

NEOPLASIA IN HEMODIALYSIS PATIENTS AND ITS EFFECT ON ANEMIA TREATMENT, VASCULAR ACCESS AND KIDNEY TRANSPLANT ELIGIBILITY

Jean J. Filipov^{1✉}, Krassimira Ashikova², Nickolay Todorov³,
Emil P. Dimitrov¹

Received on May 28, 2026

Presented by D. Damianov, Member of BAS, on September 29, 2026

Abstract

Chronic kidney disease and neoplasia are a growing problem worldwide. The aim of our study was to assess anemia treatment, type of vascular access (VA) and access to kidney transplantation (KT) in dialysis patients. We included all patients, who performed hemodialysis (HD) in two dialysis centres between 01.01.2022 and 31.12.2022. The patients were divided into two groups according to history of neoplasia (Neo). We compared patient demographics, hemoglobin levels, anemia treatment, type of VA and the number of patients on the waiting list (WL) for KT. At a second stage of the study, active malignancies were excluded. Statistical analysis included Mann–Whitney U test, Pearson's χ^2 test and Fisher exact test. Our study encompassed 139 patients (24 with Neo, in 13 cases it was the cause of CKD). Oncologic patients had higher age ($p = 0.048$) and similar sex ratio ($p > 0.05$); had similar hemoglobin levels ($p > 0.05$), but higher doses of erythropoiesis stimulating agents (ESAs) were needed ($p = 0.028$); had lower rate of arteriovenous fistulas (AVFs) ($p = 0.022$), none of them was on the WL for KT. Neo in remission had similar demographics, hemoglobin levels, need for ESAs to the control group ($p > 0.05$), though lower rate of AVFs was detected ($p = 0.017$). Malignancy was significant contributor to CKD. Neo patients on HD tended to be older, achieved similar levels of hemoglobin, based on higher ESAs need. Malignancy possibly has influenced the choice of VA and may have limited the chances for KT.

Key words: hemodialysis, neoplasia, anemia treatment, vascular access, kidney transplantation

Introduction. Chronic kidney disease (CKD) is a growing problem worldwide [1]. The global CKD pandemic is coupled with rising burden of neoplasia (Neo) [2]. Thus, an increasing number of patients are affected by CKD and Neo, complicating both health issues. Neo causes CKD and acute kidney injury (AKI) by affecting all kidney structures. Antineoplastic treatment – chemotherapy, radiotherapy, molecular targeted therapy, and surgery (nephrectomy) can have detrimental effect on kidney function too.

Additionally, CKD increases the risk of Neo. CKD patients have higher prevalence of cancer, due to chronic inflammation, impaired DNA repair and elevated parathyroid hormone levels [3]. CKD is associated with poorer response to anti-cancer therapy too [4].

Several aspects of CKD treatment are challenging in patients with CKD and Neo (CKD/Neo): treatment with erythropoiesis stimulating agents (ESAs), access to kidney transplantation (KT), and vascular access (VA) in hemodialysis.

Current KDIGO guidelines recommend cautious use of ESAs in active cancer or history of malignancy [5]. However, higher ESAs doses in multiple myeloma (MM) and CKD may be needed. Blood transfusions are avoided due to the risk of blood-borne infections and HLA sensitization. Thus, ESA treatment in CKD/Neo patients remains controversial.

VA in CKD and Neo is a challenging issue too. Chemotherapy and active neoplasia itself cause peripheral vascular damage. Therefore, arteriovenous fistula (AVF) creation may be challenging, as higher AVF failure in dialysis patients with malignancy, compared to dialysis patients without Neo was reported [6]. Cancer risk after KT is increased due to the use of immunosuppressive agents. In CKD patients, successfully treated for Neo, waiting time of two to five years is generally suggested [7]. The aim of our study was to evaluate ESAs use, choice of VA and enrollment on the waiting list (WL) for KT in patients on hemodialysis with underlying Neo.

Materials and methods. Patient selection. Our study encompassed all patients, who performed high-flux hemodialysis (HD) in two dialysis centres – University Hospital “Alexandrovska” and University Hospital “St. Anna” between 01/01/2022 and 31/12/2022. Patients with AKI, HD for less than 12 weeks, peritoneal dialysis, and those with transferrin saturation (TSAT) < 20% were excluded. Patients were divided into two groups according to their medical history for malignancy: patients with and without Neo. All malignancies were diagnosed prior to initiating HD. The following parameters were compared: patient demographics (age, gender), hemoglobin (Hb) level over the period in question, ESA dose (epoetin zeta) per month, intact PTH (iPTH) and blood transfusions. The type of VA was evaluated – use of tunneled central venous catheter (tCVC), arteriovenous graft (AVG), and arteriovenous fistula (AVF). In the two institutions AVFs are the preferred VA; AVGs were applied only in cases when AVFs could not be created as per current guidelines [8]. We assessed the composite share of AVF and AVG, then AVF prevalence separately in the two cohorts. Finally, the number

of patients on the WL for KT was assessed in both groups. At the second stage the cases with active Neo were excluded, and we compared the same indicators in patients without Neo vs. cases with Neo in remission. Active Neo was defined as malignancy which required active oncologic treatment or metastatic disease.

The study complied with the ethical guidelines of the institutions involved and was in accordance with the Helsinki Declaration of 2013. All participants gave their informed oral consent prior to inclusion in the study. As the study was retrospective in nature and standard laboratory tests and standard treatment were assessed, no other institutional approval was required.

Laboratory testing. Hb and TSAT were assessed every six weeks; biochemical parameters [serum urea and creatinine (pre- and post-HD), intact PTH levels] were tested every 3 months. Blood sampling was performed during the regular HD sessions as part of the regular follow-up.

Subjects on the WL for KT were identified by using their regular tests for HLA sensitization, performed according to the local screening policy for transplant candidates.

In order to address the relatively small number of patients, especially in the Neo arm, our statistical analysis included descriptive statistics, Mann-Whitney U test, Pearson's Chi squared test, and Fisher exact test. Continuous variables (age, Hb, ESA dose and iPTH) were presented as median and interquartile range (IQR). The level of significance adopted was $p < 0.05$. SPSS 22.0 Software (SPSS Inc., Chicago, IL, USA) was used.

Results. One hundred and thirty-nine patients met our selection criteria; 24 of them (17.27%) were identified with Neo. The most common types of malignancy were cancer of ureter/urinary bladder ($n = 5$) and colorectal cancer ($n = 5$). Table 1 demonstrates the major locations of Neo in our patients. In 13 (9.35%) cases Neo was the primary cause for CKD; nephrectomy/secondary obstruction and MM-associated nephropathy were the most common mechanisms for CKD (Table 2).

The patients were divided into two groups according to the presence of Neo (Table 3). Both groups had similar male:female ratio. The patients with malignancy were older than the control group ($p = 0.048$). Oncologic patients had lower Hb, but the difference did not reach statistical significance ($p = 0.131$). However, significantly higher monthly ESA doses were required ($p = 0.028$); Neo patients did not need more blood transfusions, compared to the controls; the two cohorts had similar iPTH levels (Table 3). The composite AVF/AVG use was significantly lower in the Neo cohort ($p = 0.042$).

Similarly, the use of AVF only was lower in the cancer arm ($p = 0.022$). Finally, the number of patients on the WL for KT was assessed. No patients with Neo were on the WL, compared to ten cases from the control arm. Although the difference was not statistically significant ($p = 0.210$), our results demonstrated a trend for poorer chance of the Neo patients for KT (Table 3).

T a b l e 1

Types of malignancy, identified in the study population, $n = 24$

Type of malignancy	Number of patients
Cancer of ureter/urinary bladder	5
Colorectal cancer	5
Renal cancer	3
Multiple myeloma	3
Lung cancer	2
Prostate cancer	1
Cancer of larynx	1
Breast cancer	1
Gastric cancer	1
Endometrial cancer	1
Cervical cancer	1

T a b l e 2

Malignancy as primary cause for chronic kidney disease (CKD)
in the study population, $n = 13$

Type of malignancy	Mechanism of CKD development	n
Cancer of ureter/urinary bladder	Secondary obstruction	4
Multiple myeloma	Multiple mechanisms	3
Renal cancer	Nephrectomy	3
Prostate cancer	Secondary obstruction	1
Lung cancer	Chemotherapy, direct toxicity	1
Cervical cancer	Radiation nephropathy	1

At the second stage of the study the patients with active malignancy were excluded (Table 4). Seventeen patients with Neo in remission were shortlisted. The comparison to the control group did not demonstrate significant difference between the two cohorts in terms of demographical and laboratory characteristics, anemia treatment, as well as number of patients on the WL for KT. The use of AVF or AVG was again lower in Neo in remission, without reaching statistical significance. The separate AVF share again was significantly lower in the neoplasia arm ($p = 0.017$) (Table 4).

Discussion. The overall prevalence of Neo in our study was 17.27%. Of these, most commonly detected were urinary tract and colorectal cancers (Table 1). A major cause for CKD were renal and ureter/urinary bladder cancers (Table 2). These findings were in accordance with a recent paper, in which renal and urinary tract cancer were associated with higher risk of CKD [9]. Nephrectomy and secondary obstruction were the most common mechanisms for kidney injury in our study. Earlier diagnosis of these cancer types could potentially reduce the risk of CKD by preventing these complications. MM was the second most

T a b l e 3

Demographic, clinical and laboratory characteristics of the study population, all patients with malignancy vs. control cohort, $n = 139$

Parameter	Patients, all malignancies, $n = 24$	Patients, no malignancy, $n = 115$	p value
Male:Female ratio	19:5	80:35	0.460
Age*	69 (64–72.75)	64 (53–72)	0.048
Hb level (g/l)*	100 (80.25–109)	104 (93–110)	0.131
Epoetin dose (IU/month)*	40 000 (15 000–48 000)	28 000 (7000–36 000)	0.028
Patients, requiring blood transfusion	3	7	0.377
iPTH (pmol/L)*	20.10 (7.35–47.40)	25.65 (9.45–50.88)	0.573
Vascular access: AVF or AVG	5	50	0.042
Vascular access: AVF	4	48	0.022
Patients on the waiting list for KT	0	10	0.210

Hb – hemoglobin, IU – international units, AVF – arteriovenous fistula, AVG – arteriovenous graft, KT – kidney transplantation * median (interquartile range)

T a b l e 4

Demographic, clinical and laboratory characteristics of the study population, patients with malignancy in remission vs. control cohort, $n = 132$

Parameter	Patients, malignancy in remission, $n = 17$	Patients, no malignancy, $n = 115$	p value
Male:Female ratio	14:3	80:35	0.393
Age*	69 (63.5–72.5)	64 (53–72)	0.109
Hb level (g/l)*	103 (79.5–111.0)	104 (93–110)	0.637
Epoetin dose (IU/month)*	32 000 (6000–48 000)	28 000 (7000–36 000)	0.291
Patients, requiring blood transfusions	1	7	1.000
iPTH (pmol/L)*	16.40 (4.00–44.10)	25.65 (9.45–50.88)	0.298
Vascular access AVF or AVG	3	50	0.062
Vascular access: AVF	2	48	0.017
Patients on the waiting list for KT	0	10	0.359

Hb – hemoglobin, IU – international units, AVF – arteriovenous fistula, AVG – arteriovenous graft, KT – kidney transplantation, * median (interquartile range)

common cause for CKD, via multiple pathways of kidney injury. The least commonly detected mechanisms for kidney injury were chemotherapy toxicity (direct damage to all structures of the nephron, or indirectly, e.g. by causing tumour lysis syndrome) and radiotherapy nephropathy (apoptosis and necrosis in endothelial, tubular and glomerular cells).

Age is a well recognized risk factor for malignancy and CKD [1]. Our findings demonstrated significantly higher age in the Neo arm (Table 3). After excluding

active malignancies higher age was detected in the Neo cohort too, though the difference was not statistically significant (Table 4). Neo is generally more prevalent in males, except for some locations (breast and thyroid cancer). However, despite the higher overall CKD prevalence in females, CKD stage 5 is more frequently observed in males [10]. This can explain the insignificant difference in male: female ratio ($p > 0.05$, Tables 3 and 4).

There are multiple pathways for anemia in Neo – epoetin and iron metabolism disturbances, bone marrow suppression, malnutrition, shorter red blood cell life span. The Hb levels in the two cohorts were not statistically different; however, significantly higher ESAs doses were needed in the Neo arm. No difference in the number of blood transfusions was detected (Table 3), probably due to the higher dose of ESAs therapy. It should be noted, that iPTH was not significantly different across the two groups, indicating that secondary hyperparathyroidism did not influence significantly Hb or anemia treatment in our cohort of patients. However, our study may be underpowered to fully evaluate the effect of iPTH on anemia therapy. Neo in remission had similar profile to the control group in terms of Hb levels, iPTH values, epoetin zeta or number of patients, requiring blood transfusions (Table 4).

Anemia treatment in CKD and Neo remains still under debate. ESAs were found to increase the risk of death of cancer in CKD patients stages 3–4 and malignancy [11]. On the basis of this study, the current recommendations regarding the use of erythropoietic agents in chronic kidney disease and active malignant diseases can be discussed, particularly where a cure is expected [5].

However, in most of our patients with active Neo cure was not anticipated. Unlike PFEFFER et al. [11], our study encompassed patients on HD, in which renal failure influences anemia more than those not on dialysis. Another aspect that differentiates our study is the use of short-acting ESA (epoetin zeta). A recent study demonstrated higher all-cause mortality in dialysis patients, treated with long-acting ESAs, compared to short-acting agents [12].

Cancer and its treatment are linked to significant cardiac and peripheral vascular abnormalities. Peripheral vessel involvement may present with venous thromboembolism, pulmonary hypertension, or Raynaud's phenomenon. Together with repeated venipuncture it can limit the effectiveness of AVF and AVG creation in HD [8]. Our results demonstrated significantly lower composite AVF/AVG use as well as for AVF alone in the overall Neo cohort ($p < 0.05$), resulting in higher use of tCVC. Neo patients in remission had lower share of AVF/AVG, compared to the control group, though the difference did not reach statistical significance (Table 4). The AVF rate was significantly lower in Neo in remission, suggesting significant changes in vascular anatomy that may influence vascular vessel formation years after successful Neo treatment. Thus, the higher tCVC need further worsens the prognosis in Neo and HD due to tCVC-associated complications [8]. Additionally, tCVC can also be used in palliative cases, like most of our active Neos, when

shorter dialysis treatment is expected [8]. However, choice of VA depends on additional factors, e.g. patient age, personal vascular anatomy, which may also influence our results and partially explain the higher overall tCVC rate in our study.

Finally, malignancy prior to KT is a serious challenge to nephrologists and oncologists. It has been estimated, that the risk of Neo recurrence in the post-transplant period reaches 10% [13]. As already mentioned, waiting time between two and five years prior to KT has been recommended [7]. None of our Neo patients was on the WL for KT. Though no statistically significant difference was observed (Tables 3 and 4), the finding demonstrated an expected trend for poorer chances of Neo patients for transplantation.

Our study has several limitations: its retrospective design and the relatively small Neo arm. Additionally, other possible factors were not assessed: malnutrition, advanced age, co-morbidities (e.g., diabetes mellitus). This underlines the need for larger prospective trials in this sphere.

In summary, a significant percentage of the dialysis patients had history of Neo; it was the primary cause for CKD in more than 9% of the cases. Malignancy demonstrated possible influence on the treatment of anemia on hemodialysis, on the choice of vascular access and patient's chances for KT, thereby likely contributing to a poorer prognosis.

Acknowledgements. We would like to thank Mrs Kremena Mihaylova-Filipova for providing the statistical calculations.

REFERENCES

- [1] KOVESDY C. P. (2022) Epidemiology of chronic kidney disease: an update 2022, *Kidney Int. Suppl.* (2011), **12**(1), 7–11.
- [2] SUNG H., J. FERLAY, R. L. SIEGEL et al. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA Cancer J. Clin.*, **71**(3), 209–249.
- [3] LEES J. S., B. M. P. ELYAN, S. M. HERRMANN et al. (2023) The “other” big complication: how chronic kidney disease impacts on cancer risks and outcomes, *Nephrol. Dial. Transplant.*, **38**(5), 1071–1079.
- [4] WEI Y. F., J. Y. CHEN, H. S. LEE et al. (2018) Association of chronic kidney disease with mortality risk in patients with lung cancer: a nationwide Taiwan population-based cohort study, *BMJ Open*, **8**(1), e019661.
- [5] Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group (2026) KDIGO 2026 Clinical Practice Guideline for the Management of Anemia in Chronic Kidney Disease (CKD), *Kidney Int.*, **109**(1S), S1–S99.
- [6] JEONG S., H. KWON, J. W. CHANG et al. (2020) Outcomes of arteriovenous access among cancer patients requiring chronic haemodialysis, *BMC Nephrol.*, **21**(1), 297.
- [7] CHADBAN S. J., C. AHN, D. A. AXELROD et al. (2020) KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation, *Transplantation*, **104**(4S1 Suppl 1), S11–S103.

- [8] LOK C. E., T. S. HUBER, T. LEE et al. (2020) KDOQI clinical practice guideline for vascular access: 2019 update, *Am. J. Kidney Dis.*, **75**(4 Suppl 2), S1-S164.
- [9] CIORCAN M., L. CHISAVU, A. MIHAESCU et al. (2022) Chronic kidney disease in cancer patients, the analysis of a large oncology database from Eastern Europe, *PLoS One*, **17**(6), e0265930.
- [10] HARRIS R. C., M. Z. ZHANG (2020) The role of gender disparities in kidney injury, *Ann. Transl. Med.*, **8**(7), 514.
- [11] PFEFFER M. A., E. A. BURDMANN, C. Y. CHEN et al. (2009) A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease, *N. Engl. J. Med.*, **361**(21), 2019–2032.
- [12] SAKAGUCHI Y., T. HAMANO, A. WADA et al. (2019) Types of erythropoietin-stimulating agents and mortality among patients undergoing hemodialysis, *J. Am. Soc. Nephrol.*, **30**(6), 1037–1048.
- [13] VIECELLI A. K., W. H. LIM, P. MACASKILL et al. (2015) Cancer-specific and all-cause mortality in kidney transplant recipients with and without previous cancer, *Transplantation*, **99**(12), 2586–2592.

¹*Department of Nephrology and Transplantation, University Hospital “Alexandrovska”,
1 Georgi Sofiiski St, 1431 Sofia, Bulgaria
e-mails: jeanphillipov@yahoo.com (<https://orcid.org/0000-0002-0951-3385>)
emilpaskalev@abv.bg*

²*Department of Nephrology, Dialysis and Transplantation, University Hospital “St. Anna”,
1 Dimitar Mollov St, 1750 Sofia, Bulgaria
e-mail: krassimiraaa@abv.bg*

³*NephroLife Dialysis Center, Transportna St, 8000 Burgas, Bulgaria
e-mail: dr.todorov@nephrolife.bg*