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Neoplastic alterations in people with chronic kidney disease on haemodialysis: a retrospective analysis

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ABSTRACT

Introduction: Chronic kidney disease is one of the ten leading causes of death in Spain, being an underdiagnosed pathology. Kidney disease and cancer have a multifactorial and bidirectional association. Kidney Disease Improving Global Outcomes estimates a 12-25% incidence of neoplasms. The Spanish Society of Nephrology has set up a multidisciplinary working group called Onconephrology to better respond to these people's needs.

Objective: To determine the incidence and prevalence of neoplasms in people on haemodialysis, as well as to describe the most commonly diagnosed types of cancer and related variables.

Material and Method: A retrospective, single-centre cohort study from January 2021-December 2023 in a haemodialysis unit. Sociodemographic and clinical data were collected from a specific nephrology database and clinical history.

Results: Thirty patients were detected with some neoplasia: prevalence 31% and incidence 17% (83% men, mean age 73±11 years). 73% dyslipidaemic, 50% diabetic, 93% hypertensive, 73% cardiovascular disease, Charlson index 9.9±2.6 points, 30% obese and 50% smokers. Aetiology of renal disease: tumour-derived (27%) and diabetic nephropathy (17%). Some 7% had a previous transplant. Most common neoplasms: 40% genitourinary-20% haematological. 27% had more than one tumour. Oncological treatment: 33% medical-surgical and 33% chemotherapy-immunotherapy. Mortality was higher in oncological tumours (40%).

Conclusions: We found a high incidence and prevalence of neoplasms and a high mortality. The results need to be confirmed in prospective studies.

Keywords: chronic kidney disease; chronic renal disease; haemodialysis; mortality; neoplasia; onconephrology.

RESUMEN

Percepción de los pacientes con terapia de hemodiálisis respecto al rol de enfermería en Perú

Introducción: La enfermedad renal crónica se sitúa entre las diez primeras causas de muerte en España, siendo una patología infradiagnosticada. La enfermedad renal y el cáncer tienen una asociación multifactorial y bidireccional. La Kidney Disease Improving Global Outcomes, estima una incidencia de neoplasias del 12-25%. La Sociedad Española de Nefrología ha puesto en marcha un grupo de trabajo multidisciplinar denominado Onconefrología con el objetivo de dar mejor respuesta a las necesidades de estas personas.

Objetivo: Determinar la incidencia y prevalencia de neoplasias en personas en hemodiálisis, así como describir los tipos de cáncer más comúnmente diagnosticados y las variables relacionadas.

Material y Método: Estudio de cohortes retrospectivo y unicéntrico de enero 2021-diciembre 2023, en una Unidad

de Hemodiálisis. Se recogieron datos sociodemográficos y clínicos de una base de datos específica de nefrología y de la historia clínica.

Resultados: Se detectaron 30 pacientes con algún tipo de neoplasia; prevalencia 31% e incidencia del 17% (83% hombres, edad media 73±11 años). El 73% dislipémicos, 50% diabéticos, 93% hipertensos, 73% enfermedad cardiovascular, Índice de Charlson 9,9±2,6 puntos, 30% obesos y 50% fumadores. Etiología de enfermedad renal: derivada del tumor (27%) y nefropatía diabética (17%). Un 7% tuvo trasplante previo. Neoplasias más comunes: 40% genitourinarias-20% hematológicas. Un 27% presentó más de un tumor. Tratamiento oncológico: 33% médico-quirúrgico y 33% quimioterapia-inmunoterapia. La mortalidad fue superior en los oncológicos (40%).

Conclusiones: Se encontró una alta incidencia y prevalencia de neoplasias y una elevada mortalidad. Los resultados deben ser confirmados con estudios prospectivos.

Palabras clave: consulta monográfica; enfermedad renal crónica; hemodiálisis; mortalidad; neoplasia; onconefrología.

INTRODUCTION

Chronic kidney disease (CKD) has become a major public health problem, both globally and nationally. In Spain, the EPIRCE study[1] reported in 2010 that CKD affects approximately 10% of the adult Spanish population and more than 20% of people over 60 years of age, with a high rate of underdiagnosis. More recently, 2 additional studies—the ENRICA-renal study[2] in 2018 and the IBERICAN study[3] in 2020—estimated CKD prevalence at 14.4% and 15.1%, respectively, higher than the estimate from The Global Kidney Health Atlas 2019[4], which places Spain at 12% for stages 3 to 5. Indeed, CKD now ranks among the top ten causes of morbidity and mortality in Spain. As with prevalence, CKD-associated mortality has increased by 30% over the past ten years in our country, and it is expected to become the fifth leading cause of death by the year 2040[5]. According to the National Institute of Statistics (INE)[6], in 2022 there were 464,417 deaths in Spain. Diseases of the circulatory system and tumors accounted for half of these deaths, making them the leading causes. These causes vary by age: while circulatory diseases are responsible for many deaths among the elderly, tumors are among the leading causes of death in individuals younger than 60 years of age. In addition, the World Health Organization (WHO) estimated that the age-standardized incidence of kidney cancer worldwide was 6.1% in men and 3.2% in women per 100,000 people in 2020 (4.6% overall). Global mortality was 1.8% in 2020[7]. The Kidney Disease Improving Global Outcomes (KDIGO)[8] estimates an incidence of neoplasms in these patients between 12–25%.

In developed countries, improved cancer survival due to more effective treatments has resulted in a growing population of cancer survivors who are at increased risk of nephropathy. Renal, oncologic, and hematologic diseases share overlapping areas of reciprocal influence, presenting a bidirectional, multifactorial, and causal relationship, since it has been demonstrated that one may act as a risk factor for the other. Cancer can affect the kidney due to the toxic effects of medications, radiation, and the tumor itself[9]. Likewise, patients requiring renal replacement therapy (RRT)—particularly those with a kidney transplant (KT)—are at high risk for cancer due to inherent immunosuppression[10,11]. Additionally, renal cancer may require nephrectomy, in patients with or without prior CKD or in those with a solitary kidney, precipitating the need for dialysis.

Due to the complexity of managing these patients, most authors agree on the importance of creating multidisciplinary working groups with proactive collaboration to address their needs through dedicated clinics, where nursing plays an essential role[12-15]. The goal of these groups is to assess the patient holistically through joint participation of various specialists, establishing the best treatment to manage the oncologic condition while preserving renal function (RF) as much as possible, with treatment individualized for each patient. Along these lines, the Spanish Society of Nephrology (SEN.) launched in 2018 a new working group called ONCONEPHROLOGY[16] aimed at better addressing the needs of these patients. They also recommend conducting epidemiological studies, using renal biopsy as a fundamental diagnostic and prognostic tool, monitoring RF, creating a biobank, establishing consensus-based protocols for inclusion and management, developing training programs, and recognizing the need for a subspecialty.

Therefore, the general objective of the present study was to determine the incidence and prevalence of neoplasms in individuals undergoing hemodialysis (HD); and, as specific objectives, to describe the most widely diagnosed cancer types, the most frequent causes of mortality, and the related variables.

MATERIAL AND METHOD

Study design and setting. We conducted a retrospective, single-center cohort study conducted through review of electronic medical records (EMR) from patients followed in the HD Unit of Hospital Universitario de la Princesa. The aim was to analyze the evolution of both conditions and the clinical and/or sociodemographic determinants. The study was conducted between January 2021 and December 2023, with a median follow-up time of 21 (IQR, 25) months.

Population and sample. All adult patients with at least three months on RRT with HD, who received treatment in the chronic HD Unit during the study period, were included. As this was a retrospective study, informed consent (IC) could not be obtained from deceased or transplanted patients; therefore, only those actively undergoing HD at the Unit were able to sign consent. Regarding patients with

onconephrologic disease, both incident and prevalent cases were included. Incident cases were those who developed the tumor while on HD; prevalent cases were those previously diagnosed with a tumor before initiating HD or those who continued with active cancer during the 3-year follow-up. Patients transferred to other centers during the study period were excluded.

Study variables Primary variables included type of neoplasm, time of onset, progression, antineoplastic treatment received, and number of neoplasms developed. Secondary variables included: age, gender, smoking status, time on HD, history of KT, and pharmacologic treatment (angiotensin-converting enzyme inhibitors [ACEIs] and proton pump inhibitors [PPIs]). Data on comorbidities, CKD etiology, and Charlson Comorbidity Index were collected, along with causes of mortality.

Data collection. Sociodemographic, clinical, pharmacological, HD duration, and renal and oncologic disease data were collected from EMRs using the HP-HCIS information system and from Nefrosoft, a nephrology-specific care management database.

Statistical analysis. Results were processed using Microsoft Excel 2019 and SPSS 28.0. Categorical variables were expressed as absolute values and percentages; quantitative variables with normal distribution as mean ± standard deviation; and tables and graphs were used for representation. Comparisons between normally distributed quantitative variables with similar variances were performed using Student's t-test. The Chi-square test was used for comparison of proportions. Mortality was analyzed using a multivariable logistic regression model. A $p < 0.05$ was considered statistically significant.

Ethical and legal aspects. Only patients undergoing active HD were informed of the study's objectives and signed IC, as previously explained. Confidentiality of collected records (anonymous and encrypted) was maintained in accordance with Organic Law 3/2018 on Personal Data Protection and Guarantee of Digital Rights. Personal data were protected and included in a file subject to the guarantees of Regulation (EU) 2016/679 of the European Parliament and of the Council (General Data Protection Regulation, GDPR). Required permissions were obtained from the Clinical Research Ethics Committee with Medicines (CEIm) of *Hospital Universitario de la Princesa* (Madrid, Spain) (5507). Ethical principles outlined in the Declaration of Helsinki (1964) were respected and supplemented by the Biomedical Research Law 14/2007 and the Basic Law 41/2022 on Patient Autonomy.

RESULTS

A total of 97 patients were evaluated, with a mean age of 73±13 years; 69% (n=67) were men, of whom 30 (31%) had developed some type of neoplasm, with an incidence of cancer after initiation of HD of 17% (n=16).

Among the 30 patients with neoplastic disease, 83% (n=25) were men with a mean age of 73±11 years and mean HD duration of 38±28 months. Regarding comorbidities: 73% (n=22) had dyslipidemia, 50% (n=15) diabetes, 93% (n=28) hypertension (HTN), and 77% (n=23) cardiovascular disease (CVD). Additionally, 27% (n=8) were overweight, 3% (n=1) obese, with a mean Charlson Index of 9.9±2.6 points. Half (50%, n=15) were smokers. The most frequent CKD etiology among patients with neoplastic disease was tumor-related in 27% (n=8), followed by diabetic nephropathy in 17% (n=5). Only 7% (n=2) had a KT.

Comparisons of sociodemographic and clinical characteristics and CKD etiology between patients with and without neoplastic disease are shown in **table 1** and **figure 1.** Significant associations were found between development of neoplasm and male sex (p=0.042), higher Charlson comorbidity index (p=0.006), and CKD etiology (p=0.002). Smoking approached statistical significance (p=0.056).

The most frequently diagnosed neoplasms were 67% (n=20) solid tumors, of which 40% (n=12) were genitourinary cancers and 23% (n=7) GI cancers. One patient could not have the primary tumor classified due to digestive metastases at diagnosis. Hematologic neoplasms accounted for 20% (n=6), and cutaneous neoplasms for 13% (n=4). A total of 27% (n=8) presented more than one tumor. Furthermore, 17% (n=16) developed a tumor while receiving active HD; of these, 31% (n=5) had had a prior tumor of a different origin before starting HD. Regarding tumor evolution, 30% (n=9) had active disease, 30% (n=9) had controlled disease, and 40% (n=12) had died. Regarding oncologic treatment, 33% (n=10) received medical-surgical management, 33% (n=10) chemotherapy–immunotherapy, 3% (n=1) radiotherapy, 20% (n=6) surgery alone, and 10% (n=3) received conservative management. Among the 30 patients with neoplasia, 12 (40%) died during follow-up, of whom 67% (n=8) had active neoplastic disease at the time of death. General characteristics of patients with neoplastic disease are shown in **table 2**.

Patients with neoplastic disease had higher mortality than those without it (40% *vs* 31%, p=0.406). Mortality causes were analyzed between the two groups **(figure 2)**, and associated factors showed significant differences in age (p=0.004), male sex (p=0.022), Charlson index (p=0.004), history of CVD (p=0.001), and ACEI treatment (p=0.038) **(table 3)**. In a multivariable model adjusted for sex, Charlson Index, diabetes mellitus (DM), and oncologic disease, history of cardiovascular events (OR 6.9, 95% CI [1.4–35.2], p=0.019) and age (OR, 1.07, 95%CI [1.01–1.13], p=0.014) were independent predictors of mortality **(table 4)**.

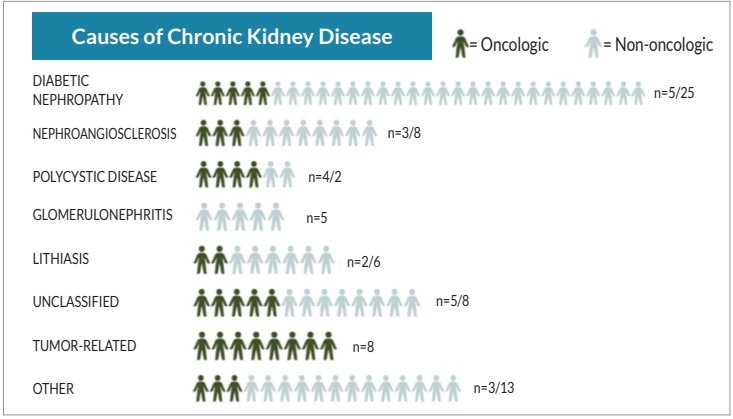
DISCUSSION

Our data show that oncologic disease is very common among individuals requiring HD. In our cohort, cancer prevalence reached 31% and incidence 17%. These data, although consistent with high cancer rates in HD patients, align with pu-

Table 1. Comparison of sociodemographic and clinical variables of the full sample according to diagnosis of neoplastic disease or no disease.

	Oncologic (n=30)	Non-oncologic (n=67)	Total (n=97)	P-value
Age (years)*	73±11	74±14	73±13	0.655^
Time on HD (months)*	38±28	41±32	39±31	0.755^
Charlson Index (points)*	9,9±2,6	8,3±2,4	8,8±2,5	0.006^
Sex				
- Male	83% (n=25)	63% (n=42)	69% (n=67)	
- Female	17% (n=5)	37% (n=25)	31% (n=30)	0.042^^
Pharmacological Treatment				
- Proton pump inhibitors	73% (n=22)	70% (n=47)	71% (n=69)	0.749^^
- ACE inhibitors	10% (n=3)	16% (n=11)	14% (n=14)	0.406^^
Comorbidity				
Diabetes %	50% (n=15)	55% (n=37)	54% (n=52)	0.633^^
Dyslipidemia %	73% (n=22)	66% (n= 44)	68% (n=66)	0.455^^
Arterial hypertension %	93% (n=28)	91% (n=61)	92% (n=89)	0.705^^
Cardiovascular disease %	77% (n=23)	72% (n=48)	73% (n=71)	0.984^^
Obesity %	3% (n=1)	8% (n=5)	6 % (n=6)	0.556^^
Overweight %	27% (n=8)	33% (n=22)	31% (n=30)	
Tobacco use %	50% (n=15)	30% (n=20)	36% (n=35)	0.056^^
Previous transplant %	7% (n=2)	18% (n=12)	14% (n=14)	0.145^^

*Mean ± standard deviation; **^** Student's t-test; **^^** Chi-square test; **n:** sample size.



CKD: chronic kidney disease; **n:** sample size.

Figure 1. Etiology of CKD among individuals with neoplastic disease and without neoplastic disease.

blished series such as the KDIGO Controversies Conference on Onconephrology (2018), which reported a neoplasm incidence of 12–25%[8], or data from the HD Unit at Hospital Universitario Infanta Sofía in Madrid, which reported a 20% incidence including peritoneal dialysis patients[13]. However, within the spectrum of advanced CKD requiring RRT, the subgroup with the highest oncologic burden is kidney transplant recipients. Although our study excluded kidney graft recipients, a recent systematic review[11] reported an incidence reaching 10–27%.

Regarding the type of neoplasm diagnosed, several studies describe solid tumors as more frequent than hematologic malignancies, with genitourinary cancers being the most prevalent[8,9,11,15,18,19]. In our study, 67% were solid tumors (40% genitourinary), compared to 20% hematologic disease. In a case series from the National Cancer Institute of Colombia (2008)[18], 61% of patients presented genitourinary neoplasms; the KDIGO Controversies Conference (2018) also supports this finding[8]. In a systematic review of KT recipients[11], most reports (11 of 14) found genitourinary tumors to be the most common, although in three studies cutaneous tumors predominated due to the increased risk of skin lesions from immunosuppressive treatment; hematologic diseases were the second most frequent. Furthermore, the *CORE Curriculum in Nephrology: Onconephrology* (2023)[9] also highlights a high prevalence of solid tumors, hematologic malignancies, and skin cancers, with higher rates in KT recipients.

Regarding variables analyzed, several studies[8,11] report that these patients tend to be older and predominantly male, except for the Colombian study[18] in which female patients predominated. Additionally, risk factors such as DM, HTN, CVD, obesity, KT, certain medications like PPIs[19], and smoking are considered associated factors[8,12]. Our findings support that comorbidity (Charlson Index) and age were associated with the presence of neoplasia. Some authors also propose ACEIs

Table 2. General characteristics of patients with neoplastic disease.

Patient	Age (years)	Sex	Tumor Type	Neoplasm Status	CKD Etiology	Treatment Received	Number of Tumors
1 E	74	M	Lymphoma	Active	Nephrotoxicity	Chemotherapy	1
2 E	85	M	Epidermoid	Active	Non-affiliated	Surgical	1
3 E	63	M	Bladder cancer	Active	Non-affiliated	Medical–Surgical	3
4 E	68	M	Colon cancer	Active	Polycystosis	Surgical	2
5 E	73	M	MDS	Controlled	Non-affiliated	Conservative	1
6 E	78	M	MDS	Active	Chronic lithiasis	Chemotherapy	1
7 E	72	M	Gastric cancer	Active	Diabetic nephropathy	Surgical	1
8 E	87	M	Bladder cancer	Controlled	Chronic lithiasis	Surgical	1
9 E	75	M	Bladder cancer	Controlled	Nephroangiosclerosis	Medical–Surgical	1
10 E	86	M	Digestive metastases	Active	Polycystosis	Conservative	1
11 E	77	M	Prostate cancer	Controlled	Nephrotoxicity	Medical–Surgical	1
12 E	82	M	Prostate cancer	Active	Tumoral	Medical–Surgical	3
13 E	80	M	Bladder cancer	Controlled	Diabetic nephropathy	Surgical	1
14 E	61	M	Bladder cancer	Active	Polycystosis	Medical–Surgical	1
15	71	M	Epidermoid	Active	Diabetic nephropathy	Chemotherapy	2
16 E	53	M	Rectal cancer	Controlled	Non-affiliated	Medical–Surgical	1
17	91	M	Kidney cancer	Controlled	Nephrectomy	Surgical	1
18 E	85	M	Prostate cancer	Active	Diabetic nephropathy	Conservative	1
19	70	M	Kidney cancer	Active	Nephrectomy	Medical–Surgical	2
20	83	M	Colon cancer	Controlled	Nephroangiosclerosis	Chemotherapy	1
21	76	M	Colon cancer	Active	Diabetic nephropathy	Medical–Surgical	2
22	76	M	Colon cancer	Active	Diabetic nephropathy	Chemotherapy	1
23	69	M	Colon cancer	Controlled	Infectious	Chemotherapy	1
24	67	M	Lymphoma	Active	Tumoral	Chemotherapy	1
25	81	F	Multiple myeloma	Active	Tumoral	Chemotherapy	1
26	75	M	Epidermoid	Controlled	Tumoral	Radiotherapy	2
27	71	M	Bladder cancer	Active	Tumoral	Medical–Surgical	1
28	61	M	Lymphoma	Controlled	Polycystosis	Medical–Surgical	1
29	76	F	Ovarian cancer	Controlled	Tumoral	Chemotherapy	2
30	61	M	Epithelioma	Controlled	Non-affiliated	Chemotherapy	1

M: Male; **F:** Female; **MDS:** Myelodysplastic syndrome; **CKD:** Chronic kidney disease.

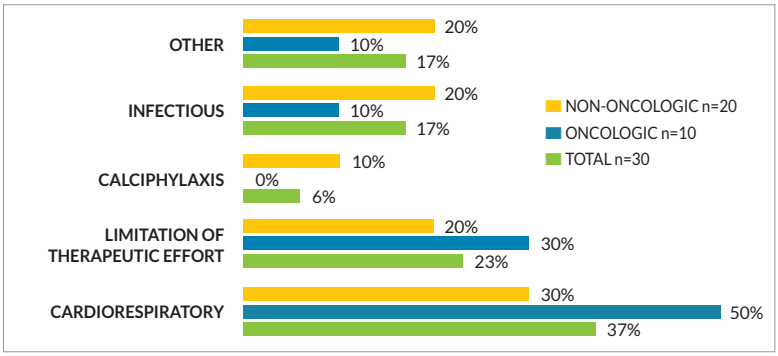


Figura 2. Causes of mortality in the entire sample.

as protective agents and recommend their use[8]; in our results, ACEI use was not significant among patients with neoplastic disease. However, when analyzing mortality-associated factors in the entire cohort, ACEI use did reach statistical significance. Regarding CKD etiology, tumor-related etiology (27%) was associated with higher rates of onco-nephrologic disease, consistent with other authors[11,15].

Cancer-related mortality was high (40%) in patients with neoplastic disease. Causes

Table 3. Comparison of sociodemographic and clinical variables between deceased and surviving patients.

n= 97	Deceased (n= 32)	Surviving (n=65)	p-value
Age (years)*	78.30±7.61	70.37±14.24	0.004^
Time on HD (months)*	41.70±31.60	39.23±30.61	0.946^
Charlson Comorbidity Index (points)*	9.91±2.17	8.28±2.56	0.004^
Sex			
Male (n=67)	84% (n=27)	62% (n=40)	0.022^^
Female (n=30)	16% (n=5)	38% (n=25)	
Pharmacologic Treatment			
PPIs (n=69)	(n=23)	(n=46)	0.910^^
ACE inhibitors (n=14)	(n=8)	(n=6)	0.038^^
Comorbidities			
Diabetes (n=52)	(n=17)	(n=35)	0.947^^
Dyslipidemia (n=66)	(n=22)	(n=44)	0.916^^
Arterial hypertension (n=89)	(n=29)	(n=60)	0.777^^
Cardiovascular disease (n=71)	(n=30)	(n=41)	0.001^^
Overweight (n=30)	(n=13)	(n=17)	0.285^^
Tobacco use (n=35)	(n=11)	(n=24)	0.806^^
Previous transplant (n=14)	(n=4)	(n=10)	0.704^^
Oncologic disease (n=30)	40% (n=12)	60% (n=18)	0.326^^

* Mean ± standard deviation; **^** Student's t-test; **^^** Chi-square test; **PPIs:** proton pump inhibitors; **ACE inhibitors:** angiotensin-converting enzyme inhibitors; **n:** sample size.

Tabla 4. Adjusted multivariable model for mortality.

Variable	Odds Ratio	95%CI (Lower/Upper)	p-value
Sex	2.551	0.741/8.788	0.138
Age	1.073	1.014/1.135	0.014
Charlson Index	1.232	0.961/1.579	0.100
CVD	6.973	1.378/35.392	0.019
Diabetes Mellitus	0.647	0.217/1.925	0.433
Enfermedad neoplásica	1.400	0.447/4.382	0.563

CVD: Cardiovascular disease; **DM:** Diabetes mellitus; **CI:** Confidence interval.

of death were analyzed, with cardiorespiratory causes being the most common (50%). Notably, 67% of patients had active neoplastic disease at the time of death. Few studies report cancer-related mortality causes, although published series highlight worse survival, especially among KT recipients[11,15,18]. This underexplored area opens opportunities for future research.

In recent years, the introduction of immunomodulatory therapies for cancer treatment (e.g., mTOR and checkpoint inhibitors) has greatly improved survival, although these treatments are not without toxic effects[15,19]. In our study, specific chemotherapy–immunotherapy regimens and their toxic effects were not collected, representing a limitation. Regarding iodinated contrast and excessive radiation exposure, our hospital does have protocols to prevent and protect RF.

Study limitations include those inherent to retrospective design. Second, being a single-center study and including only one RRT modality introduces potential selection bias and limits external validity.

It is essential to address the role of nursing in the care of individuals receiving HD for RRT, encompassing dimensions that significantly impact quality of care and patient well-being. Effective communication and understanding of individual needs are key elements for delivering person-centered, holistic care. Nursing professionals caring for HD patients with neoplastic disease must provide highly specialized and complex care, as both diseases are extremely invasive. Nurses play an important role both in prevention and in the care of these neoplastic conditions, requiring profession-specific care skills in addition to optimal mastery of treatment techniques and monitoring[20].

Based on our findings and the considerations discussed, we believe that the presence of an Advanced Practice Nurse (APN) in Onconephrology is essential to address the special needs of these patients: providing education on self-care and care strategies, monitoring the progression of both diseases, and offering high-quality, holistic nursing care while proactively accompanying patients throughout their disease process. In a recent article by Crespo-Montero R[21]. regarding APN competencies, the Andalusian Care Strategy highlights APN roles in complex oncologic conditions and CKD care, referencing several hospitals that have implemented APN positions in nephrology nursing, including *Hospital de la Princesa*[22], which is directly relevant to our study.

We conclude that our study shows that individuals requiring HD experience a high incidence and prevalence of oncologic disease, with a very poor prognosis. Although our findings should be confirmed in prospective studies, we believe that multidisciplinary onconephrologic evaluation is essential for proper management of these patients, where the APN role could be a key component of the care team.

Conflicts of interest

None declared.

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