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Original Article

ORIGINAL ARTICLE

Frailty in hemodialysis patients: results of a screening program and multidisciplinary interventions

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ABSTRACT

Background. The number of frail patients of advanced age with end-stage kidney disease (ESKD) undergoing hemodialysis is increasing globally. Here we evaluated a frailty screening program of ESKD patients starting hemodialysis, and subsequent multidisciplinary interventions.
Methods. This was a prospective observational study of ESKD patients in a hemodialysis program. Patients were evaluated for frailty (Fried frail phenotype) before and after a 12-month period. Patients followed standard clinical practice at our hospital, which included assessment and multidisciplinary interventions for nutritional (malnutrition-inflammation score, protein-energy wasting), physical [short physical performance battery (SPPB)] and psychological status.
Results. A total of 167 patients (mean ± standard deviation age 67.8 ± 15.4 years) were screened for frailty, and 108 completed the program. At screening, 27.9% of the patients were frail, 40.0% pre-frail and 32.1% non-frail. Nutritional interventions (enrichment, oral nutritional supplements, intradialytic parenteral nutrition) resulted in stable nutritional status for most frail and pre-frail patients after 12 months. Patients following recommendations for intradialytic, home-based or combined physical exercise presented improved or stable in SPPB scores after 12 months, compared with those that did not follow recommendations, especially in the frail and pre-frail population ($P = .025$). A rate of 0.05 falls/patient/year was observed. More than 60% of frail patients presented high scores of sadness and anxiety.
Conclusions. Frailty screening, together with coordinated interventions by nutritionists, physiotherapists, psychologists and nurses, preserved the health status of ESKD patients starting hemodialysis. Frailty assessment helped in advising patients on individual nutritional, physical or psychological needs.

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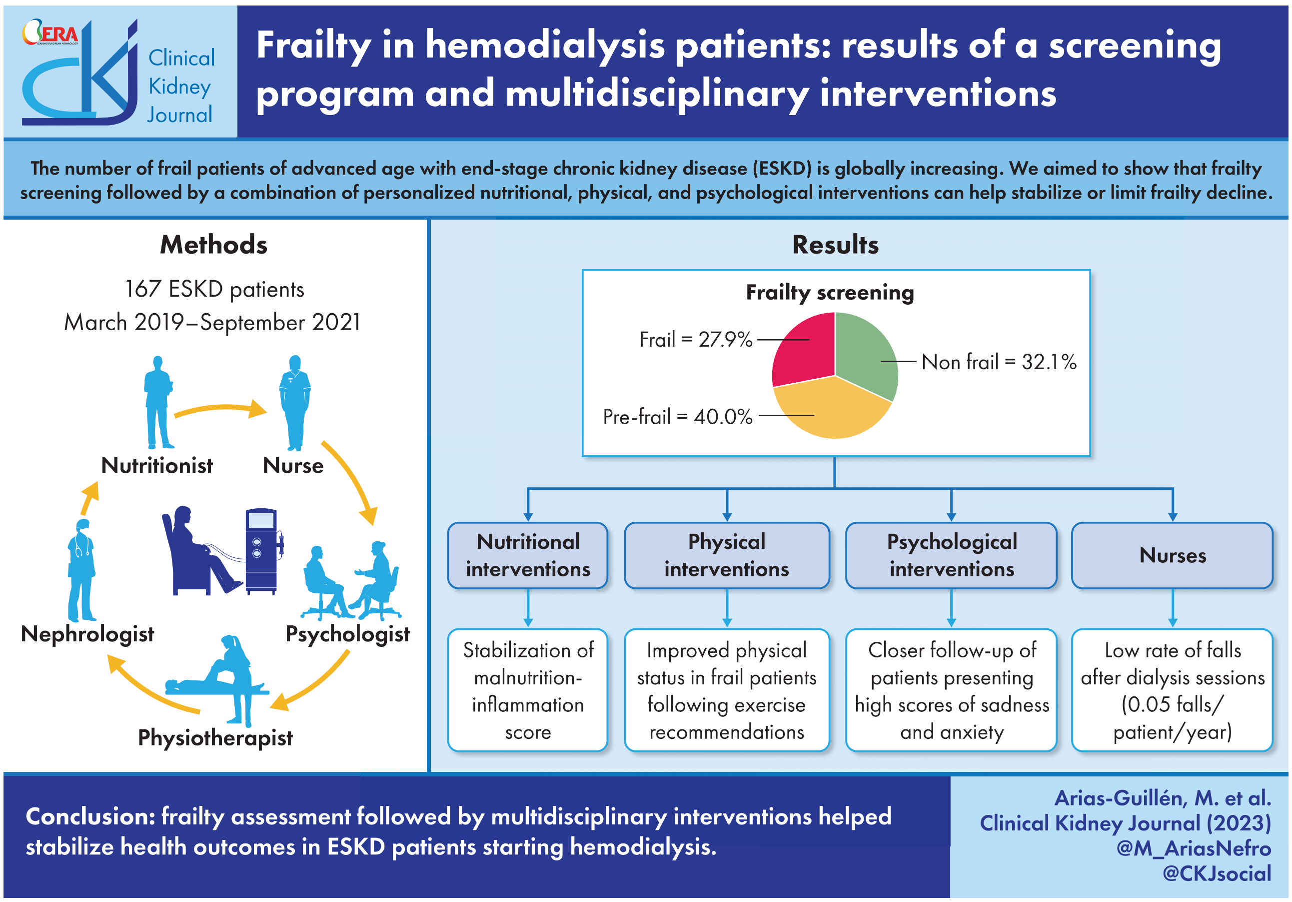
LAY SUMMARY

Increased longevity has resulted in larger numbers of patients with chronic kidney disease requiring hemodialysis. These patients are often frail and with special nutritional, physical and psychological needs. In this study we used a well-described methodology to screen patients for frailty and then used this information to advise them on actions to take to avoid health decline as they start hemodialysis. We observed that more than two-thirds of patients in the study were frail or pre-frail. Personalized advice on nutrition and physical exercise helped large proportion of these patients to avoid decline after 12 months. Frail and pre-frail patients following recommendations for physical exercise improved or stabilized compared with those who did not follow recommendations. The results of this study suggest that frailty screening is useful and should be conducted in all patients starting hemodialysis, with the goal of improving the type and quality of personalized interventions.

GRAPHICAL ABSTRACT



Keywords: end-stage kidney disease, frailty, hemodialysis, nutritional assessment, physical assessment

INTRODUCTION

The aging of the population in developed countries, together with the improved management of chronic diseases, have increased the number and the age of patients with end-stage kidney disease (ESKD) undergoing hemodialysis. Recent technological advances in hemodialysis now offer greater flexibility and tolerance to treatment, allowing the inclusion of elderly patients with more comorbidities in hemodialysis programs [1, 2]. The aging of the population starting hemodialysis has resulted in an increase in the prevalence of frailty among these patients, a condition that has been defined as a state of impaired homeostasis reserve causing an increased vulnerability to stressor events, such as infections or surgery, which could lead to a disproportionate and cumulative decline in health [3]. Frailty has been considered a predictor of disability, hospitalization, falls, loss of mobility, cardiovascular disease and death [4]. While the incidence of frailty among older people without ESKD is 3%–6%, frailty increases dramatically among people with ESKD (15%–21%), and even more so among those on hemodialysis treatment (up to 73% depending on the tool used) [1].

Studies in the past decade have demonstrated that hemodialysis patients could benefit from preventive or therapeutic measures aiming to adapt the procedures and mitigate the risks associated with frailty [5–7]. For this reason, early frailty screening of these patients by healthcare personnel has been strongly recommended, allowing for the detection of those who are frail and most vulnerable to the development of adverse health events [1, 8, 9]. The goal should be to detect not only frail patients, but also the pre-frail patients, as the latter have an increased risk of becoming frail within 3 years. However, despite the major clinical and economic implications of frailty, screening is still not routinely performed in many hemodialysis units, in part because there is no consensus regarding the optimal tool to use [10]. The current methods for assessing frailty can be divided into those based on physical frailty, such as Fried's Frailty Phenotype [11], which focuses on functional assessment and is a good predictor of clinical events [12], and multidimensional ones, such as the Frailty Index [13]; other alternatives are the Clinical Frailty Scale [14], the Edmonton Frailty Scale [15] and the FRAIL scale [16], which have been validated for the hemodialysis population. The implementation of the use of these scales in daily clinical practice is not easy, as some are time-consuming and require auxiliary instruments.

In recent years there has been increased interest in the implementation of screening programs for frailty in hemodialysis patients [8, 9, 17, 18]. However, there are few studies analyzing outcomes of interventions aimed at slowing progression or even reversing frailty in hemodialysis patients after screening. Although the nutritional, physical and psychological needs of hemodialysis patients have been extensively studied [19–22], their effects on frailty progression are not well understood. The objective of this longitudinal observational study was to determine the impact of the implementation of a frailty screening program and the subsequent multidisciplinary interventions involving nutritionists, physiotherapists, psychologists and nurses, in a population of ESKD patients undergoing hemodialysis.

MATERIALS AND METHODS

This prospective observational study was conducted from March 2019 to September 2021 at the Clinic Hospital of Barcelona (Spain). The study's recruitment was planned to ensure a minimum follow-up of 12 months between the basal and final visits. All nutritional, physical and psychological interventions followed standard routine clinical practice at our hospital and were voluntary and prescribed at the discretion of the specialist. The conduct of this study did not alter standard practice in any way. All patients provided signed informed consent and the study was conducted in accordance with the Declaration of Helsinki and local regulations. To be included in the study the patients had to be >18 years of age, with stage 5 ESKD (eGFR <15 mL/min/1.73 m^2) in a hemodialysis program, and with no hospital admissions for acute events in the month prior to inclusion.

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations including the Helsinki Declaration. The study was approved by the Clinic Hospital of Barcelona (Spain). The collection and analysis of data for this study was possible thanks to a document, evaluated, and approved by the HCB Ethics and Research Committee, signed by all patients for the use of data in review and observational studies (Reg. HCB/2018/1168). All patients provided informed consent prior to participating in the study.

Study procedures and assessments

The main assessment in this study was frailty as measured by the Fried index. Based on the five Fried frailty criteria (weight loss, exhaustion, low physical activity, slowness, weakness), the patients were divided into three phenotypes: non-frail (score 0), pre-frail (score 1–2) and frail (score 3–5) [11].

Upon inclusion in the study, the patients were assessed at the basal visit by a nutritionist, a physiotherapist and a psychologist. This multidisciplinary team evaluated and ranked each patient using well-known instruments (Table 1). These healthcare providers also prescribed interventions and monitored each patient.

The nutritional status of each patient was evaluated with the Malnutrition-Inflammation Score (MIS) [23] and the Subjective Global Assessment [24]. Protein-energy wasting was defined according to the International Society of Renal Nutrition and Metabolism criteria [25] and calculated using the Nutrendial web application (www.nutrendial.cat) [26]. The MIS provides quantitative score of the nutritional status of the patient and its severity. The severity of the MIS is composed of four grades for each component which are ranked from 0 (normal) to 3 (very severe). The overall score of the 10 MIS components ranges from 0 to 30, with high scores indicating increased severity. The Subjective Global Assessment is a semiquantitative scoring system based on history and physical examination. The history evaluates five components separately: weight loss during the preceding 6 months, gastrointestinal symptoms, food intake, functional capacity and comorbidities. The physical examination consists of two components: loss of subcutaneous fat and muscle wasting. These components are classified in terms of the three major Subjective Global Assessment scores: A, well nourished; B, mild to moderate malnutrition; and C, severe malnutrition [24].

Functional status of the patients was evaluated by a physiotherapist with the Short Physical Performance Battery (SPPB) [27], and the nurses used the Downton Fall Risk Index (DFRI) [28], and the Basic Activities of Daily Living (BADL), based on the Barthel Index (BI) [29]. The SPPB combines the results of the balance tests, gait speed and sit-to-stand, and it has been used as a predictive tool for disability and monitoring of physical function in older people. The scores range from 0 (worst performance) to 12 (best performance). The DFRI is a self-reported instrument that detects the risk of falling on a scale of 0–11 (score of ≥3 indicates a patient at risk of falling). The BI measures performance in 10 variables describing BADL and mobility, with a higher number reflecting greater ability to function independently. The time taken and physical assistance required to perform each item was used in scoring (0–100). Once the patients had been assessed by the physiotherapist, they were asked to participate in some form of physical exercise: cardiovascular work during the hemodialysis session using a pedal exerciser (intradialytic physical exercise, IPE); combined cardiovascular and strength exercise during the hemodialysis session; or functional-type home-based exercise (HBE). Patients who were already exercising on their own were advised to continue with their individual programs. Falls of patients in hemodialysis were recorded by the nursing staff and scored electronically in the hospital database.

The cognitive status of the patients was evaluated by a psychologist with Pfeiffer's test [Short Portable Mental Status

Table 1: Nutritional, physical and psychological evaluations and interventions conducted in routine clinical practice at our hospital.

Patient color coding			
Nutritional			
Instrument			
MIS	0–5	6–8	≥9
SGA	A	B	C
PEW	No	Yes/No	Yes
Intervention[a]	Diet diary[b]	Diet diary[b] Enrichment[c]	Diet diary[b] Enrichment[c] Oral nutritional supplements[d] IDPN[e]
Evaluation	After 1 year	Every 6–9 months	Every 3–6 months
Physical			
Instrument			
SPPB	>10	8–10	<8
DFRI	Low risk of falls	Medium risk of falls	High risk of falls
BADL	Autonomous	Moderate dependency	Strong dependency
Intervention	General recommendations for activity HBE, IPE Monitored for risk of falls and dependency	IPE Strength training (supervised or at home) General recommendations for physical activity Transferring to bed supervised Advise adequate shoes Measures to avoid orthostatic hypotension	Intradialytic strength training Interdialytic training in gym Bed safety measures (position, rails) Close nurse supervision All transfers supervised Home adaptation Evaluate orthopedic dynamic measures (also at home)
Psychological			
Cognitive			
Instrument			
SPMSQ	0–3	4–7	8–10
IADL	Autonomous	Moderate dependency	Strong dependency
Intervention	Monitoring	Neuropsychology Evaluate neurocognitive stimulation	Derivation to neurologist Information about Alzheimer Foundation
Evaluation	Yearly	Every 3–6 months	At neurologist's criteria
Emotional			
Instrument			
EED	0–3	4–7	8–10
Intervention	Monitoring	In-depth psychopathological interview Group therapy	In-depth psychopathological interview Evaluate HADS Evaluate derivation to psychiatrist
Evaluation	Yearly	Every 3 months	Monthly

[a]Patients with correct nutritional test results underwent no intervention, but nurses and nutritionists monitored any developing changes periodically.
[b]Diet diary: registry of all foods for a 3-day period (no dialysis day, dialysis day, holiday) in a prespecified form.
[c]Recommendations to enrich the diet (personalized by nutritionist).
[d]Nutritionally complete preparations of one or more nutrients specifically adapted to the needs of ESKD patients.
[e]IDPN was administered during regularly scheduled dialysis sessions as a supplement (commonly three times per week), and requires patients to obtain some of their nutrients orally outside of dialysis time.
HADS, Hospital Anxiety and Depression Scale; PEW, protein-energy wasting; SGA, Subjective Global Assessment.

Questionnaire (SPMSQ)] [30], and the Lawton and Brody Instrumental Activities of Daily Life (IADL) scale [31, 32]. The SPMSQ score derives from the number of errors made by the patient on a 10-item list (as errors are coded as 1 and correct answers as 0, lower values indicate better cognitive performance). Items include tasks on orientation, memory and attention. The IADL assesses independent living skills in older adults and can be used in community or hospital settings. Patients were scored according to their highest level of functioning in each of eight domains. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent).

The emotional status of the patients was evaluated with the Questionnaire to Assess Emotional Distress in Renal Patients undergoing Dialysis (EED) [33]. The EED includes five questions with different response formats (dichotomized, Likert scales and open questions) to assess sadness, anxiety, concerns, resources to cope with illness, external signs of distress, and other considerations. The score ranges from 0 to 10.

Following the evaluations, the patients were allocated into three groups (color coded green, orange and red) in each assessment (nutritional, functional, psychological), and given specific interventions (see below) depending on their nutritional, physi-

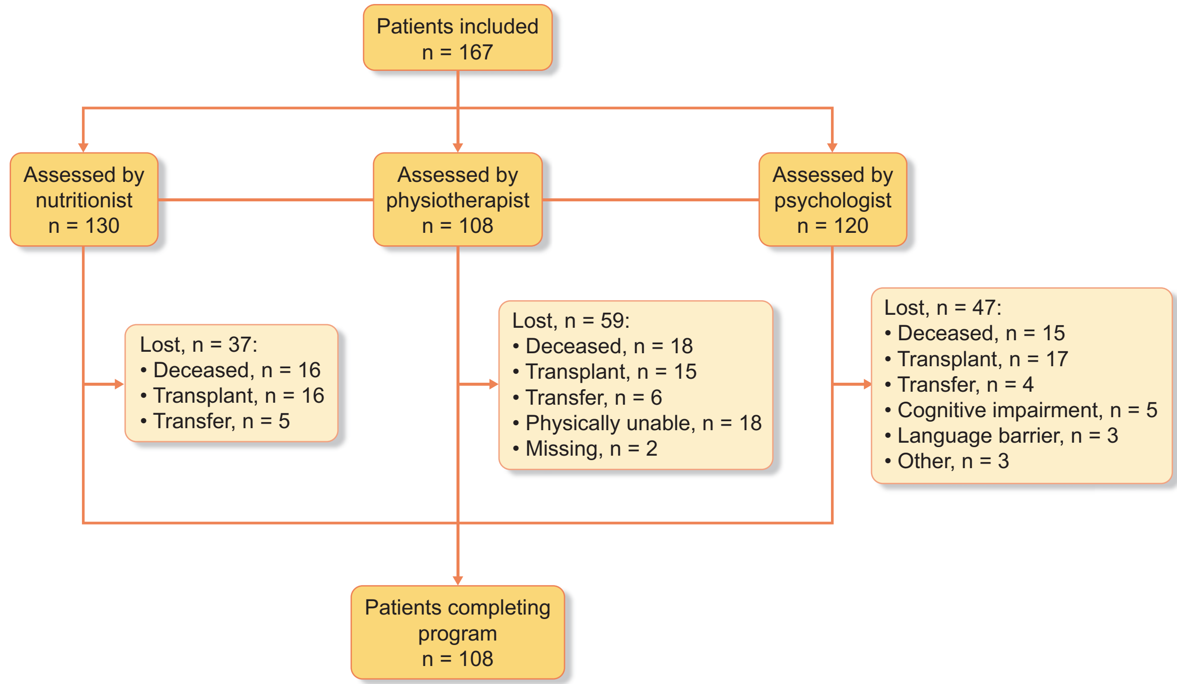


Figure 1: Patient disposition.

cal, or psychological status (Table 1). After 12 months undergoing hemodialysis, the patients were assessed again by the nutritionist and the physiotherapist, using the same instruments. Due to the limitations imposed by coronavirus disease 2019 (COVID-19) pandemic, the evaluation by the psychologist had to be postponed, which precluded assessments with a 12-month interval.

Statistical methods

A descriptive statistical analysis was performed for all variables. Continuous variables were described by the number of valid cases, mean, standard deviation (SD), median, 25th and 75th percentiles (P25–P75), and range. Categorical variables were described by means of absolute and relative frequencies of each category over the total of valid values (N).

Analysis of variance (ANOVA), the chi-square test or Fisher's exact test were used for comparisons of categorical variables. In the case of continuous variables, the Student's *t*-test or the Mann–Whitney U-test was used. For longitudinal comparisons, the repeated-measures *t*-test was used. For all comparisons, a two-tailed statistical significance α of 0.05 was applied.

Statistical analyses were performed using the SAS (Statistical Analysis System) program, version 9.3 or later on Windows platform.

RESULTS

A total of 167 patients were included in the study and 107 patients completed all assessments after 12 months (Fig. 1). The mean ± SD age was 67.8 ± 15.4 years and 67.1% were male (Table 2); 80.8% were entering the hemodialysis program and 19.2% were already in hemodialysis when the study started. The main causes of ESKD were nephrosclerosis in 41 patients (24.6%), diabetes in 26 (15.6%), glomerulonephritis in 24 (14.4%) and polycystic kidney disease in 16 (9.6%). The main comorbidities associated to ESKD were hypertension in 146 patients (87.4%) and diabetes [type 1 in 10 patients (6.0%) and type 2 in 56 patients (33.5%)]. The mean time in dialysis was 50.6 ± 48.9 months (range 3–312), with a mean daily dose of 2.3 ± 0.6 Kt/V. A total of 23 patients died during the study, and 28 underwent a renal transplant.

According to the Fried frailty phenotypes, of 165 patients with data available at the baseline visit, 53 (32.1%) were non-frail, 66 (40.0%) were pre-frail and 46 (27.9%) were frail (Fig. 2). In the final visit there were 101 patients with data available, and of these 28 (27.7%) were non-frail, 33 (32.7%) were pre-frail and 40 (39.6%) were frail. No significant changes were observed overall among the three Fried phenotypes between the two timepoints ($P = .1377$).

A nutritional assessment was conducted on 157 patients in the baseline visit and 130 in the final visit. Overall, no significant differences were observed in the MIS mean score or the proportions of patients in each of the categories for the MIS, Subjective Global Assessment or protein-energy wasting during the study period (Table 3). Also, mean values for albumin, cholesterol and transferrin did not change significantly in this patient population. When classified according to Fried phenotypes, no significant changes were observed for MIS, albumin, cholesterol or transferrin (Table 4). Patients were classified according to nutritional intervention and Fried phenotype, for baseline and final visits, revealing a higher need for nutritional intervention (dietary enrichment or supplements) in pre-frail and frail patients compared with non-frail patients (Table 5). The proportion of patients requiring these nutritional interventions was reduced between baseline and final visits.

The functional assessment (SPPB) was evaluated for 149 patients at the baseline visit and 109 at the final visit (Table 3). No statistically significant differences were observed between the two timepoints, or between the number of patients with

Table 2: Population baseline characteristics.

Variable	N = 167
Age, years, mean ± SD	67.8 ± 15.4
Sex, male, *n* (%)	112 (67.1)
Hypertension, *n* (%)	146 (87.4)
Diabetes, *n* (%)	66 (39.5)
Dialysis dose, Kt/V, mean ± SD	2.3 ± 0.6
Time on dialysis, months, mean ± SD	50.6 ± 48.9
Charlson index[a], mean ± SD	6.6 ± 2.7
Social assessment scale[b], mean ± SD	8.8 ± 3.3
BADL scale[c], *n* (%)	
Total dependency	7 (4.2)
Severe dependency	6 (3.6)
Moderate dependency	33 (19.8)
Little dependency	17 (10.2)
Independent	104 (62.3)
IADL scale[d], *n* (%)	
Total dependency	9 (5.4)
Severe dependency	6 (3.6)
Moderate dependency	21 (12.6)
Little dependency	29 (17.4)
Independent	102 (61.1)
Fall risk[d], *n* (%)	
High	18 (10.8)
Medium	52 (31.1)
Low	97 (58.1)
Cognitive impairment[f], *n* (%)	
No impairment	144 (86.2)
Mild	10 (6.0)
Moderate	9 (5.4)
Severe	4 (2.4)
Emotional distress[g], mean ± SD	
Sadness	3.48 ± 2.96
Anxiety	3.14 ± 2.74

[a]Charlson comorbidity scale [48].
[b]Gijón scale [49, 50].
[c]Delta test [51].
[d]Lawton & Brody scale [31, 32].
[e]Downton scale [28].
[f]SPMSQ [30].
[g]EED [33].

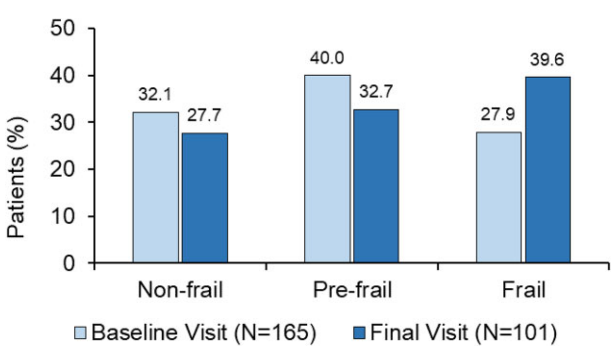


Figure 2: Fried phenotypes at the baseline and final visits.

low, moderate or normal physical status ($P = .317$). However, when the change between baseline and final functional status was evaluated against the Fried phenotypes, a significant change was found in SPPB scores, which decreased slightly in non-frail (−0.08 ± 1.19, $N = 40$) and pre-frail patients (−0.80 ± 2.02, $N = 49$), and increased in frail patients (0.39 ± 1.79, $N = 18$) ($P = .025$).

Table 3: Nutritional and functional assessments at the baseline and final visits.

Variable	Baseline visit	Final visit	P[a]
Nutritional	N = 157	N = 130	
MIS, mean ± SD	6.69 ± 3.66	6.22 ± 4.23	.312
MIS, N (%)			
0–5	68 (43.3)	70 (53.8)	.171
6–8	52 (33.1)	32 (24.6)	
≥9	37 (23.6)	28 (21.5)	
SGA, N (%)			
A	77 (49.0)	61 (46.9)	.938
B	73 (46.5)	63 (48.5)	
C	7 (4.5)	6 (4.6)	
PEW, N (%)			
Yes	30 (19.1)	16 (12.3)	.118
No	127 (80.9)	114 (87.7)	
Albumin, mean ± SD	3.86 ± 0.39	3.92 ± 0.38	.191
Cholesterol, mean ± SD	158.42 ± 37.31	156.74 ± 36.21	.701
Transferrin, mean ± SD	175.58 ± 34.79	175.54 ± 33.06	.991
Functional	N = 149	N = 109	
SPPB score, mean ± SD	9.0 ± 2.8	8.9 ± 2.8	.829
Functional categories, *n* (%)			
>10	63 (42.3)	37 (33.9)	.317
8–10	42 (28.2)	39 (35.8)	
<8	44 (29.5)	33 (30.3)	

[a]Chi-square test.
PEW, protein-energy wasting; SGA, Subjective Global Assessment.

Of 159 patients, 20 (12.6%) patients were advised to start home-based exercise, 80 (50.3%) intradialytic exercise and 25 (15.7%) a combination of home-based exercise and intradialytic exercise, and 33 (20.8%) to continue their routine physical exercise (1 patient did not receive a recommendation for medical reasons). However, of 108 patients assessed, only 75 (69.4%) accepted to follow the physical exercise proposed, while 33 (30.5%) refused to do any exercise or could not do any for other reasons (e.g. underlying pathologies, difficulty in understanding the regimen, anatomical characteristic incompatible with the continued execution of the program). Of all the patients who agreed to participate in any of the proposed physical exercise modalities, 29% had an improvement in their final SPPB score compared with baseline, in 41% it remained the same, while in 29% there was a decrease (Fig. 3A). Of the patients who declined to participate and did not perform any type of prescribed exercise, in 18% the SPPB score increased, in 27% there was no change and in 55% the SPPB score decreased. Of the patients who accepted the recommendations for the exercise program, 7 patients out of 37 (18.9%) with IPE showed an improvement in SPPB scores (Fig. 3B).

A total of 24 falls were registered during the study period (9 falls in the year 2019; 9 in 2020; and 5 in 2021), or about 0.05 falls/patient/year. Most falls were observed in the post-dialysis period.

A total of 120 patients were evaluated by the psychologist. Of these, 38 (31.7%) were non-frail, 53 (44.2%) were pre-frail and 28 (23.3%) were frail. Frail patients scored higher in the EED for sadness and anxiety (4.4 ± 2.9 and 4.4 ± 2.9, respectively) than patients who were pre-frail (3.3 ± 3.1 and 2.7 ± 2.5) or non-frail (3.1 ± 2.6 and 2.8 ± 2.8). A total of 61 patients (50.8%) presented an EED score ≥4 and most of these (>60%) were frail (Fig. 4). The psychology intervention focused on these patients and 59 of them initiated a variety of interventions, with a mean of 4.2 vis-

Table 4: Differences between final and basal scores in mean nutritional and functional parameters according to Fried phenotype.

Variable	Total	Non-frail	Pre-frail	Frail	P[a]
MIS	−0.39 ± 4.01 (N = 130)	−1.24 ± 2.48 (N = 42)	−0.11 ± 4.04 (N = 55)	0.21 ± 5.30 (N = 33)	.238
Albumin	0.05 ± 0.39 (N = 130)	0.15 ± 0.25 (N = 42)	0.00 ± 0.31 (N = 55)	−0.02 ± 0.59 (N = 33)	.101
Cholesterol	−3.79 ± 28.20 (N = 129)	0.90 ± 24.00 (N = 41)	−2.16 ± 28.42 (N = 55)	−12.33 ± 31.46 (N = 33)	.113
Transferrin	−1.54 ± 30.00 (N = 130)	1.19 ± 25.39 (N = 42)	−1.09 ± 29.54 (N = 55)	−5.76 ± 36.06 (N = 33)	.606
SPPB	−0.33 (1.76)	−0.08 (1.19)	−0.80 (2.02)	0.39 (1.79)	.025

[a]ANOVA test. The P-value shows whether there is a difference in the evolution in each of the three groups between basal and final visits.

Table 5: Differences in Fried phenotype according to nutritional intervention.

		Baseline visit				Final visit			
Nutritional intervention	Total	NA	Non-frail	Pre-frail	Frail	NA	Non-frail	Pre-frail	Frail
Monitoring	82 (100)	1 (1.2)	36 (43.9)	35 (42.7)	10 (12.2)	37 (45.1)	17 (20.7)	16 (19.5)	12 (14.6)
Diet diary	41 (100)	1 (2.4)	12 (29.3)	18 (43.9)	10 (24.4)	9 (22.0)	9 (22.0)	13 (31.7)	10 (24.4)
Diet diary + enrichment	16 (100)		1 (6.3)	9 (56.3)	6 (37.5)	7 (43.8)	1 (6.3)	2 (12.5)	6 (37.5)
Diet diary + supplements	23 (100)		3 (13.0)	4 (17.4)	16 (69.6)	11 (47.8)	1 (4.3)	2 (8.7)	9 (39.1)
IDPN	4 (100)		1 (25.0)		3 (75.0)	1 (25.0)			3 (75.0)

All data are presented as N (%).
NA, not available.

its per patient per year. Among them, nine patients received psychiatric treatment, six for major depressive disorder and three for substance disorder.

DISCUSSION

In this observational study we described the effects of the implementation of a frailty screening program in a population of ESKD patients initiating hemodialysis, and the effects of multidisciplinary interventions involving nutritionists, physiotherapists, psychologists and nurses. The screening of patients starting hemodialysis showed that about a third of them could be considered frail, and another third pre-frail. The high prevalence of frailty in this patient population is consistent with previous reports [1, 6, 8], and highlights the need for improved awareness and evaluation of the special needs of this group of patients. Worse frailty scores in ESKD patients have been associated with worse outcomes [34], and frailty assessment could be used to inform clinical decisions and to improve counselling to patients and caregivers. In our study, the frailty assessment was used to guide a multidisciplinary group of healthcare specialists to offer individualized recommendations to the patients with the goal of improving nutritional, physical and psychological outcomes.

We found a high prevalence of patients with nutritional deficiency in our cohort, as 57% of patients presented MIS scores ≥6. After 12 months of follow-up, most patients (53%) had MIS scores 0–5, suggesting that the interventions to stabilize or improve nutrition were at least partially successful. A small decrease (6.8%) in patients who were at risk for or already catalogued with protein-energy wasting was observed. Different types of nutritional interventions [food enrichment, oral nutritional supplements, intradialytic parenteral nutrition (IDPN)] were qualitatively evaluated, and it is likely that they contributed to improve MIS and protein-energy wasting results, especially in women and older patients. Our results suggest that frail and pre-frail patients required a more substantial nutritional intervention than non-frail patients. Recent work has shown that protein-rich foods/supplements should be used to improve nutritional status in ESKD patients in hemodialysis, achieving the greatest impact in those patients with the poorest baseline nutritional status [22]. A randomized study demonstrated that IDPN can help increase serum albumin, body weight, spontaneous oral intake and MIS in patients in hemodialysis [35]. A meta-analysis of randomized clinical trials studying the effects of oral nutritional supplements and IDPN in patients with maintenance dialysis therapy has shown that, although more studies are needed, modest improvement in nutritional status can be observed [36]. In our view, a periodic nutritional assessment is essential to evaluate the patient's condition, as early nutritional intervention reduces possible complications later.

Complementary to nutritional recommendations, physical activity interventions can also be implemented to prevent the loss of muscle mass and strength. In our study we observed a gain in functionality in frail patients, although globally, the SPPB score slightly decreased during the 12-month follow-up. At our hospital, both the physiotherapist and the nursing team aimed to convey to the patients the benefits of maintaining physical activity, not only during the dialysis sessions but also at their homes. Patients who accepted the recommendation to do physical exercise as part of their treatment obtained better results (70% presented improved or stable SPPB scores) compared with patients who did not accept the recommendation (50% improved or stable SPPB scores). It should be noted that during hemodialysis, the exercise was only aerobic, a form of exercise which is usually very well accepted and maintained. Combined cardiovascular and strength exercise seems to be the most effective, as seven out of nine patients who followed this recommendation presented an increase in SPPB scores. Most patients continuing their physical exercise routines (control group) or starting physical exercise at home were able to successfully maintain or increase SPPB scores. Prior studies have shown that exercise during hemodialysis can induce modest improvements in physical functioning and muscle strength [37–39], although the evidence from large randomized studies is limited and inconsistent [40].

Recent studies have concluded that focus on the identification of patients at risk, comprehensive assessment, and the

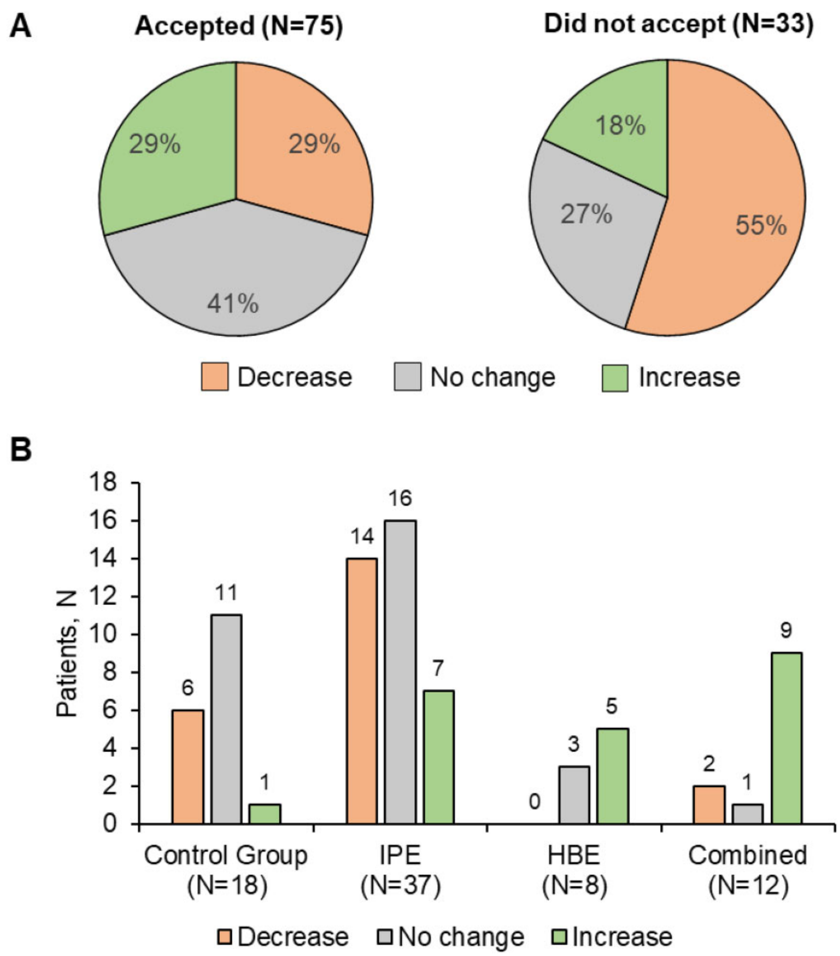


Figure 3: Changes in SPPB scores (decrease, no change, increase) according to the acceptance by the patients of the recommendations by the physiotherapist (**A**) and, in those who accepted, the type of exercise program followed (**B**).

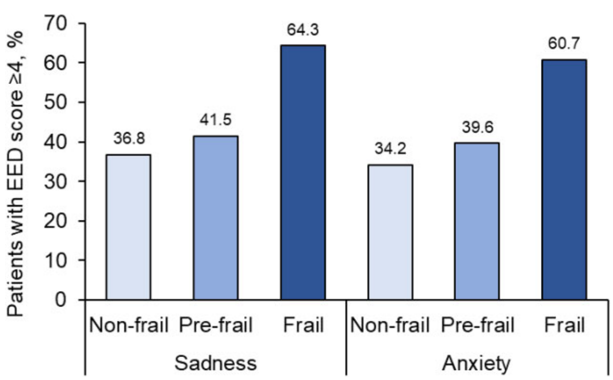


Figure 4: Psychological assessment according to Fried phenotype. Percentage of patients with EED score ≥4 (range 0–10) in the psychological evaluation. A total of 120 patients were assessed (non-frail = 38, pre-frail = 53, frail = 28). As indicated in Materials and methods, no 12-month evaluation was possible due to the limitations imposed by the COVID-19 pandemic.

implementation of prevention programs are required to reduce falls [41]. A global incidence of 0.85–1.60 falls per patient/year in hemodialysis patients has been reported [42]. In this study a remarkably low rate of 0.05 falls per patient/year was observed. At our hospital, frailty screening and the associated categorization of patients according to frailty allowed nurses to focus resources on those patients at highest risk of falling. Some patients received help for home tasks and advice on how to facilitate movement. As previous studies show that falls usually occur after dialysis sessions [43], a period at which the patient is most vulnerable, the nursing staff in charge of helping the patients was increased specifically at those periods.

Overall, although the results of our study showed that there was an increase in the percentage of frail patients after 12 months, the data suggest that the nutritional and physical interventions helped to avoid further deterioration of pre-frail and frail patients. In addition, the implementation of the frailty screening program led to major improvements in the management of the hemodialysis unit, the optimization of the nurses' workloads and more efficient allocation of resources. Similar projects have been implemented elsewhere, with generally positive results [7, 8]. In recent years, the paradigm of quality of care for patients with ESKD has changed, making necessary the introduction of models that include evaluation of frailty in clinical practice to improve resource management. The healthcare models of ESKD patients need to move from an approach segmented by specialties to a more integrated vision which considers the social situation and the patient's experience of their illness and their family context. As frailty in hemodialysis is considered a predictor of adverse outcomes such as increased hospitalization, loss of mobility, comorbidities and decreased survival [1, 4, 44–47], it is urgent to clarify the reasons that contribute to frailty decline and establish protocols aimed at mitigating them. A recent comparative study of frailty scales and clinical outcomes has shown that the Fried Frailty Phenotype used in this study was significantly associated with clinical events such as hospitalizations, fractures and/or all-cause mortality [12].

Some limitations of our study must be considered when interpreting the data. Firstly, patients were not randomized into control and intervention groups, as it seemed unethical not to treat the patients with severe malnutrition or limited physical function after the detection at screening. However, although this fact limits the overall conclusions, the results of the study still provided us with better understanding of the patients' nutritional and physical needs, as well as the necessary interventions to mitigate them. Secondly, some groups of patients might have been over- or underrepresented, as the inclusion criteria were unrestrictive to allow for a broad representation of ESKD patients in hemodialysis at our hospital. This is especially significant because most of the study was carried out during the COVID-19 pandemic, which caused a huge stress in the healthcare system and forced many patients to alter their habits. For example, the limitation of mobility due to the lockdown worsened the functional capacity of the frail population.

The main strengths of our study are the number of patients evaluated and the integrative approach to healthcare, which aimed to describe numerous interventions by different specialists in the same cohort. Although clinical trials focused on specific interventions in selected patients are necessary, our study highlights the importance of frailty screening in the general population of hemodialysis patients and the diversity of measures that can be adopted for their care.

In conclusion, the implementation of a program of assessment of frailty, together with the coordinated action of a multidisciplinary team of nutritionists, physiotherapists, psychologists and nurses, improved the health outcomes for ESKD patients at the Barcelona Hospital Clinic. Frailty assessment helped in informing patients of their prognosis at the dialysis initiation, and advising on individual nutritional, physical or psychological needs. Counseling is especially important in light of the current aging of the population, which leads to increased numbers of elderly ESKD patients in need of hemodialysis. For this reason, health professionals should include frailty assessment in their clinical practice and incorporate strategies that meet the needs of this fragile patient population.

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AUTHORS' CONTRIBUTIONS

M.A.-G. and M.Q. conceptualized and designed the study. M.A.-G. collected the data and contributed to its analysis and interpretation. M.A.-G., F.M. and B.B. wrote-up the manuscript. B.R., A.Y.-O. and A.L.-L. conducted the investigation. B.R., A.Y.-O., A.L.-L., M.G. and J.J.B. analyzed and interpretated the data. S.G., V.V., M.M., N.C. and L.R. contributed towards data collection. All authors read and approved the final manuscript.

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DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST STATEMENT

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