

Influence of hemodialysis on the physical activity and motor capacity of patients with chronic renal disease, stage 4-5 (K/DOQI): study synopsis

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ABSTRACT

Purpose: Elderly patients who undergo hemodialysis are more fragile than older persons not on dialysis. However, it is not clear if this frailty exists before hemodialysis or if it becomes evident or more acute at the time of beginning a dialysis therapy program. The purpose of this study is to analyze if changes at both the motor and cognitive levels go hand in hand with the beginning of dialysis, and, if this is the case, to identify possible risk factors associated with the functional decline in these patients.

Methods: A multicentric prospective pilot observational study was conducted in an ambulatory population with the primary objective to represent the evolution of functional gait capacity in patients before and during hemodialysis treatment, to show gait insecurity during treatment follow-up, if it is present. The secondary objectives are to identify risk factors in the development of gait insecurity, and to measure the prevalence of falls during the follow-up period.

Results: The enrolment of patients began in January 2015 and the duration of the data collection will be at least 36 months. In the first 24 months, 19 patients have been included in the study. Preliminary data analysis is not expected before July 2018.

Conclusions: The identification of frailty predictors is of major importance in order to identify and target patients at the highest risk of frailty who may be likely to benefit from preventive intervention.

Keywords: Chronic renal disease, Hemodialysis, Functional impairment, Motor impairment, Risk of fall

Purpose

Limitations in physical activity are a major problem for patients on hemodialysis (1). The incidence of falls is greater in this population compared to non-uremic patients and is associated with increased hospital admission, institutionalization, and a greater need for health care services (2, 3). It is still unclear whether the poor physical functioning in hemodialysis patients is due to uremia, advanced age, malnutri-

tion or other comorbid illnesses or if the renal replacement therapy itself plays a major role in the deterioration of gait by inactivity, reduced exercise capacity, and poor physical functioning (4). Identification of frailty predictors is of major importance in order to identify and target those patients at highest risk of frailty who may be likely to benefit from preventive interventions. The aim of this ongoing study is to assess if changes at motor and cognitive levels go hand in hand with the beginning of dialysis and, if this is the case, to identify the possible risk factors of functional decline in these patients. The essential assumption is to look for preventive measures to be studied at a later date aiming at improving quality of life, and reinforcing autonomy and safety in this population.

Methods

This is a multicentric prospective pilot observational study conducted in an ambulatory population. The patients' degree of functional autonomy and, in particular, the level of global mobility in the period preceding the start of dialysis will be assessed by means of self-evaluation grids, plus functional

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and instrumental monitoring of physical activity and gait. We want to quantify the changes in the overall degree of autonomy and mobility that accompany the start of dialysis with tests repeated in the months following the beginning of dialysis, and a quantification of the falls in the 2 subsequent years. The analysis will include the possible attendant factors linked to the control of balance and walking, to patients' frailty and/or to dialysis, which may affect the degree of mobility and autonomy in daily life, and may also influence the risk of fall.

Eligibility criteria are (i) age ≥ 18 years; (ii) chronic renal disease stage 4-5 according to the Kidney Disease Outcomes Quality Initiative™ (K/DOQI™); (iii) estimated glomerular filtration rate (MDRD equation) ≤ 20 mL/min; (iv) eligibility for a chronic intermittent hemodialysis program recognized by the Swiss Medical Association (FMH) nephrologist; (v) the ability to understand the directives in order to carry out the functional tests; (vi) the ability to walk autonomously with or without aid; and (vii) the provision of a signed informed consent. Exclusion criteria are (i) surgery (≤ 4 weeks); (ii) serious agitated depression (Score ≥ 5 according to the 10 items Geriatric Depression Scale); (iii) clinical unstable state or pre-terminal oncological disease in progress (iv) the inability to walk; or (v) dementia (Score ≥ 1 according to the Clinical Dementia Rating Scale). The study intends to enroll a minimum of 20-30 patients with severe chronic renal disease (chronic kidney disease stage 4-5, according to K/DOQI™) who are expected to start hemodialysis in one of the Ambulatory Hemodialysis and Nephrology Services of the Ente Ospedaliero Cantonale (EOC) and in the private dialysis centers in Canton Ticino. In the 6 months before the expected start of dialysis, the patients will be subjected to clinical assessments and functional tests (with controls among cases). The functional tests include the Short Physical Performance Battery, the Expanded Timed Get-up-and-Go Test, and the Performance Oriented Mobility Assessment. These assessments will be repeated after 3, 6, 12, and 24 months from the beginning of the dialysis therapy (see Tab. I). The patients who do not start the dialysis program for medical and/or technical reasons, according to the deadlines originally set by the nephrologist responsible, will be re-assessed in any case every 6 months. The protocol for the subjects enrolled on the program foresees (i) the recording of demographic data; (ii) the measurements of the patients' general wellbeing and physical activity; (iii)

the control measurements of their balance and gait; (iv) their frailty; (v) clinical laboratory parameters of the hemodialysis quality; and (vi) the prevalence of falls.

The raw data will be inserted into a database, which will be submitted for statistical analysis. The definition of a specific measure as a primary was not set, given the exploratory nature of the study; however, the more interesting variables are gait parameters (speed and variability), plus hand and lower limb strength (5). The various measurements of physical activity and motor and cognitive capacity, will be analyzed in their evolution to establish which are the more sensitive and predictive components to change, and which may be responsible for the onset of a condition of frailty. Since this is a pilot study, and therefore without a preceding collection of data on which the applicability of the statistical methodology can be assessed, and without knowledge a priori of the measurements more sensitive to change, in the next paragraph we outline a possible statistical analysis based only on the numerical measurements of mobility. A specific statistical analysis plan (SAP) will be produced.

The subjects will undergo measurements at least once before starting dialysis and several times afterwards. A possible analysis estimates these changes (before and after starting dialysis) by means of mixed linear models, taking into consideration all the measurements collected and inserting the patients into the model as random variables. In the noncorrected model, the effect of the presence or absence of dialysis will be introduced as a time-varying covariate, assessing the presence of the value of the covariate (the difference between mobility *before* and *after*) and of the value of the interaction between dialysis and time (the difference between the annual worsening *before* and *after*). Further models will be used to correct for the effect of possible confounding factors, using the following variables: (i) service where the patient is being treated; (ii) age; and (iii) co-morbidity. Since the study wants to compare values *before* with those *after* starting the dialysis program, it is also likely that possible confounders will not have a relevant influence on the estimated effect of starting dialysis. The role of possible effect modifiers will be studied using the analysis of the interactions in following models, taking into consideration the relatively small size of the sample and assessing only the important clinical variables. The SAP will be edited after a congruous number of observations

TABLE I - Study procedures

Test	-6 Mo	+3 Mo	+6 Mo	+12 Mo	+24 Mo
Well-being questionnaires	x	x	x	x	x
Physical activity monitoring (7 days)	x	x	x	x	x
Instrumental gait analysis	x	x	x	x	x
Functional assessment	x	x	x	x	x
Neuropsychological evaluation	x			x	x
Illness rating scale	x	x	x	x	x
Nephrological parameters	x	x	x	x	x
Falls monitoring	Monthly interview				

have been collected, assessing both the formal applicability of the model, and taking into consideration the opinions of the clinicians in relation to the usability of the measurements over time (e.g., excluding measurements that are too close to the time of starting dialysis or assessing which of the measurements are the strongest confounders). In the case of non-applicability of the more complex parametric methods – and in any case as analysis of sensitivity – a nonparametric analysis will be carried out, comparing the values of the measurements *before* and *after*, both as medians and median year changes.

It is thought there will be a drop-out rate close to zero, due to the clinical features of the disease (patients in nephrology centers with chronic pathologies). The type of analysis chosen (mixed-model analysis) will allow us to use all the available data without having to discard subjects due to missing data. Basal missing sociodemographic/clinical data will be dealt with by multiple imputation. The data analysis will be carried out by the Laboratory of Geriatric Neuropsychiatry, Department of Neuroscience, Istituto di Ricerche Farmacologiche “Mario Negri,” Milan, Italy.

Results

The enrollment of the patients began in January 2015 and the duration of the data collection will be at least 36 months. A total of 19 patients have been included in the study in the first 24 months. Preliminary data analysis is not foreseen before July 2018.

Conclusion

We think that this study could be important in testing our hypothesis that chronic renal disease – and especially starting

on a program of hemodialysis – can foster and seriously worsen functional motor and cognitive impairment. If the hypothesis is confirmed, it will be important to identify modifiable risk factors of the functional decline in these patients among the variables recorded in this study. This is the prerequisite to set up an intervention study to test the effect of preventive measures in order to improve the quality of life and to reinforce the autonomy and safety in this population.

Disclosures

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Conflict of interest: None of the authors has financial interest related to this study to disclose.

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