Assessment of the correlation between frailty markers and negative outcomes in elderly patients on chronic dialysis and kidney transplant: a multicenter study

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Introduction

Ageing has been defined as a process which, slowly but progressively, reduces the complexity of the body, in its biological as well as its social dimensions, which is a phenomenon that leads the individual to a situation of homeostatic imbalance and therefore to a state of frailty and vulnerability (1-3).

More than a decade ago, Fried and colleagues coined the term “frailty phenotype” based on the identification, in elderly patients, on a series of clinical conditions such as, feeling weak, a lack of resistance and energy, slow gait, limited physical activity and shrinking of the body size, which is also a characteristic of the onset of sarcopenia (4-9). The importance of detecting the *frailty phenotype* lies in its close association with a high hospitalization risk and death (4, 10-13) Nowadays, to detect as well as to establish the stage of frailty phenotype in a simple but reliable manner, the combination of a clinical score based on daily life activities (scale of clinical frailty), an assessment of the gait speed (gait test) and a record of the individual´s hand-grip are used (14-17)

On the other hand, there is increasing epidemiological evidence which links adverse social factors with the beginning and progression of chronic illnesses, as well as mortality in general; with these results showing the same or better correlation with adverse results than the classic risk factors such as hypertension or dyslipidemia (14-16). Among these social variables, it is worth to highlight *social isolation*, understood as a marked decrease in social bonds, institutional connections and participation in community activities, showing a higher risk of morbi-mortality in isolated individuals (16). In order to detect and determine the degree of *social isolation*, a score known as “social isolation score” has been developed (18).

It is worth mentioning that, much like in occidental societies there is an increase in the proportion of elderly patients (10%), there is a similar number of patients under chronic dialysis, where the elderly population reaches a 30 % and the population affected by the frailty phenotype is approximately 42% (19-21).

It then arose the question of evaluating elderly (age ≥ 65 years) patients on chronic dialysis or kidney transplant if biological frailty markers (slow gait and weak hand-grip, etc.) and negative social markers (isolation) correlate better with negative evolution markers (number of hospitalizations as well as cardiovascular and general mortality), which classic variables in the daily follow-up of these patients, such as the hematocrit, arterial blood pressure, uremia, creatininemia, glucemia, cholesterolemia, albuminemia, fosfatemia, intact parathormone, dialytic Kt/V value, and number of kidney rejections.

Objective of the project

Main

To explore the association between biological frailty markers (speed gait, hand-grip, clinical frailty score, sarcopenia by bioimpedance) as well as negative social markers (isolation) and negative results (admissions and cardiovascular as well as general mortality) in elderly on chronic dialytic treatment (hemodialysis and peritoneal dialysis) and kidney transplant.

Secondary

To explore the association between biological frailty markers (speed gait, hand-grip, clinical frailty score, sarcopenia by bioimpedance) as well as negative social markers (isolation), and Kt/V value (chronic dialysis), number of rejections (kidney transplant), blood pressure and serum biochemical variables (all).

To evaluate if there are significant differences in all the evaluated variables between old (≥65 and ≤ 75 year olds) and very old patients (>76 year olds).

Material and Methods

Design of the study
Prospective cohort

Population and study environment
Individuals older than 64 years old who are on chronic dialytic treatment or kidney transplant more than 3 months ago.

Study environment
Dialysis and transplant centers

Exclusion criteria
Less than three months at the moment of the potential admission in the cohort study.
Negative of the patient or his/her family to be included in the study.

Follow-up
One year

Potentially predictive variables

Age: continuous variable (substraction between the date of admission to the cohort and the date of birth).

Gender: dichotomic variable (1: male, 0 female)

(the following variables will be evaluated three times per year)

Frailty: using the clinical score of frailty developed by Rockwood and col[i] (Exhibit-Table 1). Ordinal number variable with seven possible categories (1 to 7).

Hand-grip: using a hand-grip meter of the hand and according to the percentile tables developed by Massy-Westropp and col. [ii] (Exhibit-Table 2)

Isolation: using the isolation score (Exhibit-Table 3)

Blood pressure: continuous variable in mm Hg.

Serum biochemical variables
Hematocrit, uremia, creatiniemia, glucemia, natremia, kalemia, total cholesterolemia and HDL fraction, albuminemia, calcemia, fosfatemia, intact parathormone: continuous variables (each one expressed in its original units).

Kt/V value: continuous variables

Number of kidney rejections: continuous variable

Lean mass evaluated by bioimpedance: continuous variable

Gait speed: Gait disorder was defined as a gait velocity < 0.8 m/s in 4.5 meters (continuous variable)

Main Out-comes

Death: each individual´s date of death will be recorded as well as its cause (cardiovascular or otherwise) or the date when it was last checked the patient was alive.

Admissions: the date of admission as well as the date of release of each time the patient is admitted will be recorded.

Annex:

Table 1: Clinical Frailty Score

Very fit	People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.
Well	People who have no active disease, symptoms but are less fit than category 1. Often, they exercise or are very active occasionally.
Managing well	People whose medical problems are well controlled, but are not regularly active beyond routine walking.
Vulnerable	While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up”, and/or being tired during the day.
Mildly frail	These people often have more evident slowing and need help in high orders (finances, medication, transportation, heavy housework).
Moderately frail	People need help with all outdoor activities. Indoors they need help with housekeeping, and often have problems with stairs. They also need help with bathing and might need minimal assistance with dressing.
	Completely dependent for

Severely frail	personal care, from either cause (physical or cognitive). Even so, they seem stable and not at high risk of dying.
Very Severely frail	Completely dependent, and approaching the end of life (within 6 months).
Terminally ill	Approaching the end of life. This category applies to any people with a life expectancy <6 months, who are not otherwise evidently frail.

If dementia is present, the degree of frailty usually corresponds to the degree of dementia

•Mild dementia: includes forgetting the details of a recent events though still remembering the event itself, repeating the same question/story and social withdrawal

•Moderate dementia: recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting

•Severe dementia: they cannot do personal care without help

Table 2: Hand-Grip

- **scoring:** The best result from several trials for each hand is recorded, with at least 15 seconds recovery between each effort. The values listed below (in kg and lbs) give a guide to expected scores for adults. These values are the average of the best scores of each hand. Other protocols will just use the score from the dominant hand, or compare the left and right hand results.

	MALES		FEMALES	
rating*	**(lbs)**	**(kg)**	**(lbs)**	**(kg)**
excellent	> 141	> 64	> 84	> 38
very good	123-141	56-64	75-84	34-38
above average	114-122	52-55	66-74	30-33
average	105-113	48-51	57-65	26-29
below average	96-104	44-47	49-56	23-25
poor	88-95	40-43	44-48	20-22
very poor	< 88	< 40	< 44	< 20

Table 2 (bis) Mean and Standard Deviation and Hand Grip Strength in kilograms, for men and women, presented in ascending age groups

Men				Women			
Age	**right**	**left**	**BMI**	**Age**	**right**	**left**	**BMI**
20 to 29	47(9.5)	45(8.8)	26.4(5.1)	20 to 29	30(7)	28(6.1)	25.1(5.8)
30 to 39	47(9.7)	47(9.8)	28.3(5.2)	30 to 39	31(6.4)	29(6)	27.3(6.8)
40 to 49	47(9.5)	45(9.3)	28.4(4.6)	40 to 49	29(5.7)	28(5.7)	27.7(7.7)
50 to 59	45(8.4)	43(8.3)	28.7(4.3)	50 to 59	28(6.3)	26(5.7)	29.1(6.4)
60 to 69	40(8.3)	38(8)	28.6(4.4)	60 to 69	24(5.3)	23(5)	28.1(5.1)
70 +	33(7.8)	32(7.5)	27.2(3.9)	70 +	20(5.8)	19(5.5)	27(4.7)

Table 3: Social Isolation Score

Four type of relationships (1 point for each).
Score ranges from 0 (highest isolation) to 4 (lowest isolation).

•Marital status: being married or living together with someone.

•Frequency of contact with other people: having 3 or more interactions with other people per week.

•Participation in religious activities: attending church or religious services 4 or more times per year.

•Participation in other club or organization activities: being member of a club or organization.

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