

# Morphofunctional Assessment with Nutritional Ultrasound in Hemodialysis Patients Undergoing Six Months of Intradialytic Aerobic and Resistance Training: A Novel Multiparametric Approach

Avinash Chandu Nanwani

[achanan@gobiernodecanarias.org](mailto:achanan@gobiernodecanarias.org)

Hospital General de Fuerteventura

**Rocío Pérez Carrascosa**

Hospital General de Fuerteventura

**Jonay Manuel García García**

Hospital General de Fuerteventura

**Jimmy Reinaldo Sánchez Gil**

Hospital General de Fuerteventura

**María Alejandra Rodríguez García**

Hospital General de Fuerteventura

**María Isabel Acosta-Ochoa**

Hospital Río Carrión

**Celia Rodríguez Tudero**

Hospital Nuestra Señora de Sonsoles

**Elena Jiménez Mayor**

Hospital Santa Bárbara

**Esperanza Moral Berrio**

Hospital General Universitario de Ciudad Real

**José Carlos De la Flor**

Hospital Central de la Defensa Gómez Ulla

---

## Research Article

**Keywords:** hemodialysis, intradialytic exercise, resistance training, sarcopenia, body composition, nutritional ultrasound, morphofunctional assessment

**Posted Date:** September 30th, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-10766157/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.  
[Read Full License](#)

**Additional Declarations:** No competing interests reported.

---

# Abstract

## Background

Sarcopenia, frailty and protein-energy wasting are highly prevalent and associated with adverse outcomes in maintenance hemodialysis. Intradialytic exercise may attenuate muscle loss, but combined aerobic-and-resistance programmes evaluated with a comprehensive morphofunctional assessment, including nutritional ultrasound (NUS), remain poorly characterised. We aimed to evaluate the feasibility of a multiparametric morphofunctional assessment, incorporating NUS, for monitoring the response to a six-month combined intradialytic exercise programme and the associated changes in muscle, nutritional status and body composition.

## Methods

In a prospective, single-centre, observational pre–post study (Hospital General de Fuerteventura, Canary Islands, Spain), patients undertook a six-month combined aerobic and resistance intradialytic exercise programme (two sessions per week). Of 44 patients assessed, 21 commenced the programme and 17 completed six months (four withdrew after kidney transplantation). Assessments at baseline and six months included handgrip strength, anthropometry, bioelectrical impedance analysis (BIA), NUS, clinical scales (Fried phenotype, SARC-F, Malnutrition–Inflammation Score (MIS), KDQOL-36) and dialysis adequacy. Within-patient changes were analysed with paired t or Wilcoxon tests and the exact McNemar test, with Benjamini–Hochberg false-discovery-rate (FDR) correction within domains.

## Results

Handgrip strength increased from 23.3 to 27.1 kg (FDR = 0.002; Cohen's  $d_z$  = 1.11) and rectus femoris cross-sectional area from 2.62 to 3.24 cm<sup>2</sup> (FDR = 0.030). Phase angle (4.53 to 5.01°; FDR = 0.028) and lean tissue index (FDR = 0.021) rose, fat tissue mass fell (40.3 to 36.7 kg; FDR = 0.028), and dialysis adequacy improved (Kt/V 1.40 to 1.62; FDR = 0.005). Frailty, sarcopenia risk and malnutrition–inflammation scores all improved (FDR < 0.05), as did physical quality-of-life and burden-of-disease scores ( $p$  < 0.05). The programme was well tolerated, no serious exercise-related adverse events and no exercise-related withdrawals.

## Conclusions

A multiparametric morphofunctional assessment incorporating NUS was feasible and captured consistent longitudinal changes during a six-month combined intradialytic exercise programme associated with improvements in muscle strength, body composition, nutritional–inflammatory status, dialysis adequacy and quality of life. NUS may represent a promising tool for longitudinal monitoring,

although its comparative performance against established techniques remains to be established. These findings warrant confirmation in larger studies with a control group.

## 1. BACKGROUND

The number of patients with end-stage kidney disease (ESKD) receiving maintenance hemodialysis (MHD) continues to rise [1], and their comprehensive management increasingly demands attention to dimensions beyond traditional comorbidities—most notably frailty, sarcopenia, and malnutrition. Frailty is a multisystem syndrome characterized by loss of physiological reserve across multiple domains and heightened vulnerability to stressors; it reflects an individual's physiological rather than chronological age and is highly prevalent in chronic kidney disease (CKD), where it is consistently associated with poor health outcomes [2, 3]. Sarcopenia, in turn, refers not only to the loss of muscle mass but also to the decline in muscle strength and to qualitative changes in muscle tissue that compromise physical function [4].

Sarcopenia is a frequent complication of CKD and is particularly prevalent in patients with ESKD undergoing kidney replacement therapy. Reported prevalence in MHD cohorts varies widely with the diagnostic criteria and population studied, ranging from approximately 28% in unselected hemodialysis patients to over 60% in those aged  $\geq 65$  years [5, 6]. Its development is driven by the accumulation of uremic toxins, metabolic acidosis, vitamin D deficiency, insulin resistance, hyperparathyroidism, proteinuria, dialytic amino acid losses, and chronic inflammation, which together activate proteolytic pathways such as the ubiquitin–proteasome system and myostatin signalling [7]. These factors increase protein degradation and reduce protein synthesis, culminating in protein-energy wasting (PEW), a hypercatabolic state that further impairs the anabolic response to any intervention. Hemodialysis itself compounds this process, as the prolonged, repetitive sessions spent largely at rest promote sedentary behavior that further erodes functional capacity, muscle strength, and quality of life. Consistently, sarcopenia and frailty have been associated with an increased risk of cardiovascular events, hospitalization, and all-cause mortality [5, 6, 8], making their early identification essential to improve clinical outcomes.

Because no single tool captures this complexity, a multiparametric approach has gained ground in recent years [9], integrating body composition, muscle strength and physical function into a single assessment and moving beyond isolated biochemical markers, anthropometry and bioelectrical impedance analysis (BIA), whose interpretation in dialysis is confounded by inflammation and fluid status. Within this framework, nutritional ultrasound (NUS) of the rectus femoris and abdominal fat compartments has emerged as a feasible, low-cost, reproducible and bedside-applicable technique. To date, however, NUS has been used almost exclusively in cross-sectional, diagnostic contexts [10, 11], and its capacity to detect longitudinal, exercise-induced muscle change remains essentially unexplored.

Intradialytic exercise—aerobic and resistance training performed during the dialysis session—is a feasible, low-cost intervention deliverable in any hemodialysis unit under existing multidisciplinary

supervision. In this setting, exercise training may improve physical function, cardiovascular and bone health, and health-related quality of life, and combined aerobic-and-resistance programmes may enhance functional capacity and dialysis adequacy [12, 13]. Resistance training may also increase muscle strength, even in established sarcopenia, and help preserve lean mass and nutritional status, with a favourable safety profile [14–16]. However, the available evidence remains limited by short intervention periods, heterogeneous protocols, and the infrequent, simultaneous assessment of muscle, nutrition and body composition within the same cohort, which has seldom incorporated NUS or other morphofunctional tools.

Against this background, we conducted a six-month prospective, single-centre study with a pre–post design in maintenance hemodialysis patients. Our primary objective was to evaluate the feasibility and construct validity of a multiparametric morphofunctional assessment – combining clinical and laboratory variables, validated scales, anthropometry, BIA and NUS – for monitoring the response to a combined intradialytic aerobic and resistance exercise programme. As secondary objectives, we described the changes observed during the programme in muscle strength, sarcopenia, frailty, nutritional status and body composition, as well as in health-related quality of life, intradialytic hemodynamic tolerance, and dialysis adequacy and treatment-related parameters.

## **2. METHODS**

### **2.1. Study design and population**

We conducted a prospective, longitudinal, single-centre observational study at the in-hospital hemodialysis unit of the Hospital General de Fuerteventura (Canary Islands, Spain). The 6-month intradialytic aerobic and resistance exercise programme was implemented as part of routine clinical practice in the unit, independently of this study, and was jointly delivered by the Departments of Nephrology and Rehabilitation. Participants were not assigned to the exercise programme by the investigators: the programme was offered to all eligible patients in the unit as part of standard care, and the research component of this study consisted solely of the prospective multiparametric morphofunctional monitoring of the patients receiving it. Throughout the six-month period the dialysis prescription and pharmacological treatment were not modified for the purposes of the study, and no structured nutritional counselling or oral nutritional supplementation was provided. No a priori sample size or power calculation was performed: the study was conceived as an exploratory, pilot-scale evaluation embedded in routine clinical practice, and recruitment followed a convenience sampling strategy in which all patients receiving maintenance hemodialysis in the unit during the study period were screened consecutively. The sample size was therefore determined by the size of the eligible unit census.

Seventeen clinically stable adults with end-stage kidney disease (ESKD) on maintenance hemodialysis (Surdial™ X hemodialysis machine) were included, and all provided written informed consent. A comprehensive morphofunctional assessment was performed at baseline and repeated after six

months. Predefined criteria for interrupting an exercise session were symptomatic hypotension, angina, severe dyspnoea, intense cramping, or blood pressure outside the predefined range (systolic blood pressure < 100 mmHg or > 180 mmHg).

## **2.2. Eligibility criteria**

Eligible patients were adults aged  $\geq 18$  years with ESKD receiving maintenance hemodialysis (> 3 months) who were able to complete the physical-fitness and handgrip dynamometry assessments and who signed the informed consent form. Patients were excluded if they had a femoral central venous catheter, a history of limb amputation, or metallic prostheses (which preclude valid bioimpedance measurement), or if dementia, inability to cooperate, intradialytic instability, or any other condition prevented completion of the functional assessment.

## **2.3. Data collection**

Demographic, clinical, and analytical variables were collected at baseline and repeated after six months of the intradialytic exercise programme.

### **2.3.1. Patient characteristics and analytical variables**

The clinical data collected comprised age, sex, chronic kidney disease etiology, hemodialysis modality, vascular access, dialysis vintage, weekly session frequency and duration, date of initiation of kidney replacement therapy, residual urine output, and interdialytic weight gain (IDWG, kg). Cardiovascular risk factors, comorbidities and pharmacological treatment (including antihypertensive, antidiabetic, anaemia, bone-mineral and potassium-lowering therapies) were also recorded.

Laboratory data comprised haemoglobin, total lymphocyte count, total protein, prealbumin, albumin, iron, transferrin saturation index, ferritin, transferrin, total cholesterol, HDL cholesterol, LDL cholesterol, non-HDL cholesterol, triglycerides, urea, creatinine, creatinine indexed to body surface area, normalised protein catabolic rate (nPCR), 25-hydroxyvitamin D, intact parathyroid hormone, calcium, phosphorus, sodium, potassium, chloride, bicarbonate, and Kt/V. Albumin, prealbumin, transferrin, total lymphocyte count, the lipid profile (total cholesterol, HDL, LDL, and triglycerides), were considered as biochemical markers of nutritional and inflammatory status. All laboratory and dialysis-adequacy parameters were obtained under standardised conditions from pre-dialysis blood samples and were determined both at baseline and after six months of the intradialytic exercise programme, enabling a paired pre-post comparison of the analytical and dialysis-related variables.

### **2.3.2. Anthropometric variables**

Anthropometric measurements comprised weight (kg), height (cm), and body mass index (BMI, kg/m<sup>2</sup>), together with mid-arm circumference (cm), waist circumference (cm), and triceps and waist skinfold thickness (mm). To eliminate inter-observer variation, all measurements were obtained by the same operator. Anthropometry, BIA, and NUS were performed together within the same assessment session,

immediately before a midweek hemodialysis session, so that all three sets of measurements were obtained simultaneously under pre-dialysis conditions.

### **2.3.3. BIA variables**

Body composition and fluid status were assessed by BIA using the Body Composition Monitor (Fresenius Medical Care), performed immediately before the second weekly hemodialysis session. The recorded parameters were phase angle, overhydration (OH), lean tissue index (LTI, kg/m<sup>2</sup>), fat tissue index (FTI, kg/m<sup>2</sup>), lean tissue mass (LTM, kg), and fat tissue mass (FTM, kg).

### **2.3.4. Muscle strength variables**

Muscle strength was measured by handgrip dynamometry, recording the highest of three measurements obtained from the dominant (non-fistula) hand. Dynapenia was defined according to the 2019 European Working Group on Sarcopenia in Older People (EWGSOP2) [4] criteria as a handgrip strength below 27 kg in men and below 16 kg in women.

### **2.3.5. Nutritional ultrasonography variables**

Examinations were performed in B-mode on a Mindray Z60 ultrasound system with a multifrequency linear probe, with the patient in the supine position and the head of the bed at 0°, both legs extended and relaxed, following the standardised morphofunctional nutritional-ultrasound protocol [10, 11]. The rectus femoris was insonated at the junction of the lower third of the line between the anterior superior iliac spine and the upper border of the patella, with the transducer perpendicular to the muscle's long axis and minimal compression to avoid tissue distortion. Femoral assessment of the rectus femoris of the dominant leg included the transverse (X-axis) and anteroposterior (Y-axis, at rest and during contraction) diameters (cm), the cross-sectional area of the rectus femoris (cm<sup>2</sup>) and its circumference, the cross-sectional area indexed to body surface area, estimated with the Mosteller formula (cm<sup>2</sup>/m<sup>2</sup>), and the subcutaneous adipose tissue thickness.

Abdominal wall assessment included total, superficial, and preperitoneal adipose tissue (all in cm). For the abdominal-wall study, the transducer was positioned on the midline at the midpoint between the xiphoid process and the umbilicus and held perpendicular to its long axis.

To minimise variability, all ultrasound examinations were performed by a single trained physician using the same ultrasound device, following a standardised protocol and always on the same day of the dialysis week; for each parameter, three measurements were obtained and the mean value was used in the analysis. All examinations were performed by a nephrologist with prior experience in nutritional ultrasound in maintenance hemodialysis [10, 11]. A formal intra-observer reproducibility study was not conducted in this cohort; the reproducibility of rectus femoris measurements has, however, been reported previously [17, 18], and the technique has been validated against bioimpedance-derived muscle mass and knee-extensor strength in maintenance hemodialysis [19].

## **2.3.6. Malnutrition, frailty, sarcopenia, and quality-of-life scales**

Nutritional status, frailty, and sarcopenia were evaluated using validated scales. Malnutrition was assessed with the Malnutrition–Inflammation Score (MIS) [20], categorised as normal (< 3 points), mild (3–5 points), moderate (6–8 points), or severe (> 8 points). Frailty was assessed with the Fried frailty phenotype [21], classifying patients as non-frail, pre-frail, or frail. Sarcopenia was screened with the SARC-F (Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls) questionnaire [22]. Health-related quality of life was assessed with the 36-item Kidney Disease Quality of Life survey (KDQOL-36) [23]. This validated, disease-specific questionnaire comprises a 12-item generic core (the SF-12, summarised as a Physical Component Summary and a Mental Component Summary) together with three kidney-disease-targeted subscales – burden of kidney disease, symptoms and problems of kidney disease, and effects of kidney disease. Scores were obtained directly from the original questionnaire template, without altering the orientation of the values beyond the coding established by that template.

## **2.4. Intradialytic monitoring, haemodynamic tolerance, and safety**

Intradialytic haemodynamic tolerance was evaluated during the exercise sessions through serial monitoring of heart rate and blood pressure, recorded before the session, every 10–15 minutes during exercise, and at the end of the session. These measurements were used to characterise the cardiovascular response to, and the haemodynamic tolerance of, intradialytic exercise.

Adverse events occurring during or in immediate relation to the exercise sessions were prospectively recorded throughout the programme. Predefined events comprised symptomatic intradialytic hypotension, muscle cramping, angina or chest pain, palpitations or arrhythmia, severe dyspnoea, dizziness, bleeding, and any vascular-access complication. Throughout, predefined stopping criteria were applied (a systolic blood pressure < 100 or > 180 mmHg, severe dyspnoea, chest pain, palpitations, dizziness, bleeding, or any vascular-access complication), and the programme was delivered by trained nursing staff in coordination with the Nephrology and Rehabilitation departments [24].

Before entering the programme, patients were assessed by the Rehabilitation Department to confirm their suitability for intradialytic exercise, identify any contraindications or functional limitations, and adapt the initial exercise prescription where necessary. Thereafter, exercise progression was tailored to each patient's clinical and functional status according to the predefined progression criteria described in the intradialytic exercise programme. The ultimate goal was for patients to achieve full autonomy to perform the programme safely and independently.

## **2.5. Statistical analysis**

Categorical variables were expressed as absolute frequencies and percentages, and quantitative variables as mean  $\pm$  standard deviation or median [interquartile range], as appropriate. The normality of the within-patient differences was assessed with the Shapiro–Wilk test, and within-patient changes from baseline to six months were evaluated with the paired Student t-test when the differences were normally distributed and with the Wilcoxon signed-rank test otherwise; paired categorical variables were compared with the exact McNemar test. To account for multiple comparisons, raw p values were adjusted within each domain using the Benjamini–Hochberg false discovery rate (FDR) procedure; both the raw and the FDR-adjusted p values are reported, and statistical significance was defined as an FDR-adjusted  $p < 0.05$ . The KDQOL-36 dimensions, analysed as a separate, exploratory secondary outcome, are reported with raw p values only, without FDR adjustment. All tests were two-tailed. Analyses were performed with R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

## 2.6. Ethics

The study was approved by the Research Ethics Committee for Medicinal Products (CEI/CEIm) of Las Palmas, Canary Islands, Spain (approval code 2025-272-1; Minutes 6/2025, 30 June 2025). It was conducted in accordance with the principles of the Declaration of Helsinki. All participating patients received a patient information sheet and provided written informed consent.

## 2.7. Intradialytic exercise programme

The programme described below constitutes the unit's routine clinical-care protocol and is described here for context and reproducibility; it was not an intervention assigned for research purposes. It consisted of a supervised, individualised combined training programme, based on previously published intradialytic exercise protocols [25–27], in which both the aerobic and resistance components were monitored. Sessions were performed twice weekly, and were carried out after the first hour of the hemodialysis session, once the nursing staff had confirmed haemodynamic stability. To avoid interfering with the vascular access, loading of the access arm was avoided during the session, while the lower limbs and, in patients with upper-limb access, the contralateral upper limb were trained (**Supplementary Fig. 1**).

Each session lasted 30 to 45 minutes according to tolerance and began with a 5–10-minute warm-up. For each prescribed exercise, three sets of 5–10 repetitions were performed (after assessing the patient's prior status and tolerance), holding each repetition for 5 seconds. The session was structured in three phases. Warm-up and resistance exercises were performed with the patient in the supine position on the dialysis bed, whereas for the aerobic component the bed was adjusted to a seated position to enable cycling on a bedside pedal ergometer positioned at the foot of the bed:

Warm-up (5–10 minutes). Ankle mobility (10 repetitions per side), alternating knee raises with a gentle movement (10 repetitions per leg), and deep breathing, inhaling through the nose and exhaling through the mouth (5 repetitions).

Aerobic component (10–30 minutes). Cycling on a bedside pedal ergometer for 10 to 30 minutes at a moderate pace.

Resistance component (10–15 minutes). Exercises targeted the main lower-limb muscle groups and included active hip flexion, combined hip and knee flexion–extension, quadriceps isometric contractions, knee extension with an elastic band, hip abduction with an elastic band, glute bridge, and ankle dorsiflexion and plantarflexion with an elastic band (**Supplementary Fig. 1**). These exercises were selected to strengthen the iliopsoas, quadriceps, gluteus medius, gluteus maximus, tibialis anterior, and triceps surae, muscles essential for gait performance, balance, and fall prevention.

For the resistance component, the training load was adjusted to a target range of 10 to 15 repetitions, with weekly review of progress. When a patient exceeded 15 repetitions in two consecutive sessions while maintaining good technique and a patient-reported moderate rating of perceived exertion (RPE 12–14 on the Borg 6–20 scale), corresponding to the moderate exercise intensity commonly prescribed in cardiac rehabilitation programmes [28], the resistance was increased slightly by progressing the elastic-band level or adding 0.5–1 kg. If the patient was unable to reach 10 repetitions, or if symptoms such as pain, dizziness, severe dyspnea, or cramping appeared, the load was reduced or the exercise was discontinued.

In patients with an arteriovenous fistula (AVF) as vascular access, the intradialytic programme focused on the contralateral upper limb, using low-to-moderate loads (RPE  $\leq$  12–14 on the Borg 6–20 scale) and high repetitions, while avoiding sustained isometric exercises and Valsalva manoeuvres. For the fistula arm, specific work was performed outside the dialysis session (interdialytic period), following vascular-access maturation guidelines, with progression of loads only once the access was fully matured. This approach protected the integrity of the vascular access while still improving shoulder-girdle and grip strength, with a positive impact on the patient's activities of daily living.

The aerobic component was delivered using pedal devices with a progressive increase in duration and intensity, targeting a moderate rating of perceived exertion (RPE 12–14 on the Borg 6–20 scale) throughout the programme [28].

## 3. RESULTS

### *3.1. Baseline characteristics of the cohort and analytical variables.*

Of 44 maintenance hemodialysis patients assessed for eligibility, 23 were not enrolled - five for haemodynamic instability, four for lower-limb amputation, three for inability to cooperate, three for metallic prostheses, two for a femoral central venous catheter, two for cognitive impairment, two for other conditions precluding functional assessment, and two who declined consent - and 21 commenced the intradialytic exercise programme. Four patients withdrew before completing six months because they received a kidney transplant, leaving a final analysed cohort of 17 patients. Participant flow is summarised in **Figure 1**. The baseline characteristics of the cohort are summarised in **Table 1**.

**Table 1. Baseline characteristics of the cohort.**

| Variable                                      | Patients (N = 17) |
|-----------------------------------------------|-------------------|
| <b>Demographics</b>                           |                   |
| Male, n (%)                                   | 11 (64.7)         |
| Female, n (%)                                 | 6 (35.3)          |
| Age, years, mean $\pm$ SD                     | 61.6 $\pm$ 16.1   |
| <b>Hemodialysis</b>                           |                   |
| Time on HD, years                             | 2.4 [1.3–3.5]     |
| Residual urine output, mL/day                 | 300 [0–1000]      |
| Vascular access – AVF, n (%)                  | 13 (76.5)         |
| Vascular access – Tunnelled catheter, n (%)   | 4 (23.5)          |
| HD modality – Online post-dilution HDF, n (%) | 16 (94.1)         |
| HD modality – High-flux HD, n (%)             | 1 (5.9)           |
| Weekly HD time, min                           | 720 [630–720]     |
| Frequency – 3 sessions/week, n (%)            | 17 (100)          |
| Interdialytic weight gain, kg                 | 1.76 [1.50–2.48]  |
| <b>Etiology of CKD, n (%)</b>                 |                   |
| Unknown                                       | 5 (29.4)          |
| Diabetic nephropathy                          | 3 (17.6)          |
| Tubulointerstitial                            | 3 (17.6)          |
| Urological                                    | 2 (11.8)          |
| Glomerular                                    | 2 (11.8)          |
| Nephroangiosclerosis                          | 1 (5.9)           |
| ADPKD                                         | 1 (5.9)           |
| <b>Comorbidities, n (%)</b>                   |                   |
| Hypertension                                  | 14 (82.4)         |
| Dyslipidemia                                  | 13 (76.5)         |
| Heart disease                                 | 10 (58.8)         |
| Diabetes mellitus                             | 9 (52.9)          |
| Gastrointestinal disease                      | 6 (35.3)          |

| Variable                              | Patients (N = 17) |
|---------------------------------------|-------------------|
| Current/former smoker                 | 5 (29.4)          |
| Malignancy                            | 5 (29.4)          |
| Peripheral vascular disease           | 4 (23.5)          |
| Stroke                                | 3 (17.6)          |
| COPD                                  | 0 (0.0)           |
| <b>Baseline treatment, n (%)</b>      |                   |
| Antihypertensive agents, median [IQR] | 3 [2–4]           |
| ACE inhibitor / ARB                   | 3 (17.6)          |
| Diabetes treatment – Insulin          | 2 (11.8)          |
| Diabetes treatment – Oral agents      | 3 (17.6)          |
| Diabetes treatment – Combination      | 3 (17.6)          |
| SGLT2 inhibitor                       | 5 (29.4)          |
| GLP-1 receptor agonist                | 2 (11.8)          |
| Non-calcium-based phosphate binders   | 15 (88.2)         |
| No phosphate binders                  | 2 (11.8)          |
| Paricalcitol                          | 9 (52.9)          |
| Calcimimetics                         | 5 (29.4)          |
| Vitamin D                             | 16 (94.1)         |
| Potassium binders                     | 8 (47.1)          |
| Intravenous iron                      | 4 (23.5)          |
| Weekly erythropoietin dose, IU        | 5000 [0–9000]     |

Continuous variables are presented as mean  $\pm$  SD (age) or median [IQR]; categorical variables as n (%).

**Abbreviations:** HD, hemodialysis; AVF, arteriovenous fistula; HDF, haemodiafiltration; CKD, chronic kidney disease; ADPKD, autosomal dominant polycystic kidney disease; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; SGLT2, sodium–glucose cotransporter 2; GLP-1, glucagon-like peptide-1; IQR, interquartile range; SD, standard deviation.

### 3.1.1. Changes in analytical and dialysis-related parameters at six months (secondary outcomes)

Laboratory and dialysis-related parameters were compared between baseline and six months (**Table 2**). Dialysis adequacy improved, with Kt/V rising from  $1.40 \pm 0.19$  to  $1.62 \pm 0.16$  ( $p < 0.001$ ; FDR = 0.005); the

normalised protein catabolic rate (nPCR) also increased, from  $1.03 \pm 0.40$  to  $1.22 \pm 0.33$  g/kg/day ( $p = 0.013$ ), although this change did not survive correction for multiple comparisons (FDR = 0.066). Serum bicarbonate decreased from  $25.30 \pm 1.84$  to  $23.09 \pm 1.99$  mEq/L ( $p = 0.001$ ; FDR = 0.008). Among the lipid parameters, non-HDL cholesterol fell significantly from  $111.24 \pm 37.62$  to  $89.88 \pm 31.46$  mg/dL ( $p = 0.003$ ; FDR = 0.028), whereas the reductions in total cholesterol ( $147.94 \pm 38.27$  to  $129.82 \pm 31.65$  mg/dL;  $p = 0.021$ ; FDR = 0.091) and triglycerides ( $146.47 \pm 62.56$  to  $117.94 \pm 57.40$  mg/dL;  $p = 0.032$ ; FDR = 0.119) were nominally significant but did not survive correction for multiple comparisons. Albumin increased from  $3.72 \pm 0.31$  to  $3.92 \pm 0.28$  g/dL ( $p = 0.010$ ; FDR = 0.062), a change that likewise did not remain significant after FDR adjustment; prealbumin showed a parallel, non-significant upward trend ( $26.18 \pm 6.81$  to  $29.06 \pm 5.24$  mg/dL;  $p = 0.070$ ), whereas transferrin and the total lymphocyte count did not change significantly (**Table 2**). Overall, after correction for multiple comparisons, intradialytic exercise was associated with a significant improvement in dialysis adequacy (Kt/V) and significant reductions in serum bicarbonate and non-HDL cholesterol.

**Table 2. Laboratory and dialysis-adequacy parameters at baseline and six months.**

| Parameter                                     | Baseline         | 6 months         | p      | p (FDR) |
|-----------------------------------------------|------------------|------------------|--------|---------|
| Hemoglobin (g/dL)                             | 12.61 ± 1.51     | 12.24 ± 1.50     | 0.485  | 0.573   |
| Total lymphocyte count (×10 <sup>3</sup> /μL) | 1515.29 ± 475.19 | 1421.18 ± 459.55 | 0.066  | 0.182   |
| Total protein (g/dL)                          | 6.58 ± 0.37      | 6.80 ± 0.58      | 0.064  | 0.182   |
| Prealbumin (mg/dL)                            | 26.18 ± 6.81     | 29.06 ± 5.24     | 0.070  | 0.182   |
| Albumin (g/dL)                                | 3.72 ± 0.31      | 3.92 ± 0.28      | 0.010  | 0.062   |
| Iron (μg/dL)                                  | 80.06 ± 38.41    | 82.59 ± 30.99    | 0.824  | 0.857   |
| TSAT (%)                                      | 40.80 ± 25.18    | 39.77 ± 18.42    | 0.864  | 0.864   |
| Ferritin (ng/mL)                              | 932.60 ± 900.25  | 863.42 ± 619.18  | 0.664  | 0.751   |
| Transferrin (mg/dL)                           | 166 [124–189]    | 141 [130–180]    | 0.124  | 0.261   |
| HDL cholesterol (mg/dL)                       | 36.00 [29–46]    | 40 [32–45]       | 0.322  | 0.441   |
| LDL cholesterol (mg/dL)                       | 85.00 ± 38.14    | 76.24 ± 31.66    | 0.217  | 0.352   |
| non-HDL cholesterol (mg/dL)                   | 111.24 ± 37.62   | 89.88 ± 31.46    | 0.003  | 0.028   |
| Triglycerides (mg/dL)                         | 146.47 ± 62.56   | 117.94 ± 57.40   | 0.032  | 0.119   |
| Total cholesterol (mg/dL)                     | 147.94 ± 38.27   | 129.82 ± 31.65   | 0.021  | 0.091   |
| Urea (mg/dL)                                  | 124 [100–129]    | 110 [100–125]    | 0.179  | 0.320   |
| Creatinine (mg/dL)                            | 7.61 ± 1.30      | 8.07 ± 1.92      | 0.261  | 0.399   |
| Creatinine/BSA (mg/dL/m <sup>2</sup> )        | 4.05 ± 0.80      | 4.32 ± 1.05      | 0.185  | 0.320   |
| nPCR (g/kg/day)                               | 1.03 ± 0.40      | 1.22 ± 0.33      | 0.013  | 0.066   |
| Intact PTH (pg/mL)                            | 233 [195–298]    | 215 [164–300]    | 0.378  | 0.491   |
| Calcium (mg/dL)                               | 9.02 ± 0.63      | 8.97 ± 0.55      | 0.718  | 0.778   |
| Phosphorus (mg/dL)                            | 4.91 ± 1.31      | 5.14 ± 1.43      | 0.478  | 0.573   |
| Sodium (mmol/L)                               | 138.47 ± 2.40    | 139.00 ± 2.60    | 0.299  | 0.432   |
| Potassium (mmol/L)                            | 4.78 ± 0.79      | 5.10 ± 0.92      | 0.131  | 0.261   |
| Chloride (mmol/L)                             | 106 [103–107]    | 105 [105–107]    | 0.129  | 0.261   |
| Bicarbonate (mEq/L)                           | 25.30 ± 1.84     | 23.09 ± 1.99     | <0.001 | 0.008   |
| Kt/V                                          | 1.40 ± 0.19      | 1.62 ± 0.16      | <0.001 | 0.005   |

Continuous variables analysed with the paired *t*-test are shown as mean ± SD; those analysed with the Wilcoxon signed-rank test as median [IQR]. *p*, raw *p* value; *p* (FDR), Benjamini–Hochberg FDR-adjusted *p*

value within the domain; significance defined as  $FDR < 0.05$ . **Abbreviations:** TSAT, transferrin saturation index; nPCR, normalised protein catabolic rate; PTH, parathyroid hormone; BSA, body surface area.

3.2. Frailty, sarcopenia, and nutritional status (secondary outcomes)

After six months of intradialytic aerobic and resistance training, all three clinical scales improved significantly, and these changes remained significant after FDR correction (**Figure 2**).

The Malnutrition–Inflammation Score (MIS) severity category improved from a median of 3.0 (IQR 2.0–3.0) at baseline to 1.0 (IQR 1.0–2.0) at six months ( $p = 0.001$ ;  $FDR = 0.002$ ), with 12 patients (70.6%) improving and none worsening. This shift was reflected in the category distribution: severe malnutrition–inflammation, present in 4 patients (23.5%) at baseline, was no longer observed at six months, while the proportion classified as normal rose from 4 (23.5%) to 9 (52.9%).

Frailty, assessed with the Fried phenotype, decreased from a median of 1.0 (IQR 0.0–2.0) to 0.0 (IQR 0.0–1.0) ( $p = 0.033$ ;  $FDR = 0.043$ ); 9 patients (52.9%) improved and 2 (11.8%) worsened. The number of frail patients fell from 5 (29.4%) to 2 (11.8%), and that of non-frail patients rose from 5 (29.4%) to 10 (58.8%).

The proportion of patients at risk of sarcopenia according to the SARC-F questionnaire dropped markedly, from 12 patients (70.6%) at baseline to 1 (5.9%) at six months (exact McNemar test,  $p < 0.001$ ;  $FDR = 0.002$ ), with 11 patients (64.7%) reclassified as being at low risk and none worsening.

3.2.1 Health-related quality of life (secondary outcome)

After six months of the programme, a significant improvement was observed in the burden of kidney disease subscale (**Table 3**), which rose from  $42.92 \pm 33.48$  to  $56.67 \pm 35.00$  points, with a mean difference of  $13.75 \pm 19.93$  points ( $p = 0.018$ ). The physical component also showed a significant increase, from  $38.33 [36.25–50.83]$  to  $51.67 [43.75–75.83]$  ( $p = 0.045$ ). No statistically significant changes were observed in the mental component ( $46.22 \pm 11.05$  vs  $44.11 \pm 10.23$ ;  $p = 0.487$ ), the symptoms and problems subscale ( $78.06 \pm 15.23$  vs  $83.33 \pm 18.73$ ;  $p = 0.091$ ), or the effects of kidney disease subscale ( $38.33 \pm 23.93$  vs  $39.82 \pm 24.03$ ;  $p = 0.677$ ).

**Table 3. Pre- vs post-intradialytic-exercise comparison of the KDQOL-36 dimensions.**

| KDQOL-36 dimension         | Pre-exercise        | Post-exercise       | Change (post-pre) | p     |
|----------------------------|---------------------|---------------------|-------------------|-------|
| Physical Component Summary | 38.33 [36.25–50.83] | 51.67 [43.75–75.83] | 5.00 [0.00–13.33] | 0.045 |
| Mental Component Summary   | 46.22 ± 11.05       | 44.11 ± 10.23       | –2.11 ± 11.46     | 0.487 |
| Burden of kidney disease   | 42.92 ± 33.48       | 56.67 ± 35.00       | 13.75 ± 19.93     | 0.018 |
| Symptoms and problems      | 78.06 ± 15.23       | 83.33 ± 18.73       | 5.28 ± 11.24      | 0.091 |
| Effects of kidney disease  | 38.33 ± 23.93       | 39.82 ± 24.03       | 1.49 ± 13.54      | 0.677 |

Continuous variables are shown as mean ± SD (paired *t*-test) or median [IQR] (Wilcoxon signed-rank test). *p*, raw (uncorrected) *p* value. PCS, Physical Component Summary; MCS, Mental Component Summary.

### 3.3. Morphofunctional assessment of body composition (primary outcome).

#### 3.3.1 Bioelectrical impedance analysis.

After six months of intradialytic exercise, body weight, BMI, and hydration status remained stable, with no statistically significant differences compared with baseline. Phase angle increased significantly from  $4.53 \pm 1.35$  to  $5.01 \pm 1.46^\circ$  ( $p = 0.011$ ; FDR = 0.028) and lean tissue index from  $11.95 \pm 3.37$  to  $13.39 \pm 3.65$  kg/m<sup>2</sup> ( $p = 0.003$ ; FDR = 0.021), while fat tissue mass decreased significantly from  $40.28 \pm 18.07$  to  $36.69 \pm 16.66$  kg ( $p = 0.008$ ; FDR = 0.028); all three remained significant after FDR correction. Fat tissue index ( $14.05 \pm 6.30$  to  $13.14 \pm 5.91$ ;  $p = 0.060$ ) and lean tissue mass ( $34.71 \pm 12.05$  to  $37.34 \pm 13.38$  kg;  $p = 0.052$ ) showed favourable trends that did not reach significance. These results indicate a favourable change in body composition and bioimpedance-derived nutritional status after the programme (**Figure 3, Table 4**).

**Table 4. BIA at baseline and six months.**

| Parameter                              | Baseline            | 6 months            | p     | p (FDR) |
|----------------------------------------|---------------------|---------------------|-------|---------|
| Weight (kg)                            | 76.00 [67.00–89.90] | 74.40 [65.00–89.40] | 0.552 | 0.631   |
| BMI (kg/m <sup>2</sup> )               | 26.75 ± 6.27        | 26.44 ± 5.82        | 0.341 | 0.454   |
| Phase angle (°)                        | 4.53 ± 1.35         | 5.01 ± 1.46         | 0.011 | 0.028   |
| Overhydration (L)                      | 1.66 ± 1.33         | 1.55 ± 0.84         | 0.721 | 0.721   |
| Lean tissue index (kg/m <sup>2</sup> ) | 11.95 ± 3.37        | 13.39 ± 3.65        | 0.003 | 0.021   |
| Fat tissue index (kg/m <sup>2</sup> )  | 14.05 ± 6.30        | 13.14 ± 5.91        | 0.060 | 0.096   |
| Lean tissue mass (kg)                  | 34.71 ± 12.05       | 37.34 ± 13.38       | 0.052 | 0.096   |
| Fat tissue mass (kg)                   | 40.28 ± 18.07       | 36.69 ± 16.66       | 0.008 | 0.028   |

Continuous variables analysed with the paired *t*-test are shown as mean ± SD; those analysed with the Wilcoxon signed-rank test as median [IQR]. *p*, raw *p* value; *p* (FDR), Benjamini–Hochberg FDR-adjusted *p* value within the domain; significance defined as FDR < 0.05.

### 3.3.2. Anthropometry and muscle strength

**Table 5. Anthropometry and muscle strength at baseline and six months.**

| Parameter                  | Baseline      | 6 months      | p      | p (FDR) |
|----------------------------|---------------|---------------|--------|---------|
| Handgrip strength (kg)     | 23.28 ± 11.28 | 27.05 ± 11.97 | <0.001 | 0.002   |
| Mid-arm circumference (cm) | 25.35 ± 4.91  | 26.29 ± 4.89  | 0.110  | 0.110   |
| Waist circumference (cm)   | 97 [88–109]   | 97 [87–105]   | 0.002  | 0.004   |
| Triceps skinfold (mm)      | 13.65 ± 8.69  | 16.06 ± 7.94  | 0.085  | 0.106   |
| Waist skinfold (mm)        | 20.18 ± 11.16 | 18.00 ± 9.30  | 0.006  | 0.010   |

Continuous variables analysed with the paired *t*-test are shown as mean ± SD; those analysed with the Wilcoxon signed-rank test as median [IQR]. *p*, raw *p* value; *p* (FDR), Benjamini–Hochberg FDR-adjusted *p* value within the domain; significance defined as FDR < 0.05.

After six months, handgrip strength increased significantly (+3.78 kg; FDR = 0.002). Central adiposity also fell, with significant reductions in waist circumference and waist skinfold (FDR = 0.004 and 0.010, respectively), whereas mid-arm circumference and triceps skinfold did not change significantly after correction for multiple comparisons (**Table 5**).

### 3.3.3. Nutritional ultrasound

On NUS, the rectus femoris increased significantly in all dimensions, including its cross-sectional area (2.62 → 3.24 cm<sup>2</sup>; FDR = 0.030) and its body-surface-area-indexed value (FDR = 0.020). In the abdominal wall, superficial adipose tissue decreased significantly (FDR = 0.004), whereas total, preperitoneal and supramuscular fat were unchanged. All muscle gains and the reduction in superficial abdominal fat remained significant after FDR correction, indicating a concurrent increase in lower-limb muscle and a reduction in superficial abdominal adiposity (**Table 6**).

**Table 6. Nutritional ultrasound (rectus femoris and abdominal wall) at baseline and six months.**

| Parameter                                       | Baseline         | 6 months         | p      | p (FDR) |
|-------------------------------------------------|------------------|------------------|--------|---------|
| Muscle X-axis (transverse) (cm)                 | 3.05 [2.56–3.27] | 3.48 [2.90–3.85] | 0.022  | 0.037   |
| Muscle Y-axis, contracted (cm)                  | 0.94 [0.77–1.22] | 1.30 [0.80–1.80] | 0.006  | 0.020   |
| Muscle Y-axis (AP) (cm)                         | 0.78 [0.63–1.03] | 1.07 [0.71–1.20] | 0.019  | 0.037   |
| RF cross-sectional area (cm <sup>2</sup> )      | 2.62 ± 2.21      | 3.24 ± 1.75      | 0.012  | 0.030   |
| RF circumference (cm)                           | 7.27 [6.15–7.91] | 7.80 [7.17–8.54] | 0.069  | 0.099   |
| RF CSA / BSA (cm <sup>2</sup> /m <sup>2</sup> ) | 1.36 ± 1.05      | 1.72 ± 0.90      | 0.005  | 0.020   |
| Supramuscular (subcutaneous) fat (cm)           | 0.53 [0.45–0.73] | 0.63 [0.37–0.80] | 0.674  | 0.674   |
| Abdominal fat – total (cm)                      | 1.66 [1.29–2.60] | 1.50 [1.12–1.99] | 0.118  | 0.148   |
| Abdominal fat – superficial (cm)                | 0.97 [0.61–1.09] | 0.70 [0.31–0.97] | <0.001 | 0.004   |
| Abdominal fat – preperitoneal (cm)              | 0.59 [0.50–0.83] | 0.57 [0.40–0.74] | 0.541  | 0.601   |

**Abbreviations:** RF, rectus femoris; AP, anteroposterior; CSA, cross-sectional area; BSA, body surface area. Continuous variables analysed with the paired *t*-test are shown as mean ± SD; those analysed with the Wilcoxon signed-rank test as median [IQR]. *p*, raw *p* value; *p* (FDR), Benjamini–Hochberg FDR-adjusted *p* value within the domain; significance defined as FDR < 0.05.

### 3.4. Intradialytic haemodynamic tolerance and safety (secondary outcomes)

Intradialytic haemodynamic monitoring confirmed good tolerance of the exercise programme. Heart rate remained stable across the session with no tachycardic response, consistent with a light-to-moderate intensity, and blood pressure showed no significant intradialytic change (**Table 7**). No episode of symptomatic intradialytic hypotension occurred, and the few transient systolic peaks above 180 mmHg were self-limiting and required no interruption of the session. Over the six-month programme no serious exercise-related adverse events were recorded – in particular, no episodes of symptomatic intradialytic hypotension or hypertensive crisis, chest pain, palpitations or arrhythmia, severe dyspnea, or exertional oxygen desaturation; no overuse injuries, loss of balance, or falls; and no vascular-access complications, including accidental needle dislodgement, puncture-site bleeding, or movement-related disturbance of

arteriovenous fistula flow. No session required definitive discontinuation on safety grounds. The only adverse effects were self-limiting muscle cramps and mild joint pain during the first sessions; all 17 patients completed the programme with no exercise-related dropout. Attendance at scheduled hemodialysis sessions was complete throughout the six-month period, and adherence to the exercise programme, calculated across the cohort as the total number of exercise sessions completed divided by the total number scheduled, was 81%. No baseline functional limitations requiring modification of the prescribed exercise programme were identified, and no participant required subsequent changes to the protocol because of adverse events during the programme.

**Table 7. Intradialytic haemodynamic monitoring before, during and after the exercise session.**

| Parameter                       | Pre-exercise | During exercise | Post-exercise | p (pre vs during) | p (pre vs post) |
|---------------------------------|--------------|-----------------|---------------|-------------------|-----------------|
| Systolic blood pressure (mmHg)  | 147.8 ± 19.0 | 145.5 ± 18.0    | 146.4 ± 20.5  | 0.37              | 0.55            |
| Diastolic blood pressure (mmHg) | 74.8 ± 9.6   | 71.4 ± 11.3     | 71.8 ± 11.5   | 0.20              | 0.28            |
| Heart rate (bpm)                | 69.8 ± 9.8   | 68.2 ± 10.4     | 69.7 ± 10.5   | 0.05              | 0.92            |

*Values are mean ± standard deviation. Blood pressure was recorded in 10 of the 17 patients and heart rate in all 17. Within-session comparisons (paired t test) showed no significant change at any phase.*

**3.5. Magnitude of effect for the principal outcomes**

To convey the magnitude rather than merely the statistical significance of the principal changes, mean differences with 95% confidence intervals and standardised within-subject effect sizes (Cohen's dz) were calculated for the key outcomes (**Table 8**). The standardised effects were moderate to large across domains, with the largest observed for dialysis adequacy (Kt/V, dz = 1.18) and handgrip strength (dz = 1.11); muscle, body-composition and lower-limb morphology outcomes showed medium-to-large effects.

**Table 8. Magnitude of change for the principal outcomes from baseline to six months.**

| Outcome                                | Mean difference (95% CI) | Cohen's dz | FDR-adjusted p |
|----------------------------------------|--------------------------|------------|----------------|
| Handgrip strength (kg)                 | +3.78 (2.02 to 5.53)     | 1.11       | 0.002          |
| Rectus femoris CSA (cm <sup>2</sup> )  | +0.62 (0.16 to 1.09)     | 0.69       | 0.030          |
| Phase angle (°)                        | +0.48 (0.13 to 0.83)     | 0.70       | 0.028          |
| Lean tissue index (kg/m <sup>2</sup> ) | +1.44 (0.58 to 2.30)     | 0.86       | 0.021          |
| Fat tissue mass (kg)                   | -3.59 (-6.11 to -1.07)   | -0.73      | 0.028          |
| Kt/V                                   | +0.22 (0.12 to 0.32)     | 1.18       | 0.005          |

*Expressed as the mean difference with its 95% confidence interval, the standardised within-subject effect size (Cohen's dz) and the FDR-adjusted p value. By convention, dz values of approximately 0.2, 0.5 and 0.8 denote small, medium and large effects, respectively. A positive mean difference indicates an increase from baseline.*

## 4. DISCUSSION

In this six-month, single-centre prospective study, a supervised programme of combined intradialytic aerobic and resistance training was associated with consistent improvements across validated clinical scales, bioimpedance-derived body composition (a higher phase angle and lean tissue index and a lower fat mass), lower-limb muscle morphology on NUS, and handgrip strength. The central finding of this study is the feasibility of a multiparametric morphofunctional assessment — anchored on NUS — for capturing this response longitudinally, with the convergence of these subjective, morphological and functional measures.

To our knowledge, this is the first study to apply a comprehensive morphofunctional assessment — integrating NUS, BIA, anthropometry, muscle strength and validated scales — to characterise the longitudinal response to an intradialytic exercise programme in maintenance hemodialysis. NUS has so far been used almost exclusively in cross-sectional, diagnostic contexts [10,11]; our data suggest that it can also detect exercise-associated change over time, and that it may therefore represent a promising tool for longitudinal monitoring rather than a purely diagnostic one. Rectus femoris cross-sectional area, validated against bioimpedance-derived muscle mass and knee-extensor strength [19], increased after the programme; its larger absolute values than in earlier cross-sectional series probably reflect differences in age, body size and measurement protocol.

Because the relative performance of NUS against established techniques is central to its proposed monitoring role, we examined the behaviour of the three body-composition methods applied concurrently in the same patients. All five rectus femoris dimensions changed significantly after FDR correction, as did three of the six BIA-derived parameters (phase angle, lean tissue index and fat tissue mass), whereas lean tissue mass and fat tissue index showed only non-significant trends. Among the anthropometric measures, neither mid-arm circumference nor triceps skinfold - those most directly reflecting

appendicular muscle and its overlying fat - changed significantly, although waist circumference and waist skinfold decreased. NUS and BIA were thus concordant in direction for the muscle compartment, while conventional anthropometry did not capture the muscle changes detected by either. This descriptive concordance should not be read as evidence of superiority: no reference standard (DXA or computed tomography) was available, the comparisons were neither pre-specified nor powered as a head-to-head validation, and FDR correction was applied within rather than across domains. What these data do support is that NUS is responsive to exercise-associated change in this population, and that it quantifies muscle with less dependence on hydration status than bioimpedance or anthropometry [10,29].

Morphofunctional assessment is also gaining increasing attention beyond the field of nephrology, as proposed in the recent expert consensus on morphofunctional assessment and subsequent studies in patients undergoing maintenance hemodialysis by García Almeida et al. and De La Flor et al. [9,10]. Recent work in cardiac rehabilitation by Amaya-Campos et al. has begun to integrate morphofunctional assessment into rehabilitation programmes, primarily to support baseline evaluation and individualized exercise prescription [30]. Our findings further support and extend this concept by demonstrating the feasibility of using morphofunctional assessment not only for patient characterization and exercise prescription but also as a practical framework for monitoring longitudinal adaptations to rehabilitation, a role that will require confirmation in controlled studies before its integration into routine clinical practice can be recommended.

The gains across the clinical scales were substantial – severe malnutrition–inflammation, present in almost a quarter of the cohort at baseline, was absent at six months; frailty fell by roughly half; and a positive SARC-F screen, present in seven of every ten patients, persisted in only one – and are concordant with previous intradialytic exercise studies [14,15,27,31] and the wider evidence base [12,13]. Because SARC-F is self-reported and the design uncontrolled, a learning or reporting effect cannot be excluded [32]; reassuringly, however, the scale changes moved in the same direction as the objective markers (phase angle, lean tissue index and lower-limb muscle morphology), arguing for a genuine treatment-associated effect rather than measurement artefact. Such an effect is biologically plausible: in hemodialysis, muscle wasting is driven by uraemic toxins, metabolic acidosis, insulin resistance and inflammation acting through catabolic pathways such as the ubiquitin–proteasome system and myostatin signalling [7], and combined training counteracts this imbalance by stimulating protein synthesis and attenuating proteolysis – the rise in phase angle, a marker of cell mass and membrane integrity, pointing to improved cellular quality rather than fluid change alone.

The body-composition findings reinforce this interpretation. Phase angle rose from 4.53° to 5.01° and lean tissue index increased while fat mass fell, indicating favourable recomposition despite stable weight and hydration – an important consideration where conventional anthropometry is confounded by fluid shifts. Wang et al. [5] identified a phase-angle threshold of approximately 4.95° for sarcopenia in this population, so the cohort's shift from just below to just above this cut-off is clinically meaningful. These gains contrast with earlier controlled studies that relied on bioimpedance alone and found no

change over twelve weeks [31], a divergence probably reflecting both the longer exposure and the greater sensitivity of a combined assessment. Because biochemical and bioimpedance markers are both vulnerable to overhydration, NUS adds value by quantifying muscle largely independently of fluid status [10,29]; congestive hemodialysis patients have been shown to display a smaller rectus femoris area [11]. Ultrasound nonetheless has its own constraints, it cannot separate intramuscular fat from contractile tissue and its echo-intensity metrics depend on acquisition settings – so standardised protocols are required for valid longitudinal use [29].

Notably, the strength gains were not confined to the lower limb. Handgrip strength, measured on the dominant non-access hand, increased significantly, as the non-access arm was itself trained (low-to-moderate loads and high repetitions, with the access arm protected), this reflects a direct response of the trained musculature, paralleling the lower-limb gains on ultrasound. That handgrip improved at all is noteworthy, since it is often resistant to change in this population [31,33,34] and responds mainly to adequately dosed training sustained for six months or longer [24,35]. Dialysis adequacy also improved, with Kt/V rising from 1.40 to 1.62, an effect likewise reported with intradialytic exercise [24,31]. This improvement was not attributable to changes in the dialysis prescription modality, session length, weekly frequency, dialyser and vascular access all remained unchanged and the parallel rise in the normalised protein catabolic rate suggests that some patients may have spontaneously improved their intake, which – together with exercise-induced increases in muscle perfusion – may have contributed to the greater solute clearance. A further, non-physiological explanation must also be considered: Kt/V is inversely related to the urea distribution volume, which is derived from body weight and composition, so the significant fall in fat tissue mass would be expected to raise Kt/V independently of any true change in solute clearance; part of the improvement may therefore be arithmetic rather than dialytic.

These findings carry two clinical implications. First, they suggest that a multiparametric morphofunctional assessment may be a useful addition to the routine evaluation of hemodialysis patients, both to diagnose sarcopenia, frailty and malnutrition and to monitor the response to intervention. Second, because both the assessment and the programme are low-cost, reproducible and deliverable within the existing multidisciplinary team, monitored intradialytic exercise is an attractive and scalable measure, with potential value as prehabilitation for kidney transplant candidates – a population in which frailty predicts delayed graft function, prolonged hospital stay and post-transplant mortality, and in which multimodal prehabilitation programmes are being formally evaluated [41]; whether intradialytic exercise combined with morphofunctional monitoring can prevent or reverse frailty before transplantation, and whether this translates into better post-transplant outcomes, remains to be tested. Its safety profile was favourable, consistent with reports in elderly and highly comorbid patients [36,37].

The magnitude of these changes warrants interpretation against known measurement variability. The increase in rectus femoris cross-sectional area (+0.62 cm<sup>2</sup>, +23.7% from baseline) is severalfold greater than the repeatability reported for this measurement in patients with chronic disease, where the typical percentage error was 7.6-9.8% [17], and than the 0.8% between-session difference observed in middle-aged and elderly adults [18]; it is therefore unlikely to be attributable to measurement error. For phase

angle no minimal clinically important difference has been established, so interpretation must rest on prognostic thresholds, such as the sarcopenia cut-off of approximately 4.95 degrees discussed above, which the cohort crossed. Conversely, the reduction in waist circumference was small - the median value was unchanged, with narrowing only of the interquartile range - and lies within the expected variability of anthropometric measurement; it should not be regarded as clinically meaningful in isolation, and the reduction in central adiposity is better supported by the concurrent decreases in waist skinfold thickness and bioimpedance-derived fat tissue mass.

These findings are best situated within the emerging literature that applies nutritional ultrasound longitudinally rather than diagnostically. In critical illness, serial assessment detected a reduction of approximately 10% in rectus femoris cross-sectional area within the first week of intensive-care admission [38]. In the opposite direction, ultrasound has also captured recovery: rectus femoris thickness and cross-sectional area increased over two weeks of post-acute care hospitalisation in older men [39], and a pilot study in severe anorexia nervosa combined bioimpedance vector analysis, nutritional ultrasound and handgrip strength to monitor physical recovery, a methodological triad closely analogous to ours [40]. Our data extend this longitudinal application to maintenance hemodialysis, a setting in which fluid overload particularly compromises the interpretation of bioimpedance and anthropometry.

This study has notable strengths – a comprehensive protocol delivered within routine clinical practice, a single trained operator for ultrasound and anthropometry, and a conservative analysis incorporating false-discovery-rate correction – but also important limitations. The small, single-centre, uncontrolled sample precludes causal inference and leaves the study underpowered for the secondary outcomes, whose non-significant findings should be read as inconclusive rather than as evidence of absence; alternative contributors such as regression to the mean, attrition bias, the closer clinical attention inherent to a supervised programme or spontaneous improvements in dietary intake and self-care cannot be excluded, although the dialysis prescription and medication remained unchanged and no nutritional counselling was provided. Because eligibility required the ability to complete the functional assessments (reasons for non-enrolment in Figure 1), the findings apply to prevalent patients with meaningful functional and nutritional compromise – the cohort had a positive SARC-F screen in 70.6% and frailty in 29.4% at baseline – but not to the most dependent patients, such as those with cognitive impairment or haemodynamic instability. Finally, intra-observer reproducibility was not quantified in this cohort, longitudinal ultrasound cut-offs for muscle change have not yet been validated in hemodialysis [19,29], and, despite within-domain FDR correction, some individual significant findings – particularly among the secondary outcomes – may still represent false positives and require confirmation. Nevertheless, to our knowledge this is one of the first studies to characterise the longitudinal response to an intradialytic exercise programme using an integrated morphofunctional assessment, and it provides a foundation that larger, controlled studies can build upon.

## 5. CONCLUSION

Six months of supervised combined intradialytic aerobic and resistance training was associated with significant improvements in frailty, sarcopenia, nutritional status and body composition in maintenance hemodialysis patients, captured by a multiparametric morphofunctional approach that included NUS - an approach that proved feasible in routine practice and that may represent a promising framework for longitudinal monitoring, pending validation against established techniques -, with gains in both lower-limb morphology and grip strength. These findings should be regarded as exploratory and hypothesis-generating. As a low-cost, feasible and scalable intervention, monitored intradialytic exercise, together with systematic morphofunctional assessment, merits evaluation as a therapeutic strategy in multicentre randomised controlled trials with larger patient populations before its incorporation into routine care can be recommended.

## Abbreviations

ACE

angiotensin-converting enzyme

ADPKD

autosomal dominant polycystic kidney disease

AP

anteroposterior

ARB

angiotensin receptor blocker

AVF

arteriovenous fistula

BIA

bioelectrical impedance analysis

BMI

body mass index

BSA

body surface area

CI

confidence interval

CKD

chronic kidney disease

COPD

chronic obstructive pulmonary disease

CSA

cross-sectional area

DXA

dual-energy X-ray absorptiometry

ESKD

end-stage kidney disease  
EWGSOP2  
European Working Group on Sarcopenia in Older People 2  
FDR  
false discovery rate  
FTI  
fat tissue index  
FTM  
fat tissue mass  
GLP-1  
glucagon-like peptide-1  
HD  
hemodialysis  
HDF  
haemodiafiltration  
IDWG  
interdialytic weight gain  
IQR  
interquartile range  
KDQOL-36  
36-item Kidney Disease Quality of Life survey  
LTI  
lean tissue index  
LTM  
lean tissue mass  
MHD  
maintenance hemodialysis  
MIS  
Malnutrition–Inflammation Score  
nPCR  
normalised protein catabolic rate  
NUS  
nutritional ultrasound  
OH  
overhydration  
PEW  
protein-energy wasting  
PTH  
parathyroid hormone  
RF

rectus femoris  
RPE  
rating of perceived exertion  
SARC-F  
Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls  
SD  
standard deviation  
SGLT2  
sodium–glucose cotransporter 2  
TSAT  
transferrin saturation index.

## Declarations

**Ethics approval and consent to participate.** The study was approved by the Research Ethics Committee for Medicinal Products (CEI/CEIm) of Las Palmas, Canary Islands, Spain (approval code 2025-272-1; Minutes 6/2025, 30 June 2025) and was conducted in accordance with the Declaration of Helsinki. All participants gave written informed consent.

**Consent for publication.** Not applicable: the manuscript does not contain identifiable data from any individual person.

**Reporting guideline.** This observational study is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

**Trial registration.** Not applicable. The intradialytic exercise programme evaluated in this study was implemented by the Nephrology and Rehabilitation departments as part of routine clinical care at the unit, independently of this study, and participants were not assigned to the programme by the investigators. The study consisted solely of the prospective observational evaluation – multiparametric morphofunctional monitoring – of patients receiving this standard of care and therefore does not meet the WHO/ICMJE definition of a clinical trial; prospective registration was accordingly not required.

**Funding.** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests.** The authors declare that they have no competing interests.

**Availability of data and materials.** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Authors' contributions.** ACN: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Software, Validation, Visualization, Resources, Project administration, Supervision, Writing – original draft, Writing – review & editing. RPC: Conceptualization, Methodology, Investigation, Resources,

Data curation, Software, Formal analysis, Validation, Visualization, Project administration, Supervision, Writing – original draft, Writing – review & editing. JMGG: Investigation, Conceptualization, Data curation, Methodology, Validation, Software, Resources, Formal analysis, Visualization, Supervision, Project administration, Writing – original draft, Writing – review & editing. JRSG: Data curation, Investigation, Methodology, Conceptualization, Formal analysis, Visualization, Software, Validation, Resources, Project administration, Supervision, Writing – original draft, Writing – review & editing. MARG: Writing – review & editing, Investigation, Data curation. MIAO: Writing – review & editing, Methodology, Validation. CRT: Writing – review & editing, Investigation, Visualization. EJM: Writing – review & editing, Data curation, Formal analysis. EMB: Investigation, Writing – review & editing, Visualization. JCF: Supervision, Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Software, Validation, Visualization, Resources, Project administration, Writing – original draft, Writing – review & editing. All authors read and approved the final manuscript.

**Acknowledgements.** Not applicable.

## References

1. Thurlow JS, Joshi M, Yan G, Norris KC, Agodoa LY, Yuan CM, et al. Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy. *Am J Nephrol.* 2021;52(2):98–107.
2. Nair D, Liu CK, Raslan R, McAdams-DeMarco M, Hall RK. Frailty in kidney disease: a comprehensive review to advance its clinical and research applications. *Am J Kidney Dis.* 2025;85(1):89–103.
3. Puri A, Lloyd AM, Bello AK, Tonelli M, Campbell SM, Tennankore K, et al. Frailty assessment tools in chronic kidney disease: a systematic review and meta-analysis. *Kidney Med.* 2025;7(3):100960.
4. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* 2019;48(1):16–31.
5. Wang Y, Hu Y, Zhang M, Jin H, Wen Y, Tang R, et al. Bioelectrical impedance analysis–derived phase angle predicts sarcopenia in patients on maintenance hemodialysis. *Nutr Clin Pract.* 2023;38(4):881–8.
6. Shen Y, Qin H, Liu X, Liu L, Chen S, Yang Y, et al. Calf circumference predicts sarcopenia and all-cause mortality in older patients undergoing maintenance hemodialysis: a prospective cohort study. *Nutr Clin Pract.* 2026;41(1):235–44.
7. Wang XH, Mitch WE. Mechanisms of muscle wasting in chronic kidney disease. *Nat Rev Nephrol.* 2014;10(9):504–16.
8. Wathanavasin W, Banjongjit A, Avihingsanon Y, Praditpornsilpa K, Tungsanga K, Eiam-Ong S, et al. Prevalence of sarcopenia and its impact on cardiovascular events and mortality among dialysis patients: a systematic review and meta-analysis. *Nutrients.* 2022;14(19):4077.
9. García Almeida JM, Ballesteros-Pomar MD, Vidal-Casariago A, Serrano-Pérez A, Cruz-Jentoft AJ, Burgos R, et al. Expert consensus on morphofunctional assessment in disease-related malnutrition: GRADE review and Delphi study. *Nutrients.* 2023;15(8):1863. 10.3390/nu15081863.

10. De La Flor JC, García-Menéndez E, Romero-González G, Rodríguez Tudero C, Jiménez Mayor E, Florit Mengual E, et al. Morphofunctional assessment of malnutrition and sarcopenia using nutritional ultrasonography in patients undergoing maintenance hemodialysis. *Med (Kaunas)*. 2025;61(6):1044.
11. De La Flor JC, Chandu Nanwani A, Rodríguez Tudero C, Jiménez Mayor E, Benites Flores IR, LLuncor Vázquez J, et al. Integrated ultrasound approach to fluid assessment and nutritional status in hemodialysis. *Cardiorenal Med*. 2026. 10.1159/000552121.
12. Hu H, Wu C, Kwok JYY, Ho MH, Chau PH, Lok KYW, et al. Effects of different exercises on physical function, dialysis adequacy, and health-related quality of life in maintenance hemodialysis patients: a systematic review and network meta-analysis. *Am J Nephrol*. 2023;54(9–10):379–90.
13. Li Y, Li C, Liu X, Yang Y, Zhu L, Zou Y, et al. Blood flow restriction training in hemodialysis patients: clinical benefits, challenges, and future perspectives. *Hemodial Int*. 2026. 10.1111/hdi.70077.
14. Chaovarín C, Chaiprasert A, Satirapoj B, Nata N, Kaewput W, Tangwonglert T, et al. Effect of intradialytic weight resistance training exercise in sarcopenic hemodialysis patients: a randomized controlled trial. *Ther Apher Dial*. 2024;28(2):182–91.
15. Assawasaksakul N, Sirichana W, Joosri W, Kulaputana O, Eksakulkla S, Ketanun C, et al. Effects of intradialytic cycling exercise on daily physical activity, physical fitness, body composition, and clinical parameters in high-volume online hemodiafiltration patients: a pilot randomized-controlled trial. *Int Urol Nephrol*. 2021;53(2):359–71.
16. Keles O, Algun ZC, Civi Karaaslan T, Harmankaya Kaptanogullari NO, Kaptanogullari H. Effects of intradialytic exercise on functional capacity and health-related quality of life in hemodialysis patients. *Ther Apher Dial*. 2026. 10.1002/1744-9987.70153.
17. Hammond K, Mampilly J, Laghi FA, Goyal A, Collins EG, McBurney C, Jubran A, Tobin MJ. Validity and reliability of rectus femoris ultrasound measurements: comparison of curved-array and linear-array transducers. *J Rehabil Res Dev*. 2014;51(7):1155-64. 10.1682/JRRD.2013.08.0187. PMID: 25437305.
18. Sørensen B, Magnusson SP, Couppé C, Suetta C, Johannsen FE, Kristensen MT, Aagaard P. Intra-Rater Reliability of Panoramic Ultrasound Imaging for Determining Quadriceps Muscle Cross-Sectional Area in Middle-Aged and Elderly Adults. *Scand J Med Sci Sports*. 2024;34(11):e14749. 10.1111/sms.14749. PMID: 39468392.
19. Matsuzawa R, Yamamoto S, Suzuki Y, Imamura K, Harada M, Matsunaga A, et al. The clinical applicability of ultrasound technique for diagnosis of sarcopenia in hemodialysis patients. *Clin Nutr*. 2021;40(3):1161–7.
20. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. *Am J Kidney Dis*. 2001;38(6):1251–63. 10.1053/ajkd.2001.29222. PMID: 11728958.
21. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research Group. Frailty in older

- adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-56. PMID: 11253156. 10.1093/gerona/56.3.m146
22. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *J Cachexia Sarcopenia Muscle*. 2016;7(1):28–36. 10.1002/jcsm.12048. PMID: 27066316; PMCID: PMC4799853.
23. Peipert JD, Bentler PM, Klicko K, Hays RD. Psychometric Properties of the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) in the United States. *Am J Kidney Dis*. 2018;71(4):461–8. 10.1053/j.ajkd.2017.07.020. PMID: 29128411.
24. Yamagata K, Hoshino J, Sugiyama H, et al. Clinical practice guideline for renal rehabilitation: systematic reviews and recommendations of exercise therapies in patients with kidney diseases. *Ren Replace Ther*. 2019;5:28. <https://doi.org/10.1186/s41100-019-0209-8>.
25. Segura-Ortí E. Ejercicio en pacientes en hemodiálisis: revisión sistemática de la literatura. *Nefrología (Madr)*. 2010;30(2):236–46.
26. García Olegario M, de Alba Peñaranda AM, Miranda B. Guía de orientación para la práctica del ejercicio físico individualizado en hemodiálisis. In: Lorenzo V, López Gómez JM, editors. *Nefrología al Día*. ISSN: 2659 – 2606. Available from: <https://www.nefrologiaaldia.org/373>
27. Yabe H, Kono K, Yamaguchi T, Ishikawa Y, Yamaguchi Y, Azekura H. Effects of intradialytic exercise for advanced-age patients undergoing hemodialysis: a randomized controlled trial. *PLoS ONE*. 2021;16(10):e0257918. 10.1371/journal.pone.0257918.
28. Mytinger M, Nelson RK, Zuhl M. Exercise prescription guidelines for cardiovascular disease patients in the absence of a baseline stress test. *J Cardiovasc Dev Dis*. 2020;7(2):17. 10.3390/jcdd7020017.
29. Prado CM, Gonzalez MC, Norman K, Orsso CE, Barazzoni R, Cederholm T, et al. Methodological standards for body composition assessment—an expert-endorsed guide for research and clinical applications: bioimpedance, dual-energy X-ray absorptiometry, computerized tomography, and ultrasound methods. *Am J Clin Nutr*. 2026;123:101283.
30. Amaya-Campos MM, Zafra R, Jiménez-Laguna L, Bernal-López MR, Gómez-Huelgas R, Pérez-Belmonte LM, et al. Functional thresholds derived from dynamometry and 6-minute walk test with morphofunctional assessment to guide individualized exercise prescription in cardiac rehabilitation. *J Clin Med*. 2026;15(11):4336. 10.3390/jcm15114336.
31. Kim S, Park HJ, Yang DH. An intradialytic aerobic exercise program ameliorates frailty and improves dialysis adequacy and quality of life among hemodialysis patients: a randomized controlled trial. *Kidney Res Clin Pract*. 2022;41(4):462–72.
32. Ahmad AM, Ghareeb MM, Mansour AE, Mousa HA. Effects of two low-frequency intradialytic cycling training programs on functional capacity in subjects undergoing hemodialysis: a randomized controlled trial. *Hemodial Int*. 2026;30(2):251–7.
33. Takahashi R, Yabe H, Ishikawa H, Hibino T, Yamaguchi T, Morishita S, et al. Age-associated effects of intradialytic exercise on physical function and nutritional status in patients receiving ambulatory hemodialysis: a multicenter cohort study. *Hemodial Int*. 2024;28(1):117–24.

34. Usui N, Yokoyama M, Nakata J, Suzuki Y, Tsubaki A, Kojima S, et al. Association between social frailty as well as early physical dysfunction and exercise intolerance among older patients receiving hemodialysis. *Geriatr Gerontol Int*. 2021;21(8):664–9.
35. Elgenidy A, Sapoor S, Abdelrhem H, Ali AS, Sulliman S, Hedawy S, et al. Utility of ultrasound in measuring quadriceps muscle thickness in patients receiving maintenance hemodialysis: comprehensive systematic review and meta-analysis. *Clin Exp Nephrol*. 2025;29(2):192–211.
36. Esteve Simó V, Junqué Jiménez A, Moreno Guzmán F, Carneiro Oliveira J, Fulquet Nicolas M, Pou Potau M, et al. Benefits of a low intensity exercise programme during hemodialysis sessions in elderly patients. *Nefrologia*. 2015;35(4):385–94.
37. Howden EJ, Coombes JS, Strand H, Douglas B, Campbell KL, Isbel NM. Exercise training in CKD: efficacy, adherence, and safety. *Am J Kidney Dis*. 2015;65(4):583–91.
38. Rosa Domingues C, Rodeia SC, Francisco AR, Santos L, Cerca C, Costa M, et al. Ultrasound monitoring of skeletal muscle wasting and relation to nutritional intervention in critically ill patients: MUScleNut study. *Intensive Care Med Exp*. 2025;13(1):122. 10.1186/s40635-025-00823-y. . PMID: 41324850; PMCID: PMC12669447.
39. Meza-Valderrama D, Marco E, Muñoz-Redondo E, Morgado-Pérez A, et al. Musculoskeletal Ultrasound Shows Muscle Mass Changes during Post-Acute Care Hospitalization in Older Men: A Prospective Cohort Study. *Int J Environ Res Public Health*. 2022;19(22):15150. 10.3390/ijerph192215150. . PMID: 36429869; PMCID: PMC9690008.
40. Romero-Márquez JM, Novo-Rodríguez M, Novo-Rodríguez C, Siles-Guerrero V, Herrera-Montes I, Garzón Navarro-Pelayo F, et al. Bioelectrical impedance vector analysis, Nutritional Ultrasound®, and handgrip strength as innovative methods for monitoring critical anorexia nervosa physical recovery: a pilot study. *Nutrients*. 2024;16(10):1539.
41. Pérez-Sáez MJ, Morgado-Pérez A, Faura A, Muñoz-Redondo E, Gárriz M, Muns MD, Nogués X, Marco E, Pascual J. The FRAILMar Study Protocol: Frailty in Patients With Advanced Chronic Kidney Disease Awaiting Kidney Transplantation. A Randomized Clinical Trial of Multimodal Prehabilitation. *Front Med (Lausanne)*. 2021;8:675049. 10.3389/fmed.2021.675049. . PMID: 34095178; PMCID: PMC8170320.

## Figures

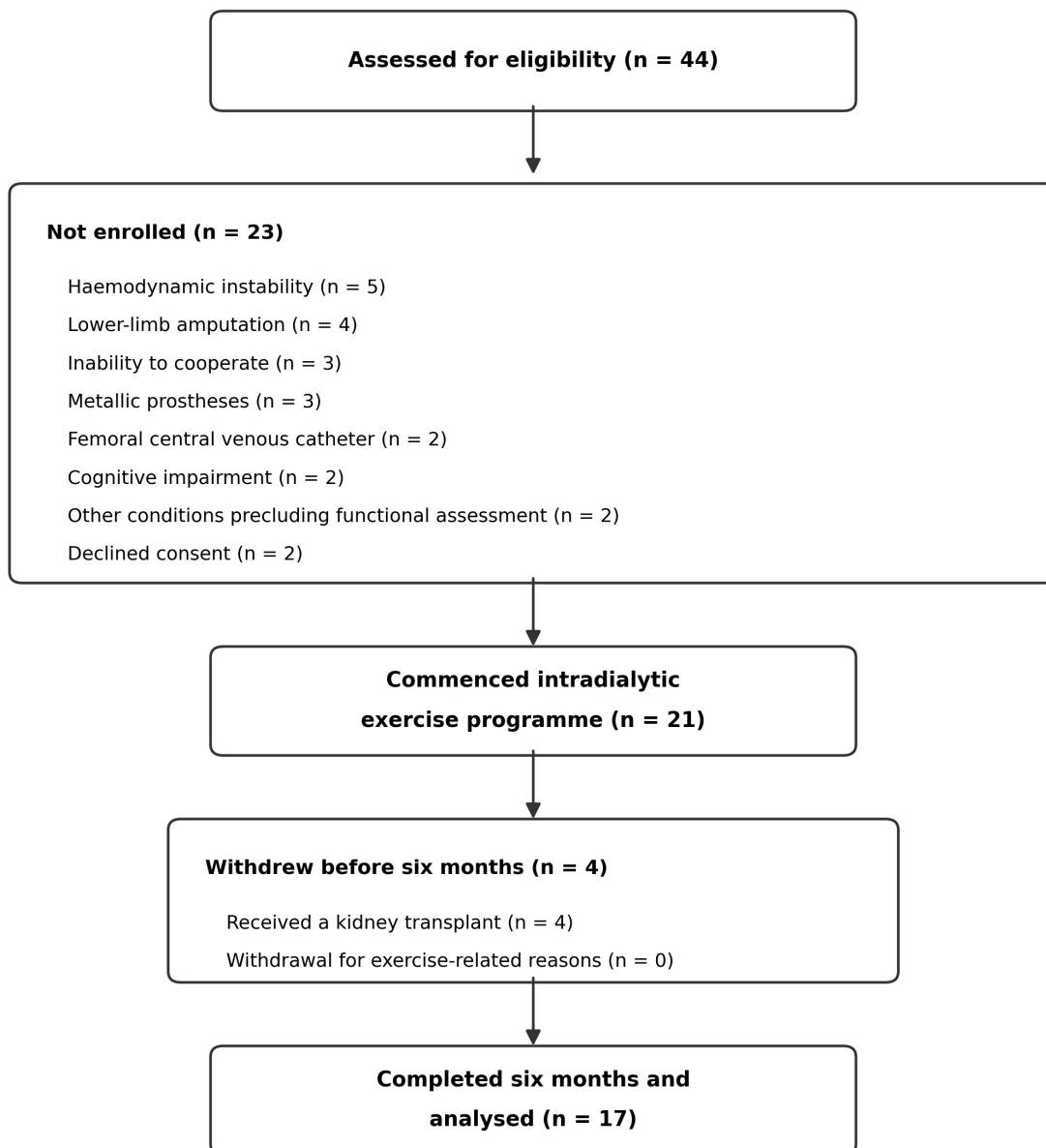


**Figure 1.** Participant flow diagram. Of 44 patients screened for eligibility, 23 were not enrolled for the reasons shown; 21 commenced the intradialytic exercise programme and four withdrew after receiving a kidney transplant, leaving 17 patients who completed six months and were analysed. No patient withdrew for exercise-related reasons.

**Figure 1**

See image above for figure legend.

**Figure 2. Frailty, sarcopenia, and nutritional status at baseline and after six months of intradialytic aerobic and resistance training.**

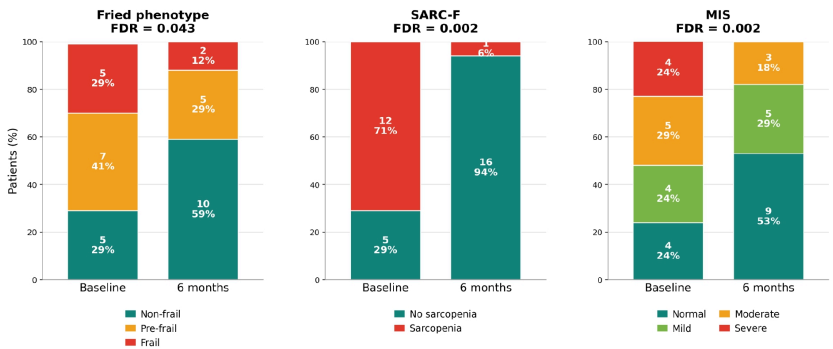


**Figure 2.** Distribution of patients ( $N = 17$ ) across the categories of the Fried phenotype (non-frail, pre-frail, frail), the SARC-F questionnaire (no sarcopenia risk, sarcopenia risk), and the Malnutrition–Inflammation Score (normal, mild, moderate, severe). For all ordinal scales, lower categories indicate better status. Within-patient changes from baseline to six months were assessed with the Wilcoxon signed-rank test (Fried, MIS) or the exact McNemar test (SARC-F);  $p$  values were adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR). All three scales improved significantly (FDR < 0.05). Abbreviations: MIS, Malnutrition–Inflammation Score; SARC-F, Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls; FDR, false discovery rate.

**Figure 2**

See image above for figure legend.

**Figure 3. Body composition by BIA at baseline and after six months.**

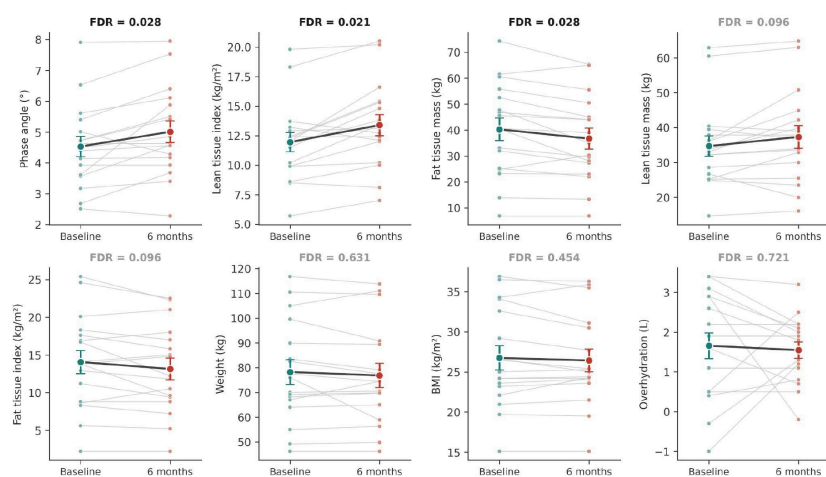


**Figure 3.** Body composition by bioelectrical impedance analysis at baseline and after six months (paired,  $n = 17$ ). Each panel shows individual patient trajectories together with the group mean and its 95% confidence interval; panel titles give the FDR-adjusted  $p$  value, and black titles denote  $FDR < 0.05$ .

## Figure 3

See image above for figure legend.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [anexoavinash16.7.2026.pptx1.jpg](#)