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Thèse

Pour le

DOCTORAT EN GERIATRIE

Diplôme d'État

par

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Profil clinique et nutritionnel d'une population gériatrique suivie dans une grande unité de néphrologie.
Comparaison entre trois cohortes définies par l'âge.

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Profil clinique et nutritionnel d'une population gériatrique suivie dans une grande unité de néphrologie.
Comparaison entre trois cohortes définies par l'âge.

De nombreuses études montrent que la prévalence de la maladie rénale chronique (MRC) augmente avec l'âge, aussi en lien avec la majoration des maladies vasculaires et du diabète.

Cette augmentation a été démontrée pour la tranche d'âge 60- 80 ans, avec une réduction de la prévalence après 90 ans, classiquement expliquée comme liée à la mortalité compétitive.

Selon les nouvelles recommandations de l'HAS, la nutrition doit faire partie intégrante de la prise en charge de la MRC à partir de ses stades initiaux. La restriction protidique est la base de la prise en charge nutritionnelle de la maladie rénale chronique, mais plusieurs experts considèrent que les patients âgés réduisent spontanément les apports protidiques et, en conséquent qu'une prise en charge ne soit pas nécessaire.

L'objectif de ce travail de thèse est d'évaluer l'applicabilité d'une prise en charge diététique de la MRC dans une population gériatrique atteinte d'une maladie rénale sévère.

La population étudiée est celle soignée dans l'Unité UIRAV (Unité pour l'Insuffisance Rénale chronique Avancée) du CH Le Mans incluant 298 patients à octobre 2020, avec un âge médian de 74 ans ; les patients inclus dans l'étude sont classifiés comme avec une maladie rénale chronique de stade 3b-5. Les comorbidités ont été évaluées selon l'index de Charlson, dont la médiane est à 7.

Pour l'évaluation globale, en incluant aussi l'état nutritionnel, deux échelles fréquemment employées en néphrologie ont été utilisées : MIS (Malnutrition Inflammation Score) et SGA (Subjective Global Assessment).

La thèse est ciblée à trois cohortes divisées selon l'âge : OLD entre 70 et 79 ans, OLD-OLD entre 80 et 89 ans et extremely- OLD > 90 ans.

Les soins médicaux sont personnalisés, associant une prise en charge néphrologique classique et une nutritionnelle en 4 étapes. 1- correction de la malnutrition, 2- normalisation de l'apport protéique à 0.8 mg/kg/jour, 3- prise en charge visée à ralentir la progression de l'insuffisance rénale et 4- éviter la dialyse. Pour la réalisation des deux dernières étapes, des régimes avec apports protéiques à 0.6 mg/kg/j éventuellement supplémentés avec des alpha-chetoanalogues sont prescrites par une petite équipe de diététiciens, spécifiquement formés.

Le premier résultat intéressant regarde les habitudes alimentaires : bien qu'avec une tendance à la réduction avec l'âge, l'apport protidique médian est, dans les trois catégories considérées, de 1.1 g/Kg/j, avec une réduction à 0.9 g/Kg/j (toujours supérieur à la définition actuelle de régime normo protidique, désormais établi à 0.8 g/Kg/j) à un âge supérieur à 90 ans. Après la prise en charge nutritionnelle, on observe, à 6 mois, une réduction des apports à une médiane de 0.9 g/Kg/j, qui se réduit ultérieurement de 0.2 g/Kg/j de protéines pour les sujets suivis pour au moins un an, en ligne avec la réduction progressive des apports.

Cette réduction des apports, probablement aussi en tenant compte du fait que moins de 10% des patients présente un état nutritionnel précaire (SGA : B), et que l'obésité a une prévalence, même dans cette population âgée, de 42%, ne s'accompagne pas à une réduction des principaux paramètres nutritionnels, dont l'albumine. Au contraire, l'albumine plasmatique montre une augmentation de 2 g/l, significative, à 3 mois depuis le début du régime.

L’adhérence thérapeutique, établie selon l’analyse des carnets alimentaires, et définie comme apport protidique non supérieure à la prescription plus 20%, est bonne, à environ 75% des patients à 3 et 6 mois d’observation. Bien que l’étude, observationnelle et non-interventionnelle, sans une cohorte contrôle, ne permet pas de juger sur l’efficacité dans le but de retarder la dialyse, une efficacité en ce sens est suggérée par le fait que tous les patients suivis en UIRAV qui ont commencé la dialyse ont bénéficié d’une approche incrémentale (début de dialyse en raison d’une ou deux séances par semaine, en lieu des trois séances « classiques »).

En conclusion : les patients âgés atteints d’une maladie rénale chronique sévère peuvent bénéficier d’une prise en charge nutritionnelle. Les apports protidiques sont probablement plus importants de ceux classiquement décrits, et la prise en charge ne s’accompagne pas à un risque de malnutrition, au moins à court terme. L’association avec un début incrémental de dialyse, moins traumatique et plus respectueux de la diurèse résiduelle, souligne les avantages potentiels, à étudier ultérieurement à long terme.

Mots clés :

Maladie rénale chronique, gériatrie, régime hypoprotidique

Clinical and nutritional profile of elderly patients in a large nephrology unit : Cmparison between old/old-old and oldest-old patients.

A considerable number of studies show that the prevalence of chronic kidney disease as well as vascular disease and diabetes increases with age.

This rise has been demonstrated for the age class 60-80 years old, with a prevalence decrease after 90 years old, classically explained as due to the competitive mortality.

According to the last HAS recommendations, nutrition must be part of the chronic kidney disease follow up from the earliest stages. Protein restriction is the base of the nutritional follow up of chronic kidney disease, but most experts think that elderly patients' spontaneously decreased protein intake ans, as consequence, they don't need to be monitored.

The objective of this thesis is the evaluation of the applicability of dietetic follow up for the CKD in a geriatric population affected by severe chronic kidney disease.

The population studies is followed in the unit UIRAV (Unité pour l'Insuffisance Rénale chronique Avancée) in the Le Mans hospital, including 298 patients in October 2020 with a median age of 74 years old ; the patients included into the study are classified stage 3b-5 of CKD. Th comorbidities was evaluated with the Charlson index with à median of 7.

For the global evaluation, including also nutritional estate, two scores usually used in nephrology were considered : MIS (Malnutrition Inflammation Score) et SGA (Subjective Global Assessment).

The thesis referred three cohorts, classified according to the age : OLD between 70 and 79 years old, OLD-OLD between 80 and 89 years old and extremely- OLD > 90 years old.

Medical care are personalized, combining a classical nephrologist and a nutritional care in 4 steps : 1- malnutrition correction, 2- normalisation of the protein intake a 0.8 mg/kg/jour, 3- followed up referred to slow down CKD 4- avoid dialysis. For the realisation on the two last steps, diet with protein intake amount 0.6 mg/kg/j eventually supplemented with alpha-chetoanalogues are prescribing for a small dietitian group, specifically trained.

The first interesting result concerns diet habits : although a trend of reduction with age, protein intake median is, in the three cohorts, of 1.1 g/kg/die, with a reduction to 0.9 g/kg/die (still more than actual definition of normal protein intake 0.8 g/kg/die) with a decrease to 0.9 g/kg/die at an age > 90 years old. After the nutritional follow up we observe, on 6 months, an intake's decrease with a median of 0.9 g/kg/die, and a further decrease of 0.2 g/kg/die of protein intake for the patients followed up for at least 1 year, due to the progressive decrease of general intake.

This decrease of intakes, probably considering that less than 10% of patients shows a poor nutritional status (SGA : B) and a prevalence of obesity, also in this elderly population, of 42%, isn't followed by a decrease of the principals nutritional parameters, as albumin level. On the contrary, plasmatic albumin shows an increase of 2 g/L, statistical significative, three months after the beginning of the diet.

Adherence, established within analysis of dietary diary, is defined as protein intake as prescribed or 20% more as good adherence for 75% of patients at follow up of 3 and 6 months.

Although the study, observational and non interventional, without a control cohort does not allow to evaluate efficacity in retarding dialysis, a kind of efficacity is suggested because all the patients en UIRAV that started dialysis, started with an incremental approach (started dialysis as one or two session a week, and not with the three « traditional » sessions).

In conclusion : elderly patients with chronic kidney disease can benefit of a diet: protein intake is probably more relevant than previously described and the prescription of a diet is not followed by an increase of malnutrition's risk, at least in the short term. The association between starting of incremental dialysis, less traumatic and more respecting residual diuresis, underlines the potentials advantages, to be studied later in the long term.

Key words :

Chronic kidney disease, geriatric, hypoprotein diet

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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et selon la tradition d'Hippocrate, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent, et n'exigerai jamais un salaire au-dessus de mon travail.

Admis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

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INDEX

1 BACKGROUND

1.1 Epidemiology of Chronic Kidney Disease

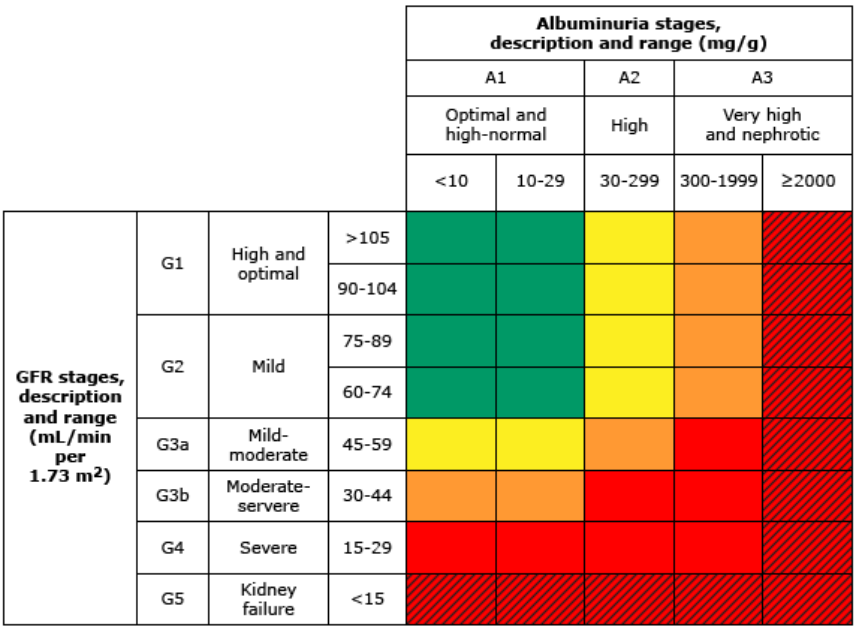
The ageing of the world's population, particularly relevant in high-income countries, has changed the profile of several specialties, shifting the focus from diseases of the young to diseases of the elderly.

This is the case, among others, of nephrology.

Chronic kidney disease (CKD) was initially acknowledged as a disease affecting young patients, and the pivotal book of Thomas Addis, which is often considered as the forerunner of nephrology, describes the history of a young man who dies of chronic glomerulonephritis. However, nowadays CKD is a disease of the elderly.

The current diagnosis and staging system of CKD on the one side underlines the importance of the early stages of CKD, by considering that all alterations of the morphology, function or urinary composition lasting for at least 3 months define the presence of CKD and, on the other side defines CKD as a long lasting decrease of the kidney function (below 60 ml/min of estimated glomerular filtration rate (e-GFR)) regardless of age. The presence of proteinuria is an ancillary criterion (figure 1).

Figure 1: CKD definition and staging (source: National Kidney Foundation).



Globally, CKD is present in 8-15% of the world population, a prevalence that is intermediate between that of diabetes, a much better acknowledged chronic, non-communicable disease, which is in the 5-8% range among the general population, according to definition and population characteristics, and that of hypertension which reaches 30% in high income, high life-expectancy settings. (Aucella, 2019).

The definition of CKD as an e-GFR below 60 mL/min for at least 3 months has challenged in particular the geriatrics and led experts to discuss whether this definition should be adapted to age, acknowledging the para-physiological decrease that is observed in older in nbdividuals (Azar, 2013). Indeed, the question is probably more semantic than clinical and reminds of the definition of hypertension, which is overall ageless, versus the need for anti-hypertensive treatment, which has to be contextualized to age, to avoid the risk of over-zealous treatment and related side effects.

What is known today in nephrology is that CKD has switched from a disease of the young to a disease of the elderly and that the most important causes, potentially progressing to end stage kidney disease (ESKD), are likewise switching from glomerulonephritis to nephroangiosclerosis or

diabetic nephropathy and multifactorial diseases. The median age of patients starting dialysis increased in parallel from less than 50 years in the eighties to over 70 years in the new millennium.

In the same period, the definition of "old" kidney transplant recipients increased from "above 50" in the late eighties to "above 70" in the new millennium, at least in high-income countries in which access to renal replacement therapy is without restrictions.

1.2 OLD / OLD-OLD / OLDEST OLD patients

Indeed, the definitions of "old" or elderly patients in nephrology, dialysis and transplantation, has changed over time and several groups are now identified, even if often differently categorized: these include the young-old, old, old-old, extremely-old, or oldest old patients (table 1).

Table 1: some examples of definition of « old patients »

Source	**Definition**	**Age**
National Policy for Older Persons Year 1999 : Ministry of Social Justice and Empowerment	**Young old or « not so old"** **Old old** **Older old or very old**	**60-69 years** **70-79 years** **>80 years**
	Young old **Middle old** **Old-old**	**60-74 years** **75-84 years** **>85**
Adam J., Garfein, A., Regula Herzog, The Journals of Gerontology, March 1995	**Young old** **Old old** **Oldest old**	**60-70 years** **70-79 years** **>80 years**

While these distinctions may further add a semantic complication to a complex domain, they have the role of underlining the fact that “not all elderly patients are alike”, and that the clinical and treatment problems faced by this age group should probably merit more precise distinctions.

1.3 Kidney function assessment in the elderly

One of the hot points in the discussion on CKD in the elderly resides in the problems of assessment of the kidney function. None of the widely employed formulae for e-GFR calculation is formally validated over 80 years of age. (Delanaye, 2019).

While most of the formulae are reported for 1.73m2, normalization to the body surface is seldom performed, which may be a problem in particular for small and thin elderly patients in which the muscle mass may be critically low. Conversely, the association between obesity and sarcopenia may be challenging especially in advanced age, and the ratio between reduced muscle mass and large body area may affect the reliability of the formulae. (Alagiarkrishnan, 2010).

Figure 2. The most commonly used formulae for e-GFR estimation (source: National Kideny foundation website)

Table 1.
Formulas used to estimate eGFR.

MDRD	$GFR = 186 \times (\text{Serum Creatinine mg/dL})^{-1.154} \times (\text{Age yrs})^{-0.203}$
Cockroft-Gault	$GFR = [(140 - \text{age yrs}) \times \text{Weight (kg)}]/\text{Serum Creatinine} \times 72$
CKD-EPI	if Serum Creatinine level ≤ 0.9 mg/dL, $GFR = 141 \times (Scr/0.9)^{-0.411} \times (0.993)^{\text{Age yrs}}$ if Serum Creatinine level > 0.9 mg/dL, $GFR = 141 \times (Scr/0.9)^{-1.209} \times (0.993)^{\text{Age yrs}}$

There are at least four good reasons for controlling the kidney function in the elderly and for detecting cases with reduced glomerular filtration rate.

The first one is that, regardless of the causes and independently from the definition of "physiological" or "pathological" reduction, most of the drugs of common use, including antibiotics, have a mainly renal clearance and, thus, referring to a correct estimate of the kidney function is fundamental to avoid toxicity.

Secondly, some drugs commonly employed in elderly patients, such as non-steroidal anti-inflammatories, ACE inhibitors and Angiotensin receptor blockers or anti-H2 receptors, are potentially nephrotoxic and, since nephrotoxicity is also increased in the case of reduced GFR, kidney function assessing may guide drug choice.

Thirdly, reduction of the kidney function is associated with frailty, and albuminuria, even at the stage of micro-albuminuria, is associated with an increased risk of cardiovascular events. While this association is more a witness of frailty and is hardly reversible, the identification of patients at higher risk may guide the clinical management.

The fourth reason regards the management of the advanced phases of CKD and the eventual need to start dialysis; while many kidney diseases of the elderly have a relatively slow course, all may

eventually lead to end stage kidney disease. Dialysis is not contraindicated at any age, but the chances that renal replacement therapy is associated with a rapid impairment in the clinical condition and with a marked and rapid reduction of the quality of life are very high. Mortality is likewise elevated in particular in the first months of dialysis, colorfully defined as “the dialysis shock”. However, the so-called conservative management (usually including medical treatment and pain management) of advanced CKD patients who refuse or are recused from dialysis is associated with shorter survival, although, often, with a more preserved quality of life. (Caudwell, 2019). (Castro, 2019). (Basile, 2019). (Drew, 2019). (Foote, 2016).

Reaching a balance between a minimalist attitude (all elderly patients may be classified as having CKD; we cannot follow-up all elderly patients) and an interventional one (all patients with CKD should be followed-up regardless of age) is not simple and the limited availability of nephrology care may further increase the discrepancies in clinical management. (Berar Yanay, 2019). (Douglas, 2014).

1.4 Multidisciplinary management of CKD patients.

Conflicting data exist on the interest for a multidisciplinary comprehensive management of CKD: while common sense and large surveys suggest that, in analogy with diabetes, specialized care and multidisciplinary follow-up may improve survival and reduce the disease burden, a few recent studies do not find such an improvement and tend to support a minimalist approach, even towards patients in advanced CKD stages. (Ahmed, 2018). (Davison, 2013).

These conflicting and perhaps frustrating results may be interpreted with caution and may witness the differences in clinical management, patient selection and, possibly, the approach to care (delivery of guideline indications, versus highly personalized care). (Freidin, 2019). The role of dietary management is likewise probably important in determining these differences. Indeed, while

the recently updated K-DIGO guidelines support protein restriction since CKD stage 3, regardless of age, this is seldom available in the clinical practice and conflicting indications regard the frail elderly patients, in which the current recommendations of the geriatric societies support, on the contrary, a diet high to very high in proteins (1.2-1.4 g/Kg/day, versus the present definition of normal protein diet, at 0.8 g of proteins per Kg of ideal body weight per day). These aspects will be further discussed in this thesis. (Brunori, 2012). (Escribano-Serrano, 2019).

At least in western countries the widening of the indications to kidney transplantation suggests that this therapy should be offered to all patients without contra-indications up to the age of 80, and that, especially in older ages, the results of kidney transplantation are better if this is performed before dialysis or immediately after its start. As a consequence, at least in settings where kidney transplantation is well developed, there is an adjunctive interest in follow-up of the “young-old and old patients, and the minimalist attitude may invest selectively the oldest, and often more fragile patients.

While the dialysis population is now monitored in most of the western countries and large registries are being developed also in medium-low income settings, thus allowing the quantification of the burden of “elderly” patients with end stage kidney diseases on renal replacement therapy, less is known on the clinical burden, on the overall characteristics and on the potential for specific therapeutic approaches in elderly patients in the pre-dialysis phase or with lesser degrees of kidney function impairment. (Berger, 2015).

2 AIM OF THE STUDY AND STUDY DESIGN

On this background, the present thesis was designed to contribute to filling these major knowledge gaps by analyzing the main clinical characteristics of elderly patients referred to a large non-university hospital in France, a country where CKD is recognized as an affection deserving fully-reimbursed care.

The study is conducted in two steps: an analysis of the prevalence and main diagnosis of CKD in the overall cohort of cases referring to at least one outpatient consultation over one year (2019). **This first part of the study allows a quantification of the disease burden and workload in a large clinical practice.**

This is followed by a more detailed analysis of the metabolic profile and dietary habits and of the indications for dietary management in a subset of this population referring to a dedicated unit for advanced CKD care (UIRAV: Unitè pour la prise en charge de l'Insuffisance Renale AVancée), and by an analysis of quality of life and adherence to the diet in the cases in which the dietary management had been performed in the context of a prospective study (pro-re-pro: reduire les proteins pour proteger les reins) presently ongoing in the same setting.

This second part of the study tries to answer the question about the interest for multidisciplinary care and dietary management in older CKD patients, a population in which protein intake is often supposed to be already reduced at baseline, and that is often considered as reluctant to change diet habits.

3 MATERIALS AND METHODS

3.1 Setting of study

The present study was undertaken at Centre Hospitalier Le Mans (CHM), one of the largest non-university hospitals in France. CHM has a nephrology service with a network of outpatient care facilities (consultations and day-hospital) and is the only hospital in the Department of Sarthe with nephrology beds (Sarthe: 560,227 inhabitants on January 1, 2020). The hospital is situated in the main city in the department, Le Mans, which counts 143,325 inhabitants.

3.2 Characterization of patients in the cross sectional analysis (2019)

All patients over the age of 18 who attended at least one consultation in 2019 in the nephrology outpatient clinics at CHM were included in this part of the study. Patients' data were retrieved from their electronic medical records (ORBIS). Demographic characteristics including age, sex and cause of kidney disease were collected. Kidney function was assessed by means of the CKD-EPI equation. Stratification was performed as per the KDIGO guidelines, in cases with at least 2 determinations of serum creatinine levels at least at 3 months intervals. When more than one visit was present in the medical records in 2019, the most recent one was used to assess CKD stage. Since all patients were observed in the outpatient units, the incidence of acute kidney injury (AKI) was considered as negligible, and the stage was calculated on the basis of the last available creatinine level, unless AKI was explicitly mentioned in the last clinical consultation report.

3.3 Analysis of cases followed in the unit dedicated to advanced CKD (UIRAV).

The second part of the study was conducted in the unit for the care of advanced kidney disease (UIRAV – [Unité pour l'Insuffisance Rénale chronique AVancée]). In this unit, there are two senior nephrologists, three dieticians, one resident and a small group of nurses. Patients are followed-up with outpatient visits or day hospitals, in case they need intravenous drug treatment or complex diagnostic assessments. Patients are followed up from CKD stage 3 to the start of dialysis.

3.4 Dietary management (UIRAV)

In central France, as in Central and Northern Europe, United States and Australia, people usually have a high-protein dietary intake. In the UIRAV a nephrologist and/or a dietician assesses the baseline protein intake and, when the protein intake is higher than the recommended one (0.8 Kg of ideal body weight), the nephrologist initially prescribes a normalization or reduction of protein intake based on baseline one, nutritional status, trajectory of CKD progression, proteinuria, age, comorbidity and life expectancy. The clinical suggestions are extensively discussed with the patient and the main nutritional strategy (mixed proteins or plant-based) is agreed; "traditional" diets, based upon the analysis of the common dietary patterns in the area, have been conceived (for example, one mainly vegetarian meal per day, based upon a vegetable soup, containing potatoes as a source of starch and small portions of dairy products), maintaining about 50% of the total protein intake from animal origin. Conversely, "plant-based" diets rely on carbohydrates such as potatoes, rice, bread, pasta as main sources of calories and favor proteins of vegetable origin (from grains and beans). Supplementation with a mixture of amino acids and ketoacids (Kestosteril, available free of charge for CKD patients in both Italy and France) may be added to low protein plant based diets, to be sure that the needs for essential aminoacids are met, and to low protein diets, or occasionally normalised diets (i.e. 0.8 g/kg/day) to avoid protein energy wasting (PEW) or nephrotic patients.

The dose, for moderately restricted diets, in keeping with the previous Italian experiences, is 1 tablet per 8–10 kg of body weight, to be further adjusted on the basis of albumin levels or protein losses.

All patients were followed up to identify signs of PEW, such as reduction in body weight (unexplained by oedema reduction), reduction in lean body mass (evaluated by clinical assessment and integration with bioimpedance on demand), reduction in serum albumin, prealbumin or total proteins, especially in the absence of acute inflammatory events, or other clinical markers of poor nutrition, deducted from the dietary journal reviewed by the dieticians, in presence of vitamin deficits or unexplained anemia.

Protein intake was assessed per kilogram of real body weight, and an average between real and ideal body weight was used only for patients whose body mass index (BMI) was >40 kg/m2.

Energy intake was tailored to 30–35 kcal/kg of body weight per day in non-obese younger patients; 20-25 kcal/Kg of body weight per day was considered acceptable for very old (>80 years) or for obese patients. In obese patients we tried to take into account not only the caloric intake, but also of the daily activities, privileging, wherever possible, increasing physical activity to reducing energy below 25 Kcal of adjusted weight per day.

Dialysis start was decided within an ‘intent to delay’ policy based on the usual clinical and biochemical markers of blood pressure control, fluid overload, hyperparathyroidism or any clinical element suggesting uremic toxicity (anorexia, weight loss, nausea, malnutrition, restless leg syndrome).

The management of sodium, potassium, phosphate, bicarbonate, folic acid, iron, erythropoietin, vitamin D, vitamin B12, followed the usual rules of good clinical practice.

3.5 Data gathered

The following data were gathered: demographic (gender, age, county of origin), type of kidney disease; whether or not the patient was on dialysis and the type of dialysis (haemodialysis or peritoneal dialysis); type of diet (previous diets, at cross-sectional analysis, at each change of type of diet and at last follow-up). Comorbidity was assessed using the Charlson Comorbidity Index (CCI, scale: 0–33). The nutritional status was assessed by means of the Malnutrition Inflammatory Score (MIS, scale: 0–30) and the Subjective Global Assessment (SGA: A, B or C).

Clinical data included height, weight, BMI, blood pressure; laboratory data including urea, creatinine, electrolytes, albumin, total serum proteins, haemoglobin, parathyroid hormone. Data not shown in tables but recorded in the database, are available upon request.

Energy and protein intake was assessed by the dietician using the patient's 3- to 7-day food diary or, in its absence (non-adherence, older age, etc.) based on the patient's dietary recall. Analysis of 24-hour urinary urea was employed for assessment of protein intake, employing the Maroni-Mitch formula, in patients able to correctly perform a 24 hour urine collection. However, in this population of mainly elderly patients, dietary journal was the basic mean for assessment.

Estimated glomerular filtration rate (eGFR) was assessed using the MDRD short and the CKD Epidemiology Collaboration (CKD-EPI) formulas.

3.6 Statistical Analysis

Statistical analyses were performed using SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA). Quantitative data were expressed as median (min–max) and qualitative data were presented as proportions and percentages.

The normality and homoscedasticity hypotheses were tested with the Shapiro-Wilk and Leven's test, respectively, for continuous series. In case of null hypothesis acceptation, Student test was performed to compare two non-appaired groups, otherwise Wilcoxon rank sum test was used. Variance analysis was applied for additional group comparisons (e.g., ND, ND supplemented, LPD, LPD supplemented), otherwise Kruskal-Wallis test was performed. Proportions were tested using the Chi-square test, or Fisher exact test in case of low subsample cohort size (<5). A two-sided alpha risk was set at 5%.

Survival was assessed by Kaplan Meier curves.

3.7 Ethical Issues

The study was conducted in accordance with the Declaration of Helsinki.

First part. Cross sectional observational study, involving the analysis of the clinical charts of patients who attended at least one consultation in a nephrology outpatient clinic in 2019; the anonymized database was built following the requests of the regional health council, to assess the number of cases in CKD, specifically stages 4 and 5. The study, performed on these data, was approved by the ethical committee (September 2020).

Second part. UIRAV. Longitudinal retrospective observational study, involving the analysis of the clinical charts of patients who attended at least one consultation in UIRAV in 2017-2020; the study, performed on these data, was approved by the ethical committee (Mars 2020).

4 RESULTS

4.1 Part one: demographic characteristics of patients referred and followed-up in a large Nephrology ward during one year (Le Mans, France, 2019).

The demographic characteristics of the entire cohort of 1992 patients referred for at least one consultation in the Centre Hospitalier Le Mans is reported in table 1.

In the context of a relatively old population, the referral patterns and the chronic kidney disease stages vary among the age groups. The highest prevalence is recorded in the age group 80-90 years (21.9%) while the extremely old patients, aged at or about 90 years, account for 5.8% of the referred cases.

Median serum creatinine steadily increases, and median eGFR consequently decreases over age, reaching 1.18 mg/dL of serum creatinine and 27 ml|min of median eGFR at or above age 90. In line with these observations, the prevalence of the most severe CKD stages (CKD stages 4 and 5) increases, and indeed, only 1.7% of the patients aged at or over 90 have a CKD stage of 1 or 2, while over 60% of the cases are in CKD stages 4-5 in this age group, versus 38.5% in the age group 80-89, and only 8.3% at age < 50 years (figure 1).

Most kidney diseases are present in all ages; the relatively high prevalence of cases categorized as with lithiasis of observed post-preeclampsia reflects specific referral patterns developed in the center of study.

In the absence of specific referral programs dedicated to the elderly, the prevalence of three categories sharply increased with age: multifactorial disease, vascular kidney disease – nephroangiosclerosis and the diabetes associated kidney disease in the variant with low proteinuria (diabetes-vascular) account for only 12.7% of the cases in the younger age group and for 80.7% in

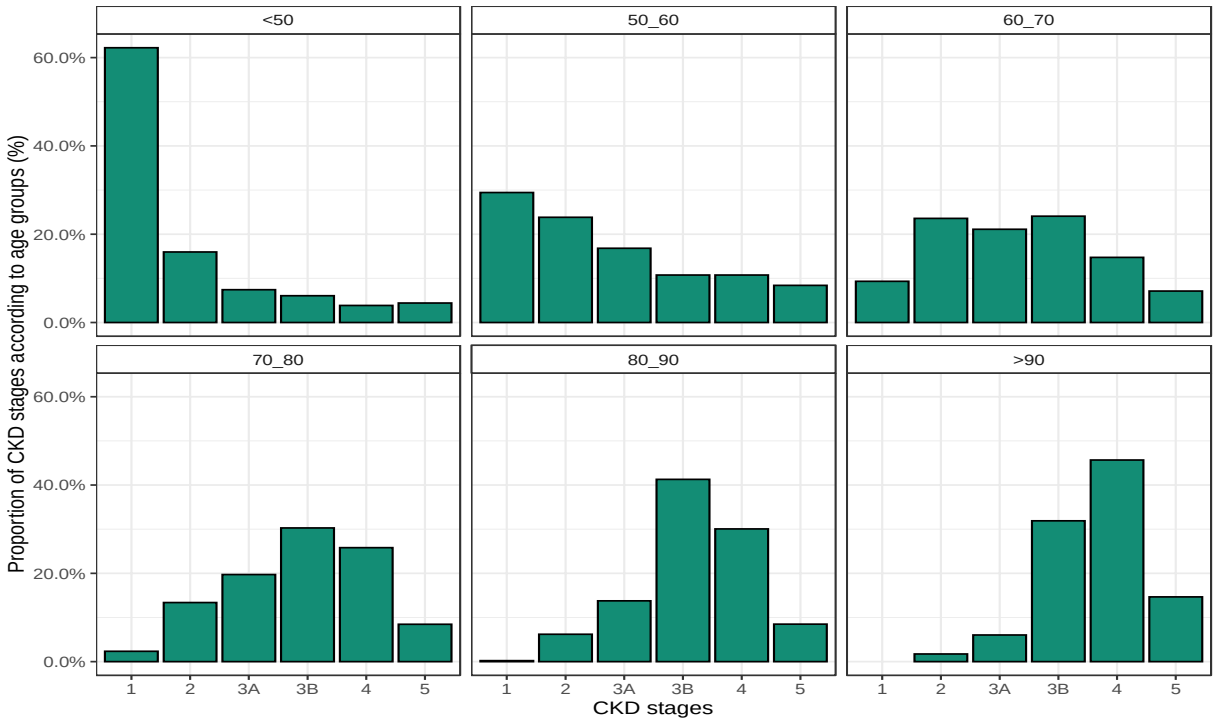
the 80-89 age group versus 84.6% in patients aged at or over 90 years (table 2). In keeping with a high prevalence of vascular nephropathies, which are usually non proteinuric or with low proteinuria, the prevalence of the cases who displayed proteinuria over 1 gram per day is low. Of note, proteinuria was missing in several cases; the lack of regular control is partly a reflection of the fact that proteinuria is not regularly checked in the patients who were classified as with vascular disease, and were known to have low or absent proteinuria in previous tests (figure 4).

Table 2. **Baseline data: the overall population followed-up in Nephrology in 2019.**

	Age groups						
	<50	50_60	60_70	70_80	80_90	≥90	P-values
N (all: 1992)	**379**	**216**	**414**	**431**	**436**	**116**	
Males/females	**154/225**	**114/102**	**263/151**	**302/129**	**245/191**	**56/60**	**<0.001**
Creatinine (mg/dl), median (IQR)	**0.85 (0.48)**	**1.09 (0.95)**	**1.39 (0.94)**	**1.65 (1.07)**	**1.67 (0.84)**	**1.88 (1.13)**	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	**100 (47)**	**66 (58)**	**47 (35)**	**38 (27)**	**33 (17)**	**27 (18)**	**<0.001**
Proteinuria (g/l), n (%)							0.147
<0.3	213 (69.4%)	119 (65.0%)	212 (60.7%)	240 (65.0%)	239 (62.3%)	67 (64.4%)	
0.3 - 1	59 (19.2)	29 (15.8%)	83 (23.5%)	53 (14.4%)	93 (24.5%)	25 (24.0%)	
≥1	35 (11.4%)	35 (19.1%)	55 (15.8%)	76 (20.6%)	50 (3.2%)	12 (11.5%)	
Stages, n (%)							**<0.001**
1	226 (62.3%)	63 (29.4%)	38 (9.3%)	10 (2.3%)	1 (0.2%)	0 (0%)	
2	58 (16%)	51 (23.8%)	96 (23.6%)	57 (13.4%)	27 (6.2%)	2 (1.7%)	
3A	27 (7.4%)	36 (16.8%)	86 (21.1%)	84 (19.7%)	60 (13.8%)	7 (6%)	
3B	22 (6.1%)	23 (10.7%)	98 (24.1%)	129 (30.3%)	180 (41.3%)	37 (31.9%)	
4	14 (3.9%)	23 (10.7%)	60 (14.7%)	110 (25.8%)	131 (30%)	53 (45.7%)	
5	16 (4.4%)	18 (8.4%)	29 (7.1%)	36 (8.5%)	37 (8.5%)	17 (14.7%)	
Main diagnosis of kidney disease							**<0.001**
ADPKD	18 (5.9%)	17 (9.3%)	17 (4.9%)	7 (1.9%)	8 (2.1%)	0 (0%)	
Isolated urinary abnormality	8 (2.6%)	2 (1.1%)	6 (1.7%)	3 (0.8%)	1 (0.3%)	0 (0%)	
Other unknown	19 (6.2%)	10 (5.5%)	11 (3.2%)	14 (3.8%)	4 (1.1%)	2 (1.9%)	
CAKUT	17 (5.5%)	7 (3.8%)	5 (1.4%)	2 (0.5%)	0 (0%)	0 (0%)	
GN	46 (15%)	20 (10.9%)	25 (7.2%)	20 (5.4%)	9 (2.4%)	3 (2.9%)	
Lithiasis and Interstitial	63 (20.5%)	56 (30.6%)	61 (17.5%)	34 (9.2%)	9 (2.4%)	1 (1%)	
Multifactorial	**22 (7.2%)**	**26 (14.2%)**	**60 (17.2%)**	**67 (18.2%)**	**71 (18.7%)**	**12 (11.5%)**	
NAS and Diabetes	**5 (1.6%)**	**11 (6%)**	**54 (15.5%)**	**69 (18.7%)**	**55 (14.5%)**	**14 (13.5%)**	
NAS and vascular	**12 (3.9%)**	**14 (7.7%)**	**51 (14.6%)**	**96 (26%)**	**180 (47.5%)**	**62 (59.6%)**	
Diabetic nephropathy	12 (3.9%)	11 (6%)	34 (9.7%)	20 (5.4%)	17 (4.5%)	2 (1.9%)	
Obstructive and PNA	0 (0%)	0 (0%)	4 (1.1%)	8 (2.2%)	10 (2.6%)	2 (1.9%)	
Post-AKI	2 (0.7%)	1 (0.5%)	4 (1.1%)	4 (1.1%)	5 (1.3%)	3 (2.9%)	
Post-transplantation	4 (1.3%)	0 (0%)	2 (0.6%)	3 (0.8%)	1 (0.3%)	0 (0%)	
Post-preeclampsia	66 (21.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Single kidney	1 (0.3%)	0 (0%)	1 (0.3%)	1 (0.3%)	0 (0%)	1 (1%)	
Systemic	12 (3.9%)	8 (4.4%)	14 (4%)	21 (5.7%)	9 (2.4%)	2 (1.9%)	

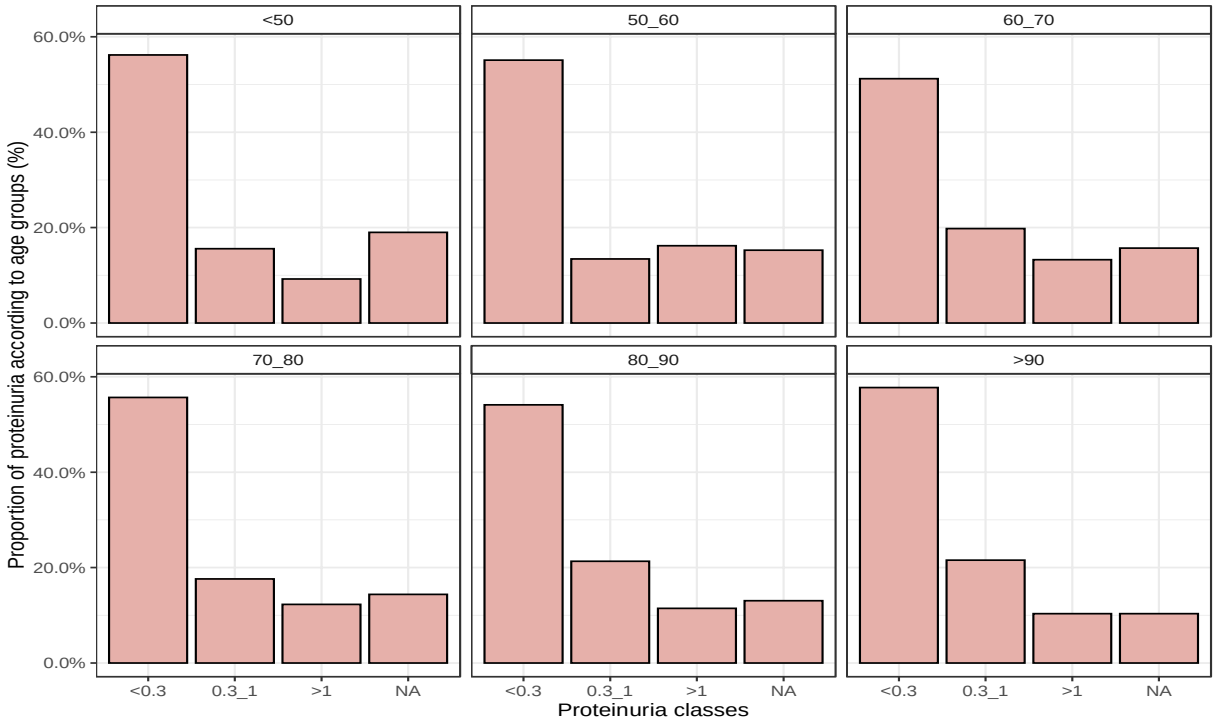
IQR: Inter-quartile range; GN: Glomerulonephritis; NAS: nephroangiosclerosis; ADPKD: autosomic dominant Polycystic Kidney Disease; CAKUT: congenital anomalies of the kidney and urinary tract; AKI: Acute kidney disease; PNA: acute pyelonephritis; eGFR-EPI: estimated glomerular filtration rate according to the Chronic Kidney Disease EPIdemiology collaboration

Figure 3. Distribution of the CKD stages among age groups (overall cohort referred or followed-up in Nephrology in 2019).



Legend: CKD: chronic kidney disease

Figure 4. Distribution of classes of proteinuria among age groups (overall cohort referred or followed-up in Nephrology in 2019).



Legend NA: Not available

4.2 Part two: demographic characteristics and clinical details in patients referred and followed-up in the Unit dedicated to the care of advanced kidney disease (UIRAV, Le Mans, France, 2017-2020).

4.2.1 Baseline data (UIRAV)

The UIRAV is the setting of the care of three subsets of patients, including at-risk pregnancies, patients needing particular attention (intellectual deficit, rare diseases etc), most of the cases, considered in the present study, are affected by advanced or progressive CKD (stages 3-5). This subset was selected for the present analysis. Of note, we considered in this analysis the functional data at enrollment and included also three cases in which the indication for being followed-up in UIRAV was posed when the patients were in stage 3, but who where found in stage 2 at the first assessment at enrollment.

The main demographic characteristics of the 438 patients with complete baseline data, referred to the Unit dedicated to advanced CKD (UIRAV), since the start of its activity (November 15th 2017) to June 30th 2020 are reported in table 3. Fundamental baseline data include kidney functional data, Charlson comorbidity index (CCI), Malnutrition inflammation score (MIS) and subjective global assessment (SGA); at least one of these data is missing in 94 cases, mainly since the three indexes CCI, MIS and SGA are calculated on the basis of an extensive clinical and biochemical evaluation, usually performed in the day hospital, after a first nephrology consultation. The missing data regard therefore either patients who are in the evaluation phase, or cases that performed one consultation only.

In keeping with the selection criteria, serum creatinine levels and e-GFR were more homogeneous in this cohort. Of note, the same e-GFR level corresponds to a serum creatinine that decreases across age groups.

The distribution of the CKD stages confirms a trend towards referring later the oldest patients with advanced CKD, possibly also because the kidney diseases in the oldest are less frequently characterized by proteinuria, which is one of the main elements considered in assessing the potential progression of the functional kidney impairment (figure 3). The disease pattern reflects what was observed in the general population referred to the Centre Hospitalier Le Mans with an increasing predominance of vascular and multifactorial diseases with increasing age and a consequent lower prevalence of relevant proteinuria (at or above 1 g/24 h).

Table 3. **Baseline data: the cohort followed-up in the unit UIRAV (15 November 2017, 30 June 2020)**

	Age groups						
	<50	50_60	60_70	70_80	80_90	≥90	P-values
N (all: 438)	23	39	74	108	140	54	
Males/females	11/12	25/14	51/23	77/31	79/61	18/36	**<0.001**
Creatinine (mg/l), median (IQR)	2.85 (3.39)	2.50 (2.24)	2.58 (1.37)	2.22 (1.09)	2.02 (1.04)	1.86 (1.17)	**<0.001**
eGFR EPI (ml/min/1.73m²), median (IQR)	22 (25)	23 (23)	23 (18)	26 (14)	26 (15)	25 (17)	0.613
Proteinuria (g/24h), n (%)							**<0.001**
<0.3	2 (15.4%)	6 (31.6%)	11 (26.8%)	36 (48.0%)	53 (53.5%)	25 (71.4%)	
0.3 - 1	3 (23.1%)	3 (15.8%)	7 (17.1%)	11 (14.7%)	25 (25.3%)	5 (14.3%)	
≥1	8 (61.5%)	10 (52.6%)	23 (56.1%)	28 (37.3%)	21 (21.2%)	5 (14.3%)	
Stages, n (%)							**<0.008**
2	2 (8.7%)	0 (0%)	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	
3A	1 (4.3%)	6 (15.4%)	5 (6.8%)	8 (7.5%)	9 (6.5%)	5 (9.3%)	
3B	5 (21.7%)	11 (28.2%)	20 (27%)	33 (30.8%)	41 (29.7%)	15 (27.8%)	
4	7 (30.4%)	14 (35.9%)	34 (45.9%)	47 (43.9%)	71 (51.4%)	22 (40.7%)	
5	8 (34.8%)	8 (20.5%)	15 (20.3%)	18 (16.8%)	17 (12.3%)	12 (22.2%)	
Main diagnosis of kidney disease							**<0.001**
ADPKD	2 (8.7%)	3 (7.7%)	4 (5.4%)	1 (0.9%)	2 (1.4%)	1 (1.9%)	
CAKUT	3 (13%)	4 (10.3%)	2 (2.7%)	0 (0%)	1 (0.7%)	1 (1.9%)	
GN	4 (17.3%)	2 (5.1%)	3 (4.1%)	2 (1.8%)	2 (1.4%)	2 (3.8%)	
IN	2 (8.7%)	2 (5.1%)	8 (10.8%)	4 (3.7%)	1 (0.7%)	0 (0%)	
Multifactorial	5 (21.7%)	6 (15.4%)	6 (8.1%)	20 (18.5%)	25 (18%)	6 (11.3%)	
VN	3 (13%)	2 (5.1%)	11 (14.9%)	27 (25%)	63 (45.3%)	31 (58.5%)	
NAS.diab	3 (13%)	15 (38.5%)	33 (44.6%)	42 (38.9%)	40 (28.8%)	9 (17%)	
DN	0 (0%)	1 (2.6%)	0 (0%)	3 (2.8%)	0 (0%)	0 (0%)	
PNA	0 (0%)	0 (0%)	2 (2.7%)	2 (1.9%)	2 (1.4%)	1 (1.9%)	
Others	1 (4.3%)	4 (10.3%)	4 (5.5%)	6 (5.5%)	3 (2.1%)	2 (2.8%)	

IQR: Inter-quartile range; GN: Glomerulonephritis; NAS: nephroangiosclerosis; ADPKD: autosomic dominant Polycystic Kidney Disease; CAKUT: congenital anomalies of the kidney and urinary tract; AKI: Acute kidney disease; PNA: acute pyelonephritis; eGFR-EPI: estimated glomerular filtration rate according to the Chronic Kidney Disease EPIdemiology collaboration

Figure 5. **Distribution of CKD stages at referral: the cohort followed-up in the unit UIRAV (15 November 2017, 30 June 2020)**

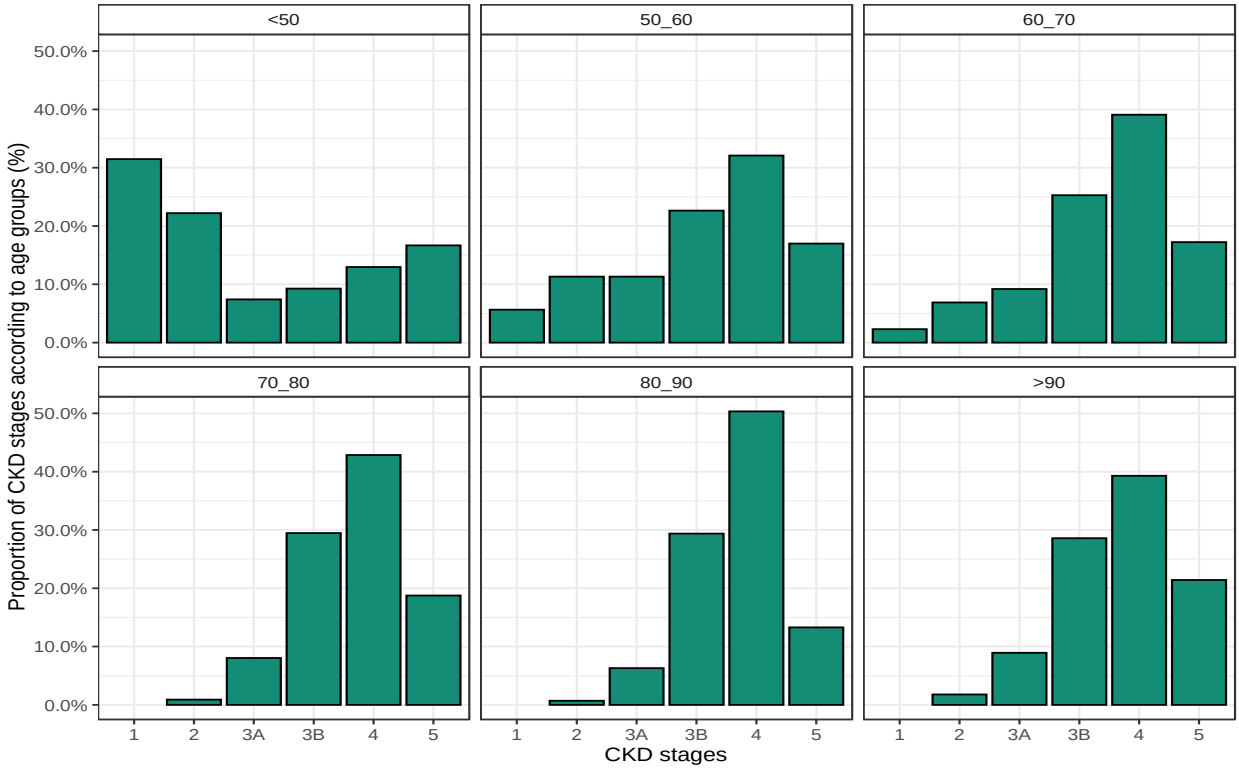
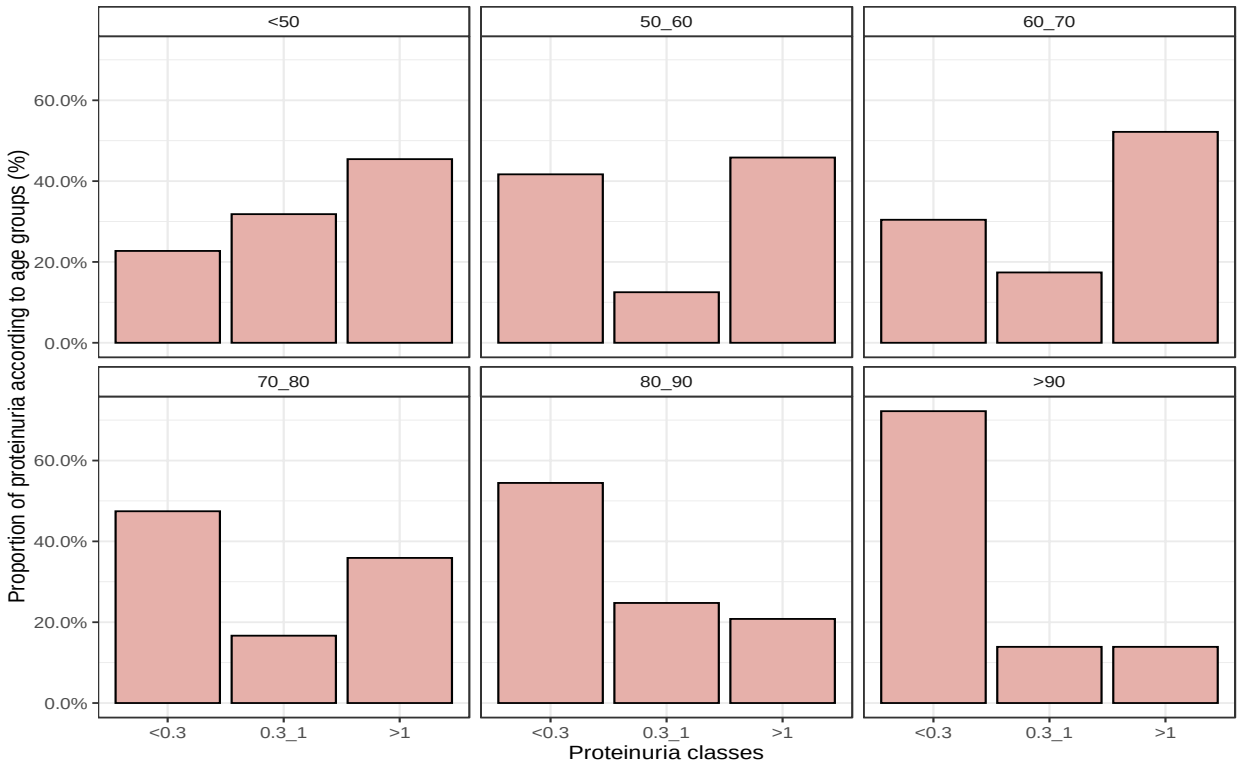


Figure 6. **Distribution of proteinuria assessed at referral: the cohort followed-up in the unit UIRAV (15 November 2017, 30 June 2020)**



3.2.2. Functional scores and comorbidity (UIRAV)

Table 4 and figures 7-10 report the distribution of the main comorbidity nutritional and comprehensive indexes commonly employed in the definition of CKD patients.

The Charlson comorbidity index overall increases across age groups; part of this increase is due to the effect of age *per se*, since the age-related component accounts for 1 point for each decade of life, since the age of 50 (1 point), and up to >=80 years (4 points) (figure 7 et 7bis).

Not considering age, the median comorbidity index is around 5 (2 points for severe CKD) (figure 8).

The prevalence of diabetes is the highest in the age groups 60-69 and 70-79, and decreases thereafter, suggesting a role of competitive mortality in this subset of cases, while the prevalence of neoplastic diseases peaks at 80-89 years; heart diseases, mainly ischemic, are more fluctuating, being present in about 40% of the patients above age 50, underlining the strict relationship between chronic kidney disease and cardiac impairment.

The subjective global assessment defines our population as overall well nourished, and only a minority of the cases is considered as with a severely impaired nutritional status (less than 3% in the overall cohort). Moderate nutritional impairment, conversely, increases over age, reaching 53.7% at age at or above 90; of note the definition is not “age adjusted” and may read age-related sarcopenia, more than the effect of CKD. In keeping with this observation, the median BMI is in the overweight range at all ages in the population followed-up in UIRAV is stable at around 29 kg/m2 in the age groups 50-79 years old, and to 25.7 kg/m2 at or above 90 years.

MIS index, which is the malnutrition inflammation score, shows likewise an increasing value with increasing age, as graphically plotted in figure 10.

Table 4. **Functional scores and comorbidity: the cohort followed-up in the unit UIRAV (15 November 2017, 30 June 2020)**

	Age groups						
	<50	50_59	60_69	70_79	80_89	≥90	P-values
N (all: 438)	23	39	74	108	140	54	
Males/females	11/12	25/14	51/23	77/31	79/61	18/36	**<0.001**
Charlson index, median (IQR)	2 (3)	5 (2)	7 (4)	8 (2)	8 (3)	9 (1)	**<0.001**
MIS, median (IQR)	4 (5)	4 (4)	5 (4)	5 (4)	5 (3)	7 (4)	**<0.001**
SGA, n (%)							**<0.001**
A	21 (91.3%)	37 (94.9%)	60 (81.1%)	96 (88.9%)	106 (75.7%)	23 (42.6%)	
B	2 (8.7%)	1 (2.6%)	13 (17.6%)	11 (10.2%)	31 (22.1%)	29 (53.7%)	
C	0 (0%)	1 (2.6%)	1 (1.4%)	1 (0.9%)	3 (2.1%)	2 (3.7%)	
Diabetes, n (%)	4 (17.4%)	18 (47.4%)	40 (56.3%)	56 (54.4%)	57 (42.2%)	13 (25.5%)	**<0.001**
Cardiopathy, n (%)	4 (17.4%)	22 (43.1%)	24 (33.8%)	35 (34.0%)	59 (43.7%)	22 (43.1%)	**0.010**
Neoplasia, n (%)	1 (4.3%)	2 (5.3%)	13 (18.3%)	18 (17.3%)	33 (24.4%)	8 (15.7%)	**0.048**
BMI ($kg.m^{-2}$), median (IQR)	26.2 (16.9)	29.3 (8.9)	29.0 (10.1)	29.6 (8.8)	27.8 (5.5)	25.7 (6.3)	**0.001**

Figure 7. **Distribution of the Charlson comorbidity index among age groups in the UIRAV cohort**

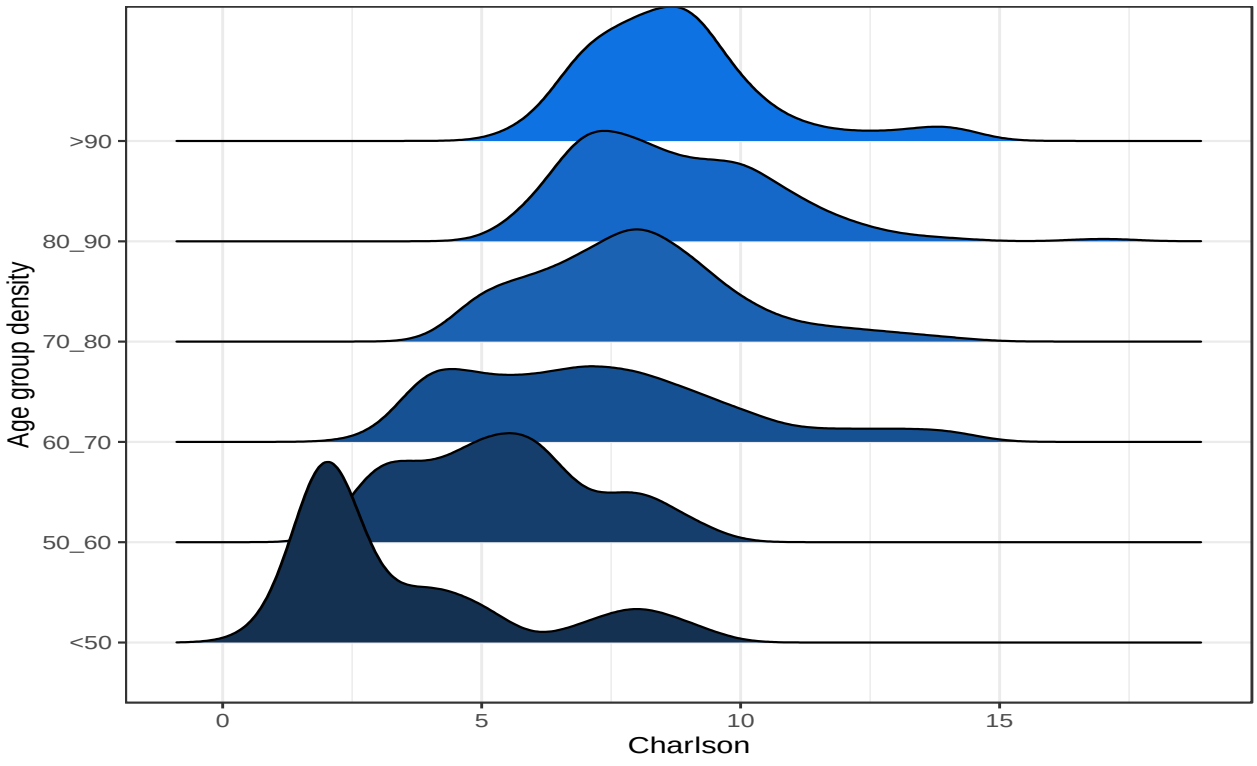


Figure 7 bis **Distribution of the Charlson comorbidity index among age groups in the UIRAV cohort**

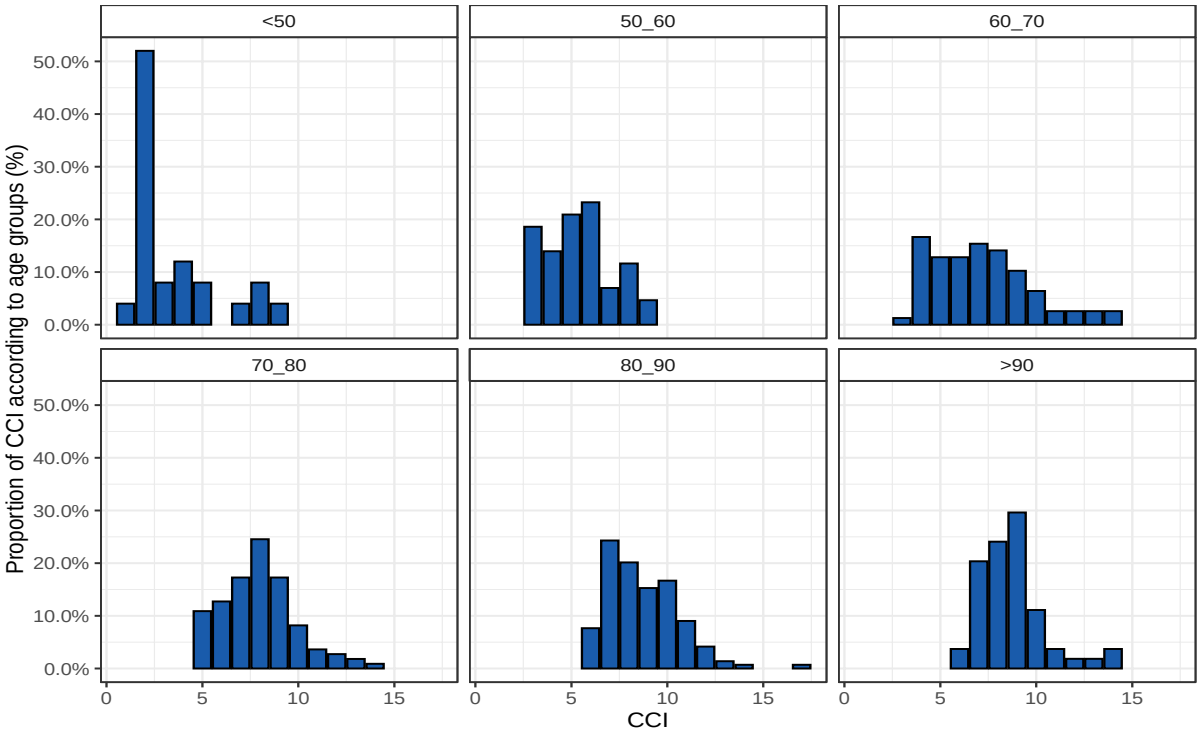


Figure 8. **Distribution of the Charlson comorbidity index among age groups (calculated without counting age)**

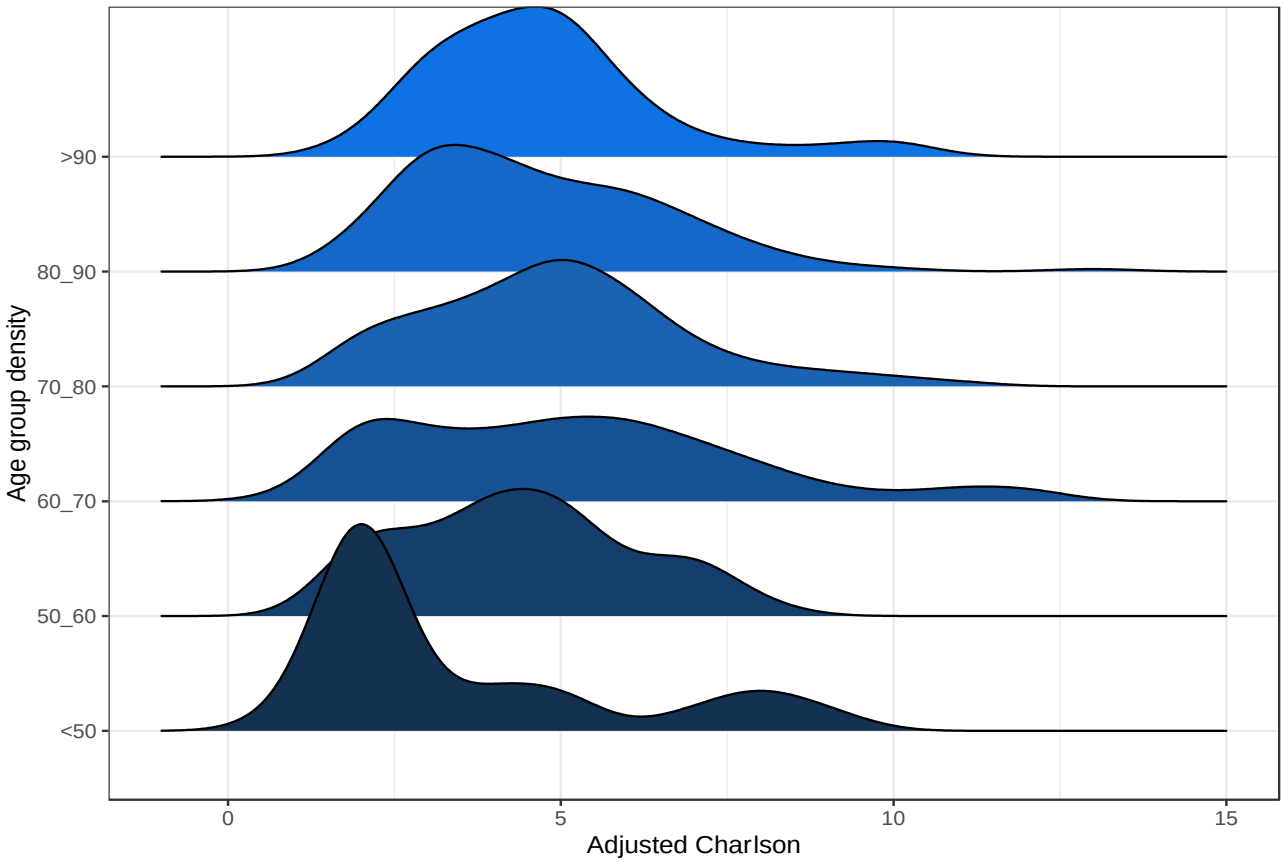


Figure 9. **Distribution of the SGA score among age groups**

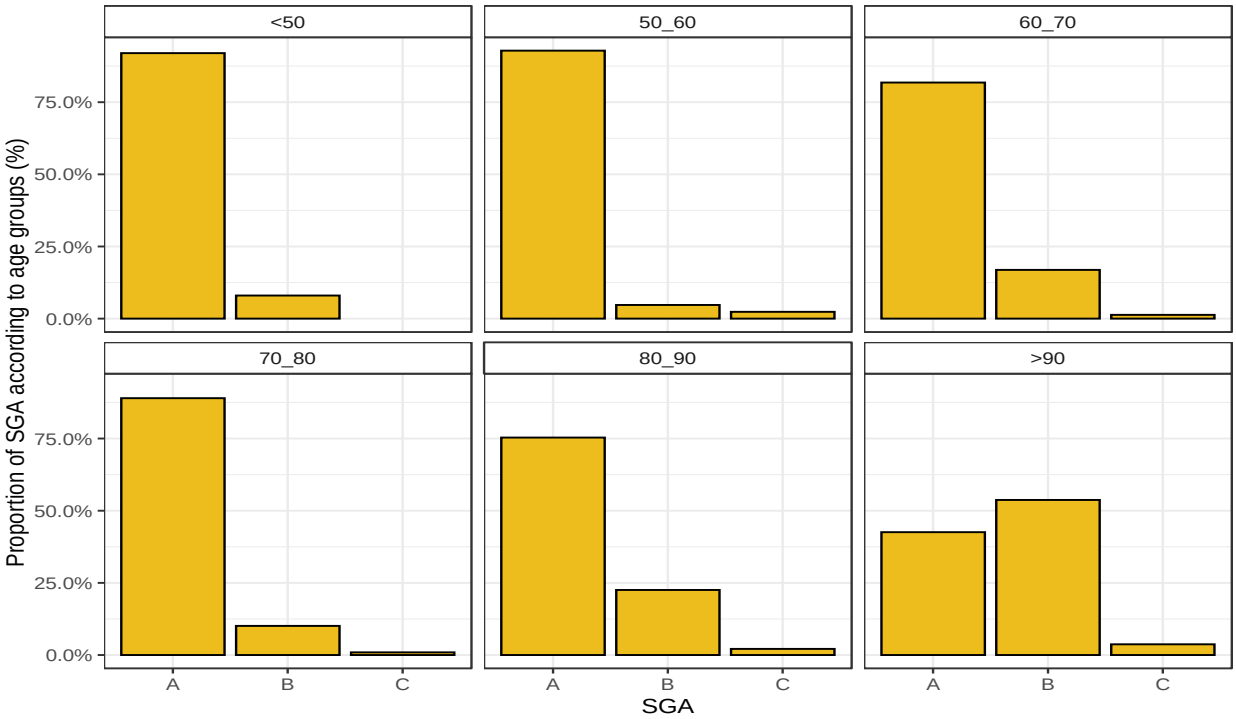
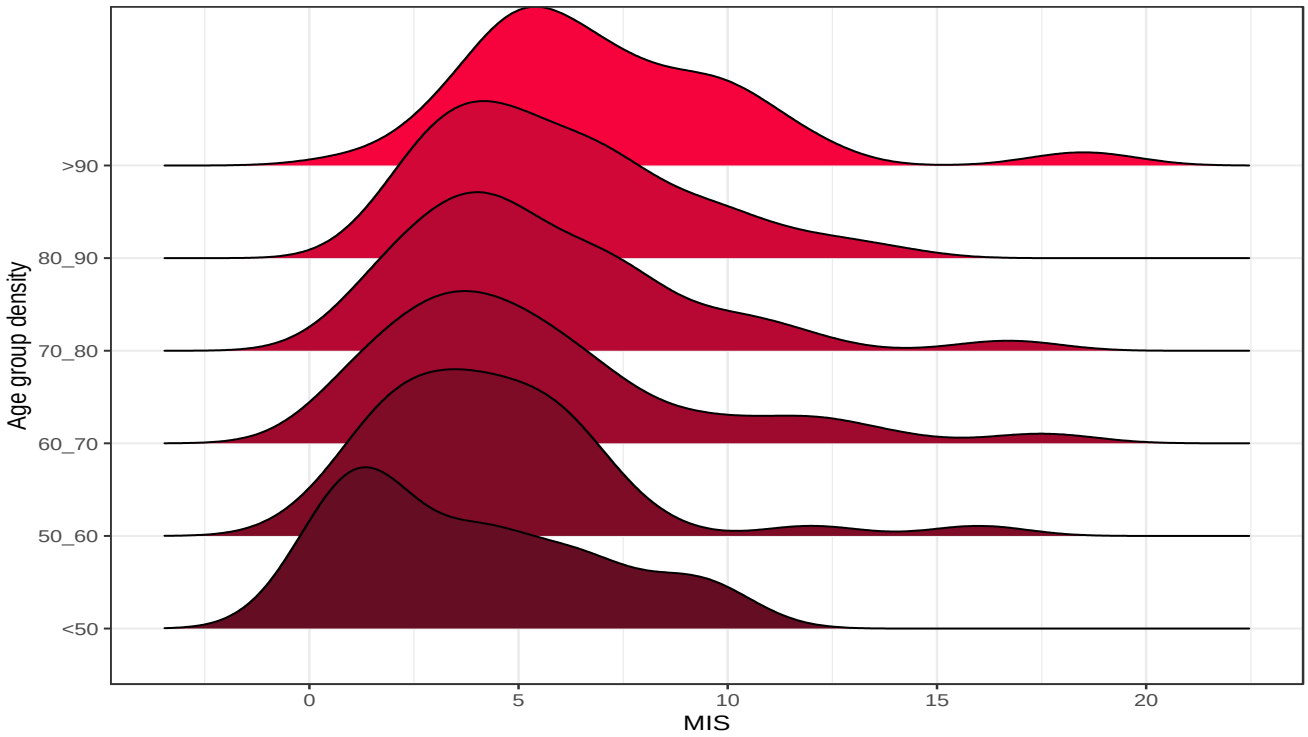


Figure 10. **Distribution of the MIS score among age groups**



3.2.3 Biochemical profile across age groups.

The following tables (table 5) describe the biochemical profile across the age groups. Overall, the trends are similar and the minor differences reflect more the evolution across stages, overall similar in each age group, than the effect of age per se, suggesting that the metabolic impact of CKD is modulated by stage more than by age.

Table 5. **Biochemical data across the different age groups (UIRAV cohort)**

	Age groups						
	<50	50_60	60_70	70_80	80_90	≥90	P-values
N	23	39	74	108	140	54	
Creatinine (mg/l), median (IQR)	2.85 (3.39)	2.50 (2.24)	2.58 (1.37)	2.22 (1.09)	2.02 (1.04)	1.86 (1.17)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	22 (25)	23 (23)	23 (18)	26 (14)	26 (15)	25 (17)	0.613
Proteinuria (g/24h), n (%)							**<0.001**
<0.3	2 (15.4%)	6 (31.6%)	11 (26.8%)	36 (48.0%)	53 (53.5%)	25 (71.4%)	
0.3 - 1	3 (23.1%)	3 (15.8%)	7 (17.1%)	11 (14.7%)	25 (25.3%)	5 (14.3%)	
≥1	8 (61.5%)	10 (52.6%)	23 (56.1%)	28 (37.3%)	21 (21.2%)	5 (14.3%)	
Albumin (g/dl), median (IQR)	3.45 (0.83)	3.50 (0.50)	3.70 (0.60)	3.80 (0.50)	3.60 (0.50)	3.52 (0.33)	**0.003**
PTH (ng/ml)	110 (248)	125 (205)	87 (120)	105 (105)	85 (77)	77 (59)	0.099
BUN (mg/dl)	33.5 (24.2)	43.4 (35.0)	43.1 (40.5)	39.5 (28.7)	42.7 (23.4)	41.9 (23.7)	0.859
Bicarbonate (mmol/l)	20 (6)	22 (3)	22 (5)	24 (5)	24 (5)	24 (4)	**<0.001**
Hemoglobin	11.6 (1.8)	12.2 (3.5)	11.7 (3.1)	11..8 (2.7)	11.6 (2.3)	11.5 (2.2)	0.962
Ferritin (µg/l)	92 (96)	154 (248)	179 (231)	189 (222)	158 (176)	180 (195)	**0.004**
Transferrin (g/l)	2.41 (0.71)	2.16 (0.48)	2.29 (0.61)	2.20 (0.57)	2.27 (0.58)	2.22 (0.44)	0.233
Uric acid (µmol/l)	426 (303)	415 (147)	447 (193)	434 (160)	470 (195)	441 (148)	0.110
Total Cholesterol	4.84 (1.65)	4.53 (3.01)	5.06 (1.76)	4.33 (1.45)	4.46 (2.03)	5.08 (2.14)	**0.034**
Vitamin D	26 (10)	23 (21)	30 (26)	27 (21)	30 (18)	32 (22)	**0.037**
Sodium	140 (4)	141 (3)	140 (4)	140 (4)	140 (4)	140 (4)	0.542
Potassium	4.45 (0.50)	4.55 (0.70)	4.20 (0.70)	4.20 (0.60)	4.30 (0.60)	4.30 (0.60)	0.155
Calcium	2.30 (0.15)	2.34 (0.13)	2.35 (0.19)	2.34 (0.16)	2.34 (0.17)	2.33 (0.14)	0.930
Phosphate	1.01 (0.66)	1.26 (0.40)	1.10 (0.36)	1.04 (0.32)	1.10 (0.28)	1.14 (0.32)	0.020
Diabetes, n (%)	4 (17.4%)	18 (47.4%)	40 (56.3%)	54 (54.4%)	56 (42.2%)	12 (25.5%)	**<0.001**
HbA1$_c$ (%) *, median (IQR)	6.4 (-)	7.1 (1.6)	7.1 (1.9)	6.9 (1.5)	6.8 (1.5%)	7.2 (1.1)	0.993

* only for those with diabetes, with 88% available data (for age groups: 2, 12, 27, 54, 55, 12, respectively)

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Table 6. **Biochemical data across 60-69 years old patients**

60-69 years (n=74)					
	CKD Stages				
	3A	3B	4	5	P-values
N	5	20	34	15	
Creatinine (mg/l), median (IQR)	1.35 (0.07)	1.93 (0.28)	2.77 (0.66)	5.17 (2.48)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	54 (3)	34 (4)	20 (6)	10 (6)	**<0.001**
Charlson index, median (IQR)	9 (5)	6 (4)	8 (3)	7 (3)	0.111
MIS, median (IQR)	7 (2)	3 (3)	5 (4)	5 (4)	0.051
SGA, n (%)					0.845
A	5 (100%)	17 (85%)	26 (76.5%)	12 (80%)	
B	0	3 (15.0%)	7 (20.6)	3 (20.0%)	
C	0	0	1 (2.9%)	0	
Diabetes, n (%)	2 (50%)	7 (35%)	23 (67.6%)	8 (61.5%)	0.128
Cardiopathy, n (%)	4 (100%)	5 (25%)	11 (32.4%)	4 (30.8%)	**0.035**
Neoplasia, n (%)	1 (25%)	5 (25%)	7 (20.6%)	0 (0%)	0.290
BMI (kg.m^{-2}), median (IQR)	24.8 (12.8)	29.2 (10.1)	29 (8.0)	28.7 (9.7)	0.930
Albumin	3.90 (1.70)	3.65 (0.60)	3.60 (0.55)	3.70 (0.60)	0.804
PTH	59 (54)	47 (46)	92 (86)	226 (815)	**<0.001**
BUN	28.0 (8.7)	34.2 (26.3)	40.5 (24.8)	71.3 (49.1)	**0.002**
Bicarbonate	26 (1)	24 (4)	22 (6)	21 (3)	**0.006**
Hemoglobin	13.0 (0.7)	12.4 (3.4)	11.5 (1.9)	10.1 (2.9)	0.088
Ferritin	295 (295)	164 (247)	143 (163)	217 (475)	0.456
Transferrin	2.33 (1.03)	2.40 (0.52)	2.30 (0.69)	2.03 (0.56)	0.110
Uric acid	276 (144)	427 (159)	474 (187)	443 (158)	0.175
Cholesterol	4.66 (1.88)	5.55 (1.06)	4.97 (1.39)	3.87 (2.6)	0.104
Vit D	30 (18)	32 (33)	24 (27)	41 (24)	0.261
Sodium	142 (10)	139 (4)	140 (4)	141 (5)	0.432
Potassium	3.60 (1.20)	4.00 (0.50)	4.30 (0.45)	4.30 (0.90)	**0.021**
Calcium	2.30 (0.16)	2.43 (0.17)	2.33 (0.15)	2.26 (0.23)	0.085
Phosphate	0.87 (0.26)	0.98 (0.16)	1.14 (0.31)	1.40 (0.27)	**<0.001**
Diabetes, n (%)	2 (50.0%)	7 (35.0%)	23 (67.6%)	8 (61.5%)	0.128
HbA1c (%) *, median (IQR)	8.89 (-)	8.2 (2.8)	7.0 (1.5)	5.8 (2.2)	0.150

* only for those with diabetes in this group, with 68% available data (for CKD stages: 1, 5, 17, 4, respectively)

Table 7: **Biochemical data across 70-79 years old patients**

70-79 years old (n=106)					
	CKD Stages				
	3A	3B	4	5	P-values
N	8	33	47	18	
Creatinine (mgl/l), median (IQR)	1.26 (0.27)	1.82 (0.36)	2.58 (0.59)	4.58 (1.66)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	47 (7)	35 (6)	22 (5)	11 (5)	**<0.001**
Charlson index, median (IQR)	7 (4)	7 (2)	8 (2)	8 (3)	**0.001**
MIS, median (IQR)	5 (5)	4 (2)	6 (3)	5 (5)	**0.046**
SGA, n (%)					0.302
A	6 (75.0%)	31 (93.9%)	43 (91.5%)	14 (77.8%)	
B	2 (25.0%)	2 (6.1%)	3 (6.3%)	4 (22.2%)	
C	0	0	1 (2.1%)	0	
Diabetes, n (%)	3 (37.5%)	11 (34.4%)	30 (66.7%)	10 (62.5%)	**0.027**
Cardiopathy, n (%)	2 (25%)	9 (28.1%)	18 (40%)	6 (37.5%)	0.669
Neoplasia, n (%)	0 (0%)	5 (15.6%)	6 (13.3%)	5 (29.4%)	0.251
BMI (kg.m^{-2}), median (IQR)	26.2 (5.5)	29.4 (6.5)	30.5 (9.6)	29.4 (13)	0.494
Albumin	3.9 (0.8)	3.9 (0.3)	3.7 (0.5)	3.75 (0.8)	**0.018**
Protide	71 (6)	75 (8)	72 (11)	73 (8)	0.509
CRP	4 (29)	4 (4)	4 (5)	8 (16)	0.299
PTH	72 (27)	56 (51)	120 (83)	257 (166)	**<0.001**
BUN	25.9 (6.4)	32 (11.8)	51 (23.8)	64.4 (28.3)	**<0.001**
Bicarbonate	25 (2)	24 (4)	24 (5)	22 (4)	**0.026**
Hemoglobin	11.4 (3.7)	13.1 (2.5)	11.6 (2.2)	11 (1.6)	**0.002**
Ferritine	219 (409)	184 (216)	211 (197)	175 (396)	0.867
Transferrine	2.19 (0.46)	2.36 (0.62)	2.19 (0.7)	2.2 (0.43)	0.097
Uric acide	425 (157)	426 (96)	439 (187)	468 (168)	0.643
Cholesterol	4.45 (2.4)	4.69 (1.71)	4.1 (1.17)	4.01 (1.73)	0.299
Vit D	23 (30)	28 (19)	27 (23)	26 (17)	0.936
Sodium	138 (5)	139 (3)	140 (4)	141 (2)	0.136
Potassium	4.3 (0.9)	4.2 (0.5)	4.2 (0.7)	4.5 (0.7)	0.377
Calcium	2.33 (0.18)	2.41 (0.12)	2.32 (0.18)	2.29 (0.14)	**0.028**
Phosphore	1 (0.21)	0.98 (0.21)	1.05 (0.31)	1.52 (0.5)	**<0.001**
Diabetes, n (%)	3 (37.5%)	11 (34.4%)	30 (66.7%)	10 (62.5%)	**0.027**
$HbA1_c$ (%) *, median (IQR)	6.5 (-)	6.9 (1.7)	7.2 (1.9)	7.2 (2.1)	0.267

* only for those with diabetes in this group, with 98% available data (for CKD stages: 3, 11, 29, 10 respectively)

Table 8: **Biochemical data across 80-89 years old patients**

80-89 years old (n=138)					
	CKD Stages				
	3A	3B	4	5	P-values
N	9	41	71	17	
Creatinine (mgl/l), median (IQR)	1.04 (0.27)	1.69 (0.33)	2.27 (0.78)	3.85 (1.57)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	50 (2)	35 (5)	22 (8)	10 (5)	**<0.001**
Charlson index, median (IQR)	7 (1)	8 (3)	9 (2)	8 (3)	**0.001**
MIS, median (IQR)	4 (2)	6 (4)	5 (4)	6 (6)	0.141
SGA, n (%)					0.107
A	7 (77.8%)	32 (78%)	57 (80.3%)	10 (58.8%)	
B	2 (22.2%)	8 (19.3%)	14 (19.7%)	5 (29.4%)	
C	0	1 (2.4%)	0	2 (11.8%)	
Diabetes, n (%)	1 (11.1%)	14 (35.9%)	35 (50.7%)	6 (37.5%)	0.093
Cardiopathy, n (%)	4 (44.4%)	13 (33.3%)	34 (49.3%)	7 (43.8%)	0.461
Neoplasia, n (%)	0 (0%)	13 (33.3%)	19 (27.5%)	1 (6.3%)	0.052
BMI (kg.m^{-2}), median (IQR)	29.9 (7.7)	26.7 (3.8)	28.4 (5.4)	26.1 (4.4)	0.105
Albumine	3.8 (0.3)	3.7 (0.6)	3.6 (0.4)	3.4 (0.5)	**0.013**
Protide	70 (6)	71 (9)	74 (7)	72 (10)	0.197
CRP	3 (2)	6 (9)	3 (6)	5 (7)	0.340
PTH	42 (38)	74 (60)	91 (74)	172 (149)	**<0.001**
BUN	24.2 (15.9)	31.2 (13.7)	46.4 (19.4)	57 (29.7)	**<0.001**
Bicarbonate	25 (5)	26 (6)	24 (4)	20 (4)	**<0.001**
Hemoglobin	12.3 (1.7)	11.8 (2.4)	11.6 (2)	9.9 (1.8)	**0.005**
Ferritine	161 (200)	170 (196)	143 (143)	180 (191)	0.451
Transferrine	2.43 (0.79)	2.14 (0.39)	2.36 (0.47)	2.14 (0.8)	**0.035**
Uric acide	434 (71)	446 (210)	519 (211)	485 (193)	0.189
Cholesterol	4.81 (1.77)	4.38 (2.02)	4.29 (2.2)	4.87 (1.49)	0.122
Vit D	41 (14)	26 (18)	33 (17)	31 (26)	0.293
Sodium	141 (4)	141 (3)	140 (4)	139 (6)	0.063
Potassium	4.15 (0.5)	4.2 (0.6)	4.3 (0.5)	4.3 (0.6)	0.774
Calcium	2.28 (0.21)	2.36 (0.19)	2.34 (0.15)	2.34 (0.26)	0.273
Phosphore	1.03 (0.13)	1.01 (0.25)	1.12 (0.26)	1.43 (0.35)	**<0.001**
Diabetes, n (%)	1 (11.1%)	14 (35.9%)	35 (50.7%)	6 (37.5%)	0.093
$HbA1_c$ (%) *, median (IQR)	6.61 (-)	7.3 (1.7)	6.9 (2.0)	6.4 (2.2)	0.664

* only for those with diabetes in this group, with 98% available data (for CKD stages: 1, 14, 34, 6, respectively)

Table 9: **Biochemical data across ≥90 years old patients**

≥90 years old (n=53)					
	CKD Stages				
	3A	3B	4	5	P-values
N	5	15	22	11	
Creatinine (mgl/l), median (IQR)	1.07 (0.2)	1.44 (0.22)	2.09 (0.66)	4.06 (1.08)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	46 (4)	34 (7)	22 (9)	10 (4)	**<0.001**
Charlson index, median (IQR)	8 (1)	9 (2)	8 (2)	9 (2)	0.596
MIS, median (IQR)	6 (1)	6 (4)	7 (4)	9 (4)	0.269
SGA, n (%)					0.233
A	2 (40.0%)	6 (40.0%)	10 (45.5%)	4 (36.4%)	
B	3 (60.0%)	9 (60.0%)	12 (54.5%)	5 (45.5%)	
C	0	0	0	2 (18.2%)	
Diabetes, n (%)	1 (20%)	4 (28.6%)	4 (20%)	3 (27.3%)	0.931
Cardiopathy, n (%)	4 (80%)	4 (28.6%)	7 (35%)	6 (54.5%)	0.164
Neoplasia, n (%)	0 (0%)	2 (14.3%)	4 (20%)	2 (18.2%)	0.739
BMI (kg.m^{-2}), median (IQR)	24.9 (8.1)	27.9 (5.1)	23.8 (4.4)	27.8 (6.2)	0.230
Albumin	3.7 (0)	3.6 (0.3)	3.45 (0.5)	3.5 (0.2)	0.336
Proteins	71 (3)	73 (9)	73 (9)	71 (5)	0.918
CRP	3 (3)	3 (2)	8 (11)	10 (11)	0.164
PTH	64 (63)	66 (68)	59 (56)	162 (203)	**0.049**
BUN	28.3 (7.8)	33.3 (13)	45.7 (20.1)	70 (49.6)	**0.013**
Bicarbonate	24 (3)	25 (5)	23 (7)	22 (7)	0.207
Hemoglobin	12.8 (1.9)	12.6 (2.5)	11.3 (1.7)	10.5 (1.8)	**0.004**
Ferritin	135 (136)	134 (182)	237 (220)	176 (216)	0.556
Transferrin	2.33 (0.25)	2.25 (0.46)	2.15 (0.43)	2.06 (1)	0.588
Uric acid	459 (73)	431 (149)	450 (155)	500 (164)	0.736
Cholesterol	4.66 (1.33)	5.06 (2)	5.29 (2.1)	5.02 (3.56)	0.768
Vit D	34 (11)	34 (18)	32 (22)	22 (33)	0.428
Sodium	141 (3)	141 (6)	140 (4)	139 (6)	0.745
Potassium	4.3 (0)	3.9 (0.6)	4.4 (0.5)	4 (2.1)	0.051
Calcium	2.38 (0.15)	2.34 (0.17)	2.35 (0.15)	2.29 (0.17)	0.058
Phosphate	0.98 (0.06)	1.06 (0.17)	1.14 (0.24)	1.48 (0.69)	**0.001**
Diabetes, n (%)	1 (20.0%)	4 (28.6%)	4 (20.0%)	3 (27.3%)	0.931
HbA1$_c$ (%) *, median (IQR)	7.43 (-)	7.2 (0.7)	6.6 (1.6)	7.4 (-)	0.647

* only for those with diabetes in this group, with 98% available data (for CKD stages: 1, 4, 4, 3, respectively)

3.2.4 Protein intake and dietary prescription in the different age groups.

Protein intake was assessed at baseline in all cases and a dietary prescription was proposed to over 90% of the patients, the missing cases being either still undergoing evaluation or having refused all diet approaches. In the case of patients in nursing homes, the evaluation and prescription were done in agreement with the structure of care.

In a context of an overall well-nourished and overweight population, the median protein intake was higher than the recommended protein intake of 0.8 g/Kg of body weight per day, according to the WHO, in all age groups. However, the baseline protein intake decreases from 1.2 g/Kg of body weight per day in cases ages less than 50 years, to 1.1 g/Kg/day at the age 50-59 and to 1.0 thereafter.

However, the prevalence of cases with a spontaneous normal protein intake or a lower one increases with age.

3.2.5. Outcome analysis: survival, renal survival, total drop-out

Three main time-dependent outcomes were analyzed by Kaplan Meier analysis: patient survival, renal survival, whose outcome is the start of renal replacement therapy, and the so-called total drop-out curve, in which patients are censored in the occasion of death or dialysis or loss to follow-up. This latter analysis defines the "persistence" of the patients in the setting of care (figures 11, 12, 13).

As expected, patient survival is highly dependent on age and, one year after the start of follow-up, over 80% of the "old patients" were still alive, versus less than 70% of the extremely old patients, a figure that may be underestimated considering that about 20% of the oldest patients are lost of sight every year.

Conversely, due to the effect of the competitive mortality, younger patients have a much higher chance of starting dialysis during follow-up (figure 13).

The persistence into the system of care (total drop-out curve) was however non negligible even in the oldest subsets of the population, and about half of the oldest patients (age at or over 90) were followed for at least 400 days.

Figure 11: **Patient survival in patients followed-up in the UIRAV, according to age at referral**

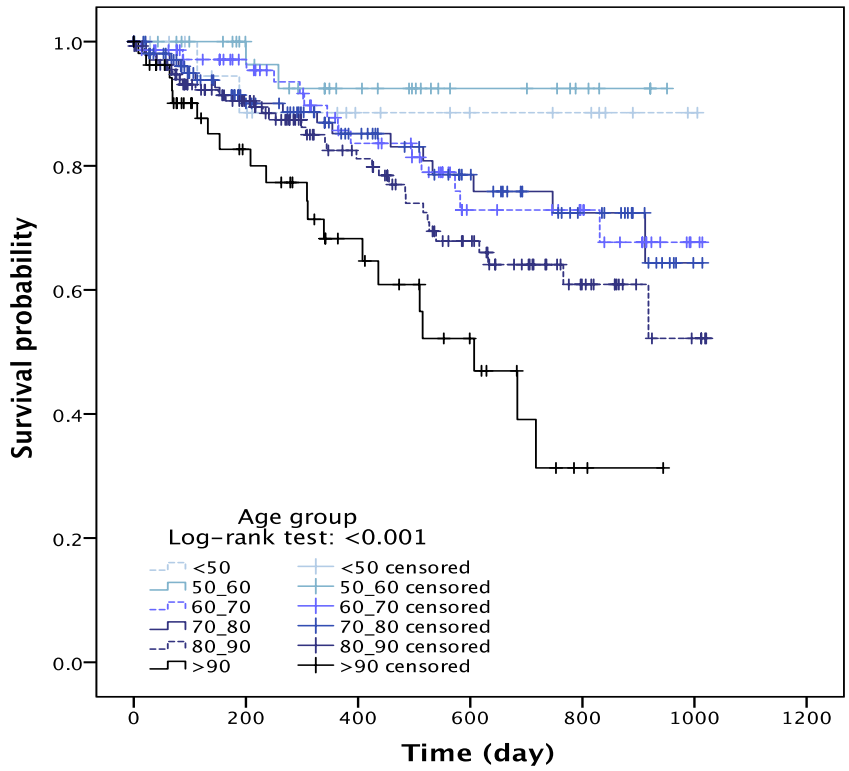

Figure 12. **Renal survival in patients followed-up in the UIRAV, according to age at referral**

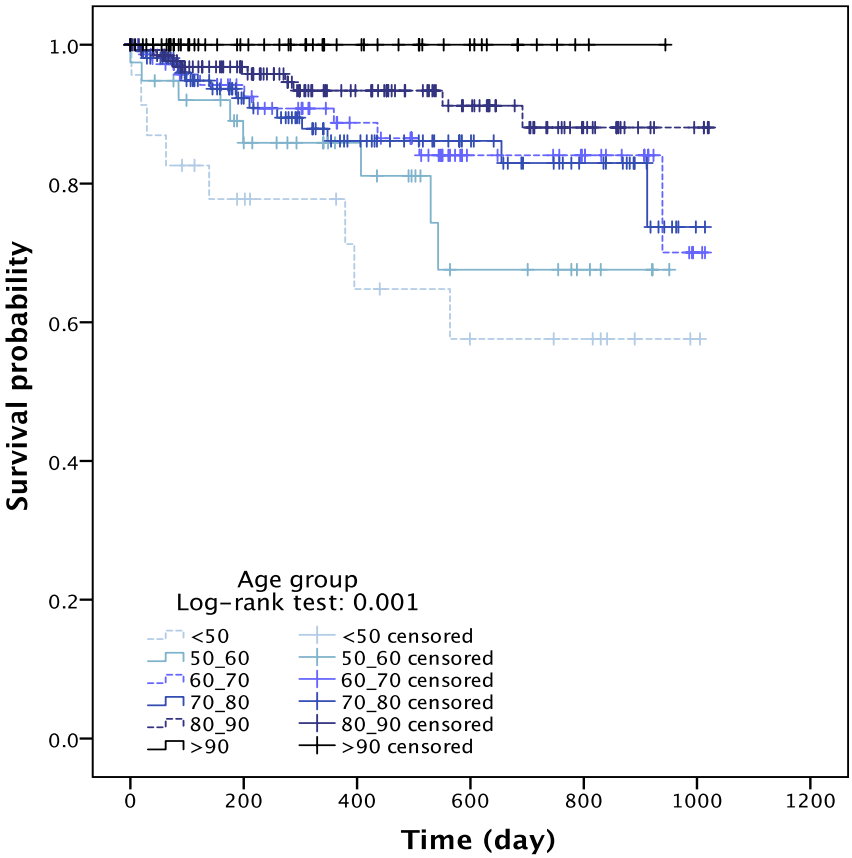

Figure 13. **Total drop-out (death, dialysis, loss of sight) in patients followed-up in the UIRAV, according to age at referral**

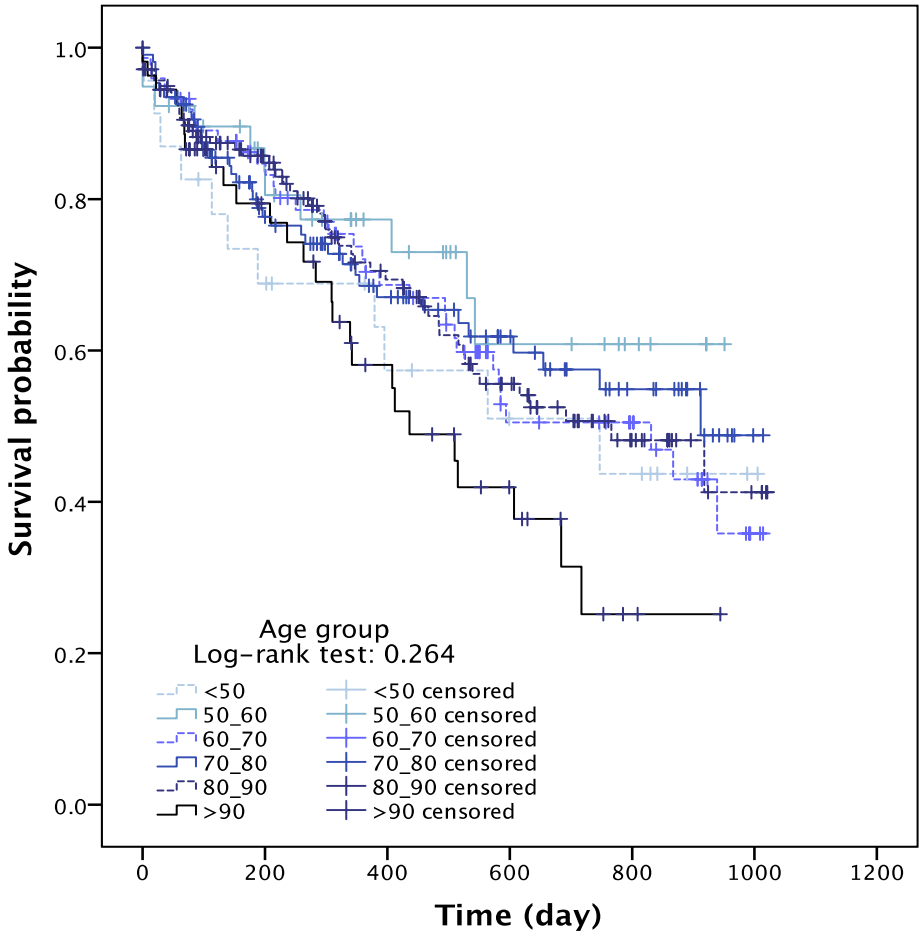

Table 10. **Quality of life and dietary compliance**

	Age groups						
	<50	50_60	60_70	70_80	80_90	≥90	P-values
N (all: 438)	23	39	74	108	140	54	
Creatinine (mg/l), median (IQR)	2.85 (3.39)	2.50 (2.24)	2.58 (1.37)	2.22 (1.09)	2.02 (1.04)	1.86 (1.17)	**<0.001**
eGFR EPI (ml/min/1.73m^2), median (IQR)	22 (25)	23 (23)	23 (18)	26 (14)	26 (15)	25 (17)	0.613
Stages, n (%)							**<0.008**
2	2 (8.7%)	0 (0%)	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	
3A	1 (4.3%)	6 (15.4%)	5 (6.8%)	8 (7.5%)	9 (6.5%)	5 (9.3%)	
3B	5 (21.7%)	11 (28.2%)	20 (27%)	33 (30.8%)	41 (29.7%)	15 (27.8%)	
4	7 (30.4%)	14 (35.9%)	34 (45.9%)	47 (43.9%)	71 (51.4%)	22 (40.7%)	
5	8 (34.8%)	8 (20.5%)	15 (20.3%)	18 (16.8%)	17 (12.3%)	12 (22.2%)	
Protein intake at baseline (g/kg/24h), median (IQR)	1.20 (0.42)	1.10 (0.30)	1.00 (0.39)	1.00 (0.30)	1.00 (0.30)	1.00 (0.30)	**<0.001**
≤0.8 g/kg/24h, n (%)	1 (5.3%)	6 (15.4%)	17 (23.6%)	36 (35.6%)	37 (27.6%)	20 (39.2%)	**0.012**
≥1.2 g/kg/24h, n (%)	12 (63.2%)	15 (38.5%)	19 (26.4%)	22 (21.8%)	25 (18.7%)	10 (19.6%)	**<0.001**
Diet prescribed, n (%)	21 (91.3%)	36 (92.3%)	67 (90.5%)	101 (93.5%)	133 (95.0%)	49 (90.7%)	0.702
Details of the diet prescribed, n (%)							**0.045**
0.8 g /kg/24	2 (8.7%)	19 (48.7%)	31 (41.9%)	57 (53.3%)	86 (61.4%)	35 (64.8%)	
0.8 g /kg/24h with ketosteril	11 (47.8%)	2 (5.1%)	4 (5.4%)	14 (13.1%)	13 (9.3%)	8 (14.8%)	
0.6 g /kg/24h	2 (8.7%)	11 (28.2%)	22 (29.7%)	26 (24.3%)	27 (19.3%)	5 (9.3%)	
0.6 g /kg/24h with ketosteril	5 (21.7%)	4 (10.3%)	10 (13.5%)	3 (2.8%)	7 (5%)	1 (1.9%)	
No diet	3 (13.0%)	3 (7.7%)	7 (9.5%)	7 (6.5%)	7 (5%)	5 (9.3%)	

4. DISCUSSION ET CONCLUSION

The study described in this thesis was performed with the double aim of quantifying the burden of elderly patients in an outpatient unit of Nephrology and of exploring the potential for a comprehensive nephrology and nutritional management in the work-up in particular of the oldest old.

4.1 Part 1: what is the burden of elderly patients in a large outpatient nephrology unit?

The analysis of the large cohort of about two thousand patients (1992), referred of followed-up the presence of any clinical condition of nephrological interest, clearly confirms that the present nephrology needs geriatric competences: in spite of two specific outpatient units, dedicated to complicated lithiasis and to the follow-up post preeclampsia, recruiting mainly or exclusively young patients, the vast majority of the cohort followed up in the setting of study (a large non-university hospital in central France) was “old”. The patients aged 60 years or more accounted for 70% of the overall cohort, one patient out of four is aged 80 or is older, and the most numerous subsets is recorded the one in age group 80-90 years (21.9%) while the extremely old patients, aged at or about 90 years, account for 5.8% of the cases (table 2).

The referral pattern is in line with a selective early referral of younger patients and a later referral of elderly ones; indeed, in this cohort, the median eGFR decreases over age, reaching 27 ml|min at or above age 90. In line with these observations, the prevalence of the most severe CKD stages (CKD stages 4 and 5) increases with age, and indeed, only 1.7% of the patients aged at or over 90 has a normal or slightly reduced kidney function at referral, and over 60% of the cases are in CKD stages 4-5, versus 38.5% in the age group 80-89, and only 8.3% at age < 50 years (figure 3).

This figure on one side reassures about the frequently reported concern that, since the commonly used formulae are less reliable in the elderly, elderly patient may be over-referred, at levels of the

kidney function that do not define a “true kidney disease”. This gray area, as per clinical relevance, mainly regards stage 3 patients, in which the trajectories of the kidney function impairment is more important than the impairment level *per se*. While this present cross-sectional study does not allow analyzing trajectories, there is little concern about the fact that patients in CKD stage 4 and 5 are prone to develop severe metabolic derangements and have a higher risk of death and of need for starting renal replacement therapy.

The subset of cases in the late CKD stages (e-GFR < 30mL/min) increases sharply with age, thus raising more the concern of late referral than of an overzealous, and possibly not cost-effective, use of the nephrology resources.

This point may be further stressed by the more in-depth analysis of the patients followed-up in the new dedicated patient unit (UIRAV), which is progressively taking in charge the patients in the more advanced CKD stages. In this context, the analysis per age groups highlights the same metabolic derangements in all ages, with a striking similar pattern in CKD stage 5 (hyperparathyroidism, anemia, increased phosphate levels) 60-69 to at or over 90 years (tables 5-9).

As for the kidney diseases, the prevalence of three categories increases with age: multifactorial diseases, vascular kidney diseases - nephroangiosclerosis, and the diabetes associated kidney disease in the variant with low proteinuria (diabetes-vascular). The three diseases account for 80.7% of the diagnoses in the 80-89 age group, versus 84.6% in patients aged at or over 90 years (table 1). The diagnoses of vascular kidney diseases- nephroangiosclerosis are eminently clinical (hypertension, signs of central or peripheral vascular disease, small kidneys, absent or scant proteinuria and no hints for a different kidney disease), and may also reflect a minimalist attitude towards the diagnoses of the kidney diseases of the elderly. Notwithstanding this limitation, this first portrait of the elderly population suggests that the main focus of nephrology care in this patient should be more on the clinical and metabolic needs, than on the diagnostic pathways. These needs,

as well as the prevalence of the major comorbidities, are analyzed more in detail in the second section of the discussion.

4.2 Part 2: what is the importance of comorbidities, with particular regard to nutritional status, in elderly patients followed up in a nephrology unit dedicated to advanced CKD stages?

The UIRAV is the setting of the care of three subsets of patients, including at-risk pregnancies, patients needing particular attention (intellectual deficit, rare diseases etc), most of the cases, considered in the present study, are affected by advanced or progressive CKD (stages 3-5). This subset was selected for the present analysis.

The main baseline demographic characteristics of the 438 patients analyzed define an overall elderly population, with a prevalence of extremely old patients that is in line with that observed in the overall population on follow-up. The distribution of the CKD stages and the disease pattern confirms what was observed in the general population referred to the Centre Hospitalier Le Mans, with an increasing predominance of vascular and multifactorial diseases with increasing age and a trend towards referring later the oldest patients with advanced CKD, possibly also because the kidney diseases in the oldest are less frequently characterized by proteinuria, which is one of the main elements considered in assessing the potential progression of the functional kidney impairment.

In this population at high comorbidity, as expected, the Charlson comorbidity index overall increases across age groups; the prevalence of diabetes is the highest in the age groups 60-69 and 70-79, and decreases thereafter, suggesting a role of competitive mortality in this subset of cases; the prevalence of heart diseases is around 40% without consistent age-related differences, underlining the strict relationship between chronic kidney disease and cardiovascular impairment.

In spite of the high comorbidity, the subjective global assessment defines our population as overall well nourished, with only a minority of cases with a severely impaired nutritional status (less than 3%). Once more, the high mortality of these patients may compete with nephrology referral, and indeed moderate nutritional impairment, increases over age, reaching 53.7% at age at or above 90; however, the definition of the SGA is difficult in extreme ages, as sarcopenia is an almost invariable finding and the distinction between what is physiological and what is not is subtle. In keeping with an overall well-nourished population, the median BMI is in the overweight range at all ages but decreases to 25.7 kg/m^2 at or above 90 years. The more comprehensive malnutrition inflammation score (MIS), which combines nutritional, functional and comorbidity indexes, may be a more reliable marker in this population, as indeed suggested by its increase over age.

The biochemical profiles, as previously mentioned, are essentially similar across ages, and follow the well-known development of the metabolic derangement characteristics of uremia in stages 4 and 5.

The practical meaning of similarity of the pattern across ages, including the old-old and the oldest-old, is two folds: on one side, it reassures on the fact that the population taken in charge is not over-treated and over-referred, also considering the relative increase in severe CKD stages in elderly patients referred to the nephrology units, and on the other it defines a role for the nephrology work-up, in taking care of the metabolic derangement of advanced CKD in all ages.

Furthermore, in keeping with the need for a nutritional management in this population, median protein intake is higher than recommended in the overall population in all ages; the therapeutic room is even higher if we consider that the current recommendations of protein restricted diets apply to all metabolically stable patients since stage 3, and that a protein intake of 0.4-0.6 g/Kg/day is recommended without any specific age restriction. Our policy, of a stepwise reduction in the protein intake, applied to all ages, even if normalization of a too-high intake was often the only

approach in elderly patients. The concomitant supplementation with essential aminoacids and ketoacids was a tool to try to stabilize or improve the nutritional status.

While only long-term studies may allow a better understanding of compliance and efficacy of this policy, an indirect marker of the interest towards a comprehensive approach to elderly CKD patients may come from the total drop-out curve, that measures the persistence into the system of care. While mortality and dialysis start show a competitive pattern, mortality being higher in the oldest, and dialysis start being more frequent in the youngest, persistence in the system (drop-outs, mortality and dialysis start are considered as "events" in this analysis) was relevant even in the oldest subsets of the population, and about half of the oldest patients (age at or over 90) were followed for at least 400 days.

In conclusion, nephrology and geriatrics need to be more interconnected, on the account of the fact that about 70% of the cases followed up in nephrology may be labeled as "old", and the oldest age groups (at or above age 80) represent the most relevant subset of the population.

The metabolic alterations occur, in late CKD stages, in all age groups, thus identifying a role for the nephrology work-out. In a well-nourished elderly population, there is also room for nutritional management, in keeping with the most regent guidelines.

Prospective studies are needed to highlight the potential, benefit and indication of nephrology care in elderly CKD patients, and to define areas of cooperation, in the optics of a multidisciplinary management of this fragile population.

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De la Faculté de Médecine de Tours

Tours, le

64 pages - 10 tableaux – 13 figures

L'objectif de ce travail de thèse est d'évaluer l'applicabilité d'une prise en charge diététique de la MRC dans une population gériatrique attente d'une maladie rénale sévère.

La population étudiée est celle soignée dans l'Unité UIRAV du CH Le Mans ; les patients inclus dans l'étude sont classifiés comme avec une maladie rénale chronique de stade 3b-5. Les comorbidités ont été évaluées selon l'index de Charlson, dont la médiane est à 7.

La thèse est ciblée à trois cohortes divisées selon l'âge : OLD entre 70 et 79 ans, OLD-OLD entre 80 et 89 ans et extremely- OLD > 90 ans.

Le premier résultat intéressant regarde les habitudes alimentaires : bien qu'avec une tendance à la réduction avec l'âge, l'apport protidique médian est de 1.1 g/Kg/j, avec une réduction à 0.9 g/Kg/j (toujours supérieur à la définition actuelle de régime normo protidique, désormais établi à 0.8 g/Kg/j) à un âge supérieur à 90 ans. Après la prise en charge nutritionnelle, on observe, à 6 mois, une réduction des apports à une médiane de 0.9 g/Kg/j, qui se réduit ultérieurement de 0.2 g/Kg/j de protéines pour les sujets suivis pour au moins un an, en ligne avec la réduction progressive des apports. Cette réduction des apports, probablement aussi en tenant compte du fait que moins de 10% des patients présente un état nutritionnel précaire (SGA : B), et que l'obésité a une prévalence, de 42%, ne s'accompagne pas à une réduction des principaux paramètres nutritionnels, dont l'albumine. Au contraire, l'albumine plasmatique montre une augmentation de 2 g/l, significative, à 3 mois depuis le début du régime.

L'adhérence thérapeutique est bonne, à environ 75% des patients à 3 et 6 mois d'observation. Bien que l'étude, observationnelle et non-interventionnelle, sans une cohorte contrôle, ne permet pas de juger sur l'efficacité dans le but de retarder la dialyse, une efficacité en ce sens est suggérée par le fait que tous les patients suivis en UIRAV qui ont commencé la dialyse ont bénéficié d'une approche incrémentale.

En conclusion : les patients âgés atteints d'une maladie rénale chronique sévère peuvent bénéficier d'une prise en charge nutritionnelle. Les apports protidiques sont probablement plus importants de ceux classiquement décrits, et la prise en charge ne s'accompagne pas à un risque de malnutrition, au moins à court terme. L'association avec un début incrémental de dialyse, moins traumatique et plus respectueux de la diurèse résiduelle, souligne les avantages potentiels, à étudier ultérieurement à long terme.

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