

Translational Article

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Characteristics and Treatment Course of Patients Older Than 75 Years, Reaching End-Stage Renal Failure in France. The PSPA Study

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Background. The age of patients with end-stage renal disease is increasing in Europe and United States. In France, patients older than 75 years represent 40% of the patients who start renal replacement therapy (dialysis or renal transplantation). In these elderly patients with many comorbidities, the benefit of dialysis remains controversial. To provide clear information to patients about diagnosis, prognosis, and all treatment options, more data are needed on their clinical characteristics, therapeutic projects, and outcome.

Methods. Researchers present here the ongoing Parcours de Soins des Personnes Agées (PSPA) multicenter prospective study, which includes 581 patients with a mean age of 82 ± 5 years and an estimated glomerular filtration rate (by SMDRD) of 14 ± 4 ml/min/1.73m² without dialysis.

Results. Despite a high prevalence of associated comorbidities, most of the patients are autonomous, living at home. Less than 10% are followed jointly by a nephrologist and a geriatrician. At inclusion, postponed dialysis decision due to stable estimated glomerular filtration rate was reported in 43%, 17% of the patients are under evaluation, the decision to start dialysis was chosen in 24% of the patients, nondialysis decision was decided in 16%.

Conclusions. Geriatricians' expertise may help nephrologists to identify patients at high risk of early death for who nondialysis care may be discussed. They also may be more able to evaluate and anticipate the impact of such restricting treatments. A multidisciplinary approach of these old and frail patients' needs to be reinforced.

Key Words: Elderly—ESRD—CKD stage 5—Dialysis—Outcome.

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CHRONIC kidney disease (CKD) is now recognized as a common condition that elevates the risk of cardiovascular disease, as well as kidney failure and other complications. In the United States, based on a cross-sectional analysis of the National Health and Nutrition Examination Survey in 1999–2004, the overall prevalence of CKD among men was 11.1%, and 15.0% among women (1). The prevalence of CKD was about 48% after the age of 70 years. With improvement in the mean life expectancy in general population, the aging of the population will result

in a progressive increase in the number of patients reaching the stage 5 of CKD. Currently, because age is no more a contra-indication in most of the western countries for renal replacement therapy, in France, as in the whole of Europe and United States, incident elderly patients with CKD stage 5 starting renal replacement therapy is increasing (2–4). In France in 2010, the median age of patients starting dialysis was 71 years and the proportion of patients older than 75 years was nearly 40% of incident dialysis patients (2). Although dialysis aims to prolong life (5,6), in these

elderly dialysis patients who present lots of comorbidities, the benefit associated to dialysis is questionable (6–9). In fact, mortality rate and dialysis withdrawal is particularly high in this elderly subgroup within the dialysis population (8,10–12). In France, the survival rates are 27% and 15% at 5 years in patients aged 75–84 years and older than 85 years, respectively. Prognostic factors of quality of life and survival rate were previously studied in incident dialysis patients (13,14), but very few studies have focused on the elderly subgroup (15). Recently, based on the French end-stage renal disease REIN registry data, Couchoud et al. (10). constructed a prognosis score for patients older than 75 years predicting survival rate after 6 months of dialysis. The objective of this score was to help clinicians, especially nephrologists and gerontologists, in the decision of starting dialysis. Cohen et al. (16). developed also a 6-month-prognosis score in dialysis patients but with an additional question for nephrologist. This question was “would I be surprised if this patient died within the next 6 months in dialysis”. Those studies were able to identify patients that would benefit from dialysis with a high probability of survival after 6 months. But these studies included patients who already started dialysis, and this constitutes a selection bias. No such study has been done before the stage of dialysis, and in general, very few studies are focused on these elderly patients before the stage of dialysis. This is of particular importance because previous studies showed that in patients older than 75 years and with less than 20 mL/min/1.73 m² of glomerular filtration rate (GFR), the risk of death is higher than the risk of dialysis start (17,18).

Few studies suggested that elderly CKD patients could be treated for a long time by a conservative approach (ie nondialysis care) and a coordinated follow-up by nephrologists, gerontologists, general practitioners, or palliative care structures (19). Other studies have shown lower survival rates when compared with patients who started dialysis (5). But the evaluation of conservative treatment is limited by the design of the published studies including retrospective, single center, small size, and dialysis registry data (20). In a single center retrospective study, in a sample of octogenarian patients reaching end-stage renal failure with estimated GFR (eGFR; Cockcroft Equation) less than 10 mL/min/1.73 m², patients who underwent dialysis showed a significant increase in survival rate compared with the patient with a conservative treatment (30% of the sample) (6). In the United Kingdom, comparison of survival rate between conservative treatment and dialysis in elderly with stage-5 CKD showed a significantly better survival rate for the dialysis option compared with conservative treatment in the subgroup of low comorbidity patients. However, this was not significant in the subgroup of high comorbidity patients (7,9,19). One explanation can be that kidney failure may be a part of irreversible multiorgan dysfunction in these frail patients, and the treatment of one of the components will

not have any effective effect (8,15). Because it would be unethical to randomize patients to dialysis or conservative management, other methodological approaches and further studies have to be developed.

Furthermore, trend among nephrologists to start dialysis earlier in the course of end-stage renal disease has led to an increasing debate about benefit of this early start (21–23). Observational studies showed that a higher level of eGFR at the start of dialysis is associated with decreased patient survival. A recent randomized trial, designed to evaluate the benefit in survival between strategies of starting dialysis at higher levels of eGFR versus starting dialysis at lower levels of eGFR failed to show any difference. However, patients older than 65 years were excluded (24). This result and a recent study based on the French REIN registry data suggest that age and patient condition strongly determine the decision to start dialysis and may explain most of the inverse association between eGFR and survival (25). What about the elderly patients? In the French REIN registry, 40% of patients older than 75 years have had eGFR more than 10 mL/min/1.73 m² at the start of dialysis, and the mean eGFR is 12 mL/min/1.73 m² in the United States Renal Data System registry (13,26). In the elderly patients, eGFR and clinical uremic signs are difficult to appreciate for various reasons: eGFRs have been shown to be inaccurate and imprecise indicators of renal function in this population especially at advanced stages (27), the symptoms of CKD stage 5 overlap those of geriatric syndrome (28), and dialysis is associated with higher risk of residual renal function decline.

Another aspect that is really poorly explored in the literature is the collaboration between nephrologists, general practitioner, gerontologists, and family in the process of dialysis start decision making (29). Exploring the role of geriatric evaluation such as cognitive, autonomy, and functional status may help facilitate more appropriate use of resources and improve decision making for dialysis. In general elderly population, the geriatric evaluation is associated with increased survival rate but nothing is known in CKD population (30,31). Collaboration between nephrologists and geriatrician for the evaluation and the follow-up of patient reaching end-stage renal failure has also to be evaluated.

Finally, according to the most recent guidelines on “shared decision making” from the Renal Physicians Association (32), not to start dialysis may be considered in elderly CKD stage 5 patients older than 75 years who meet two or more of the following prognostic criteria: clinicians responding “No” for “would I be surprised if this patient died within the next 6 months”, high comorbidity score, significantly impaired functional status, and severe chronic malnutrition. Given the fact that prediction scores are never absolute, in the researchers’ opinion, the decisions made according to these guidelines should be thoroughly evaluated in future studies. The discussion between the physicians and the patients about starting dialysis or not may

be improved when the burdens of dialysis can be predicted. The information given to the patient and his family must substantially outweigh the benefits with application of the ethical principles of respect for autonomy, beneficence, nonmaleficence, and justice (32,33).

In consequence, facing the problem of dialysis of elderly patients, many questions remain to be answered: Who is a candidate for nondialysis care? Which elderly patient will benefit from dialysis? When should we start dialysis? Because no randomized study can be ethically done to answer those questions, we constructed a prospective multicenter French cohort study entitled “Parcours de Soins des Personnes Agées (PSPA)” (“Treatment course and outcome for elderly patients”). This study aims to describe the characteristics of elderly patients with severe CKD, to better understand their outcomes before dialysis stage, to describe the current nephrological practices, and to elaborate “tools” to improve decision making for physicians, patients, and families in situations prior to dialysis.

In this article, researchers will present the design and the characteristics of the population such as different therapeutic projects planned by nephrologists at inclusion time.

POPULATION AND METHOD

Twenty-four nephrology centers participated in this study, including more than 70 nephrologists (list in Annex 1). Inclusion criteria for the patients were age older than 75 years, CKD with eGRF less than 20 mL/min/1.73 m² for a period of 3 months (by sMDRD formula), and at least one consultation with a nephrologist. Out-patients or hospitalized patients could be included. Exclusion criteria were acute renal failure and late referral defined by dialysis starting without previous nephrologist follow-up.

Inclusion time was 4 months in each center, total inclusion time for all centers was 1 year (2009–2010), and the follow-up will be 4 years.

Inclusion questionnaire asked for demographic data, clinical condition (primary renal disease, comorbid conditions, and disabilities), mobility (walk without help, need assistance with mobility, and totally dependent for transfers), way of living (Home living [alone or with someone] or institutionalized), biological data (blood and urine), treatment (including medication for hypertension and renal protection), type of follow-up physicians (general practitioner, gerontologist, and nephrologist, other), and therapeutic projects about the option for dialysis for each patient. The presence of dementia is based on nephrologists' declaration. These therapeutic project options for dialysis were previously defined in a French pilot study (34) and are as follows: (a) ongoing evaluation of the patient's clinical condition; (b) decision about dialysis is postponed due to a stable eGFR; (c) decision has been made to start dialysis when required; (d) nondialysis due to nephrologist or patient request. Therapeutic project is reevaluated at each time

point during the follow-up, according to possible changes of nephrologists' or patients' opinion. As it is an observational study of current practices, no additional tests were mandatory either at inclusion time or during the follow-up. During the follow-up, at each visit will be recorded renal function, clinical condition, way of life, mobility, treatments, therapeutic project options for dialysis, dialysis start, death, and stopping follow-up by nephrologist. Nephrologists will specify the criterion of dialysis start and the modality of treatment. Date and cause of death for patients who started dialysis will be obtained from the French REIN registry. For patients who stopped being followed by a nephrologist, dialysis start or death will be obtained from French REIN Registry and the national registry of death. The study was approved by the Institutional Review Board of the researchers' institution and is conducted in accordance with good international clinical practice guidelines.

Statistical Analysis

Patient characteristics are described for the overall cohort and according to therapeutic project at inclusion. Normally distributed variables are expressed as means (\pm SD) and non-normally distributed variables are expressed as median and interquartile range. Qualitative values were compared using the chi-square test and quantitative value with analysis of variance or Wilcoxon test and Tukey test for subgroups. All *p* values were two-tailed, with <.05 considered as statistically significant. Analyses were performed using SAS, version 9.1 (SAS Institute, www.sas.com).

RESULTS

Between 2009 and 2010, 581 patients have been included in the PSPA study in 24 centers all over France (Supplementary Figure 1): Mean age at entry in the study was 83 \pm 5 years and 57% were men. General characteristics are presented in Table 1. As expected, the prevalence of severe comorbidity is high. Among patients with active malignancy, 35% had urologic cancer and 20% hematologic cancer.

Kidney function was appreciated as follows: mean eGRF was 14 \pm 4 mL/min/1.73 m² and median proteinuria was 0.9 [0.3–1.5] g/g of creatinuria (available for 64% of the patients), with 50% of population treated with angiotensin converting (ACE) inhibitors or angiotensin receptor blockers (ARBs). Renal biopsy was performed only in 9% of the patients. The presumed primary renal disease was vascular nephropathy in 39% of the cases, diabetic nephropathy in 20%, chronic glomerulonephritis in 11%, tubulointerstitial in 9% and other in 21%. Mean number of drug tablets per day was 11 \pm 5 corresponding to 9 \pm 3 classes of drugs. Mean blood pressure (BP) was within limits with 93 % of the patients receiving at least one antihypertensive drug (mean 2.7 \pm 1.2 classes) comprises 75% diuretics, 49% ACE inhibitors or ARB, 57% calcium channel inhibitor, and 47% betablocker.

Table 1. Patient's Baseline Characteristics at Entry in the Study

Baseline Characteristics	N = 581 pts
Age: mean \pm SD	83 \pm 5
Men	57%
BP (mmHg)	
Systolic: mean \pm SD	144 \pm 23
Diastolic: mean \pm SD	74 \pm 11
BMI mean \pm SD	26.5 \pm 4.9
BMI <18.5 kg/m ² - n(%)	17 (3.3%)
BMI > 30 kg/m ² - n(%)	106 (21%)
Missing data - n(%)	70 (12%)
Comorbidities	
Diabetes	37%
Chronic heart failure	34%
Peripheral vascular disease	25%
Cerebrovascular disease	13%
Dysrhythmia	28%
Active malignancy	8%
Dementia	5%
Way of living	
Home living	88%
Living alone	33%
Mobility; Unassisted with walking	81%
Nephrologist follow-up > 6 months	82%
Outpatient vs hospitalized at inclusion	77%
Joint follow-up with a geriatrician	9%

Notes: BMI, body mass index; SD, standard deviation.

Median hemoglobinemia was 11.5 [10-12] g/dl with 45% of patients treated with Erythropoiesis Stimulating Agent, hyperkalemia was present in 9% (ie K⁺ \geq 5.5 mmol/L) and metabolic acidosis in 30% (ie tCO₂ < 22 mmol/L).

At baseline, therapeutic project about dialysis options were ongoing evaluation for 17% of the patients, postponed dialysis decision due to stable eGFR in 43%, decision to start dialysis in 24% (among them 50% have dialysis access), and nondialysis in 16%. Of these former, 50% of dialysis withholding cases were due to nephrologist decision and the remaining due to patients or family's request. The nephrologist's reasons for not performing dialysis were dementia (31%), cognitive disturbance (17%), age (21%), active malignancy (17%), disability (10%), and chronic heart failure (4%). Few follow-up by geriatricians were reported at inclusion (9%).

The characteristics of the patients according to the various therapeutic projects are presented in Table 2. As expected, case-mix varied according to the therapeutic project at study inclusion. In patients with an ongoing evaluation or postponed dialysis, median eGFR was significantly higher than in patients for whom decision to dialysis was chosen and for patients with nondialysis option. In the group with nondialysis option at this point due to patient's requests, patients were older and predominantly women. In the group with nondialysis option at nephrologist request, patients were older with more comorbidity such as active malignancy and dementia, less home living and more dependent.

DISCUSSION

The growing population of elderly CKD and end-stage renal disease patients presents a major challenge to health care systems worldwide.

Clinical practice guidelines on shared decision making regarding dialysis encourage physicians to provide clear information to patients about "diagnosis, prognosis and all treatment options which should include (1): available dialysis modalities (2); not starting dialysis and continuing conservative management including end-life care (3); a time-limited trial of dialysis; and (4) stopping dialysis and receiving end-life care (32,35,36)". To be able to provide such clear informations, PSPA study is a large prospective cohort study whose objectives are to describe the characteristics of elderly patients with severe CKD; to better understand their outcomes before dialysis stage; to describe the current nephrological practices; and to find tools that can help clinician, patients, and families for dialysis decision making. In this article, researchers presented the design of the study and the baseline characteristics of patients at inclusion. From these characteristics, some points can already be discussed.

Baseline characteristics of these patients show that elderly patients who are referred to nephrologists are probably highly selected. Most of the patients are autonomous and living at their home; few have dementia or active cancer. Biological characteristics show that according to a high

Table 2. Patient's Characteristics Depending on Therapeutic Projects

Projects Concerning Dialysis	Ongoing Evaluation n = 99 (17%)	Stable GFR n = 255 (44%)	Option for Dialysis n = 135 (23%)	Nondialysis Option at Patient's Request n = 45 (7.8%)	Nondialysis Option at Nephrologist's Request n = 48 (8.2%)	Overall comparison p value
Age; m \pm SD	82 \pm 5	82 \pm 5	81 \pm 4	85 \pm 5	86 \pm 5	<.001
Men; n(%)	58 (59%)	148 (58%)	82 (61%)	18 (40%)	27 (56%)	.04
eGFR; median [IQ]	14 [11-17]	16 [13-17]	12 [9-15]	10 [9-15]	12 [9-16]	<.001
Dementia	5 (5%)	3 (1%)	2 (1%)	4 (9%)	17 (35%)	<.001
Active cancer	5 (4%)	17 (7%)	9 (7%)	4 (9%)	11 (23%)	.002
Unassisted walking	87 (88%)	218 (85%)	123 (91%)	28 (62%)	16 (33%)	<.001
Home living	88 (88%)	231 (91%)	124 (92%)	39 (87%)	29 (60%)	<.001

Notes: IQ, interquartile; GFR, glomerular filtration rate; eGFR, estimated GFR

number of pills (more than 10, corresponding to more than 9 different classes...), these patients have BP within limits and few biological consequences of end-stage renal failure: anemia, metabolic acidosis, and hyperkalemia. With this “conservative support” (control of metabolic disturbances and BP), a large number of patients included in this cohort are considered by the nephrologist as “non progressor” for renal failure, and only for 24% of the cohort, dialysis is reported as the main project. The follow-up will tell us if those initial prognoses were valuable. Researchers need more information on the role of comorbidities, cognitive status, and functional status in the decision making and outcome of patients with end-stage renal failure. A prognosis score in this group of patient that may help to identify patients with a high probability of survival would be useful for physician and for discussion with patients and family. The score Couchoud et al. developed on elderly patients after the start of dialysis has to be evaluated at the earliest stage, and the follow-up of the PSPA population will help to validate this score or to determine another one. Of course, prediction tools are helpful but only when balanced with physician instinct and family principles. That is why scores should not be used alone to withhold dialysis.

Less than 10% of these highly comorbid patients are declared to be follow-up jointly by a nephrologist and a geriatrician. Collaboration between general practitioner, geriatrician, and nephrologist is indeed crucial to follow these patients and decide together with the patient and his family to start dialysis or not and when. According to the fact that after dialysis start, 25% and 35% of the patients aged 75–84 years and older than 85 years will die within the first year, geriatricians’ expertise may help nephrologists to evaluate the prognosis of one patient before starting a renal replacement therapy. They may help to identify patients at high risk of early death with whom conservative treatment may be discussed. Moreover, geriatricians may be more able to evaluate and anticipate the impact of such heavy and restricting treatment on the quality of life of those patients. Geriatrician evaluation may help to go to individualized versus disease-based approaches (37). In case of dialysis withholding, nephrologists need help from geriatricians and palliative care to manage nonaggressive care with relevant medications and diet for conservative treatment.

Clinical signs of uremia, which often is the starter for renal replacement therapy, are absolutely not specific in elderly patients (nauseas, loss of appetite, sleeping disorders, and cramps) and can be confounded with aging clinical signs. At the same time, serum creatinine level is under dependence of muscular mass and, in consequence, decreases with aging. In consequence, the expertise of the nephrologist is important to evaluate the stage of the CKD and the appropriate timing for discussion of dialysis options with the patient and his family. Nephrologist may help

geriatrician to distinguish symptoms due to chronic renal failure that could be specifically treated from symptoms due to another pathology that will not be relieved by dialysis and specific renal management therapy.

After discussion with the patient and his family, if the decision to consider dialysis is taken, it should be planned early in good condition of preparation, at least in patients timely referred to the nephrologist. International guidelines are consistent in recommending starting dialysis whenever signs of uremia or malnutrition are present, or BP or hydration status cannot be controlled, but they differ regarding the level of eGFR at which it should be best initiated in the absence of these conditions, ranging from 8 to 12 mL/min/1.73 m², according to countries and expert panels (38–42). This threshold can be discussed in light of the results of this study.

Major strengths of this study include the prospective and multicentre design. Researchers will be able to get an idea on the evolution of renal function over time and evolution of the therapeutics projects.

CONCLUSION

PSPA is a large multicenter French cohort study whose objective is to help clinicians to manage elderly patients reaching the stage of dialysis. Baseline characteristics already show that nondialysis care is largely done by nephrologist in order to stabilize patients but that collaboration between geriatricians and nephrologists needs to be reinforced. Follow-up data will help us establish tools to help physicians, patients, and families in dialysis decision making process.

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SUPPLEMENTARY MATERIAL

Supplementary material can be found at: <http://biomedgerontology.oxfordjournals.org/>

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