22).

A meta-analysis of prospective cohort studies evaluated the association between HGS and all-cause mortality in CKD patients found that the summary risk ratio of all-cause mortality in patients with low HGS was 1.88 (95 % confidence interval, 1.51-2.33; $p < 0.001$), while the summary risk ratio of all-cause mortality associated with a 1-kg unit increase in HGS was 0.95 (95 % confidence interval, 0.93-0-97; $p < 0.001$) (23).

These results suggest that HGS could be a strong predictor of malnutrition, inflammation, and all-cause mortality, as well as providing valuable information regarding the muscle mass of HD patients.

Our study has some limitations. First, due to the small sample size do not allow for the conclusion that the measurement of PF can represent the quality of muscle mass at any age in this patient group. Second, the patients did not undergo familiarization with the different PF tests, which may yield a biased result due to the poor standardization of the patients at the time of the tests.

CONCLUSION

The measurement of MM in HD patients is challenging due to frequent changes in the hydration status. Our data suggest that the evaluation of HGS and other low-cost and easy- to-perform PF measurements can provide important information related to MM. Additional studies are needed that include patient populations with larger sample sizes, across a wider age range, and including patients across the spectrum of kidney disease.

PRACTICAL APPLICATIONS

The measurement of physical function and handgrip strength are both low cost and easy to perform, and both measurements can give clinicians important information about the muscle mass of patients who are undergoing chronic hemodialysis.

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