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Lung cancer and kidney injury: an updated review

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ABSTRACT

Lung cancer is the leading cause of cancer deaths worldwide, accounting for an estimated 1.8 million deaths. Lung cancer is also the most common primary cancer leading to soft tissue (ST) metastasis. Renal disease may occur as a direct or indirect consequence of the cancer itself (e.g., post-renal obstruction, compression, or infiltration), its treatment (e.g., radiotherapy or chemotherapy), or its related complications (e.g., opportunistic infection). Existing evidence shows that the most frequent primary solid tumor responsible for renal metastasis is pulmonary carcinoma, followed by gastric, breast, soft tissue, and thyroid carcinomas. Chronic kidney disease is a potential risk factor in the survival of patients with lung cancer. In this review, we will discuss causes of kidney injury in relation to lung cancer, potential mechanisms of kidney injury, and treatment options.

Implication for health policy/practice/research/medical education:

The most common primary solid tumor responsible for renal metastasis is pulmonary carcinoma. In this review, we showed that chronic kidney disease harmfully affects the survival of individuals with pulmonary malignancy.

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Introduction

Onco-nephrology is concerned with the complex problems associated with cancer and kidney disease (1). The development of renal disease in patients with cancer may lead to increased toxicity of chemotherapeutic agents or decreased distribution of chemotherapeutic agents (2). Kidney disease is usually predictive of a diagnosis of an underlying cancer, simultaneously or through the disease process (3). Therefore, close attention of the oncologists is vital for a quick diagnosis and treatment of renal disease in cancer patients. The incidence and severity of kidney disease differ according to the type and stage of cancer, treatment sequence, and co-morbidities (3). In patients

with active non-renal cancer, diagnostic evaluation of a malignant renal mass could be either an asynchronous primary renal tumor or metastatic disease (4). A study by Humphreys et al indicated recent developments in controlling different types of renal diseases are associated with cancer and its treatment; with specific emphasis on certain conditions such as uric acid nephropathy, drug induced thrombotic microangiopathy, bisphosphonate-induced collapsing glomerulopathy, and hematopoietic cell transplant (HCT)-associated renal failure. Although renal disease in cancer patients is complicated; it is helpful to clinically considering of acute kidney injury as pre-renal, intrinsic, and post-renal causes (5). Another

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common cause of kidney damage in cancer patients is the medications that are prescribed for their existing cancer(s) (6). In a study of Renal Insufficiency and Anticancer Medications (IRMA) among 445 lung cancer patients with renal insufficiency (7), the baseline serum was calculated using KDIGO-KDOQI (Kidney Disease Improving Global Outcome-Kidney Disease Outcome Quality Initiative) definition (7,8). Between the 445 IRMA lung cancer patients, 14.4% had serum creatinine level ≥ 1.24 mg/dL (110 μ mol/L) and 62.1% had abnormal renal function using the formula of Cockcroft–Gault and 55.9% using aMDRD (Abbreviated Modification of Diet in Renal Disease) formula (7).

Lung cancer is recognized as the second most common malignancy and the leading cause of tumor-related deaths around the globe (9). It is generally divided into two types; small cell lung cancer (SCLC; 15% of the cases) and non-small cell lung cancer (NSCLC; 85% of the cases) (10). Lung cancer is also the most common primary cancer resulting in soft tissue (ST) metastasis. Due to the difficulty of diagnosing NSCLC in its early stages of cancer, more than 30% of NSCLC patients are diagnosed with distant metastasis (11,12). Kidneys receive about 20 to 25% of the cardiac output (about 1.0 to 1.1 L/min) making those susceptible to hematogenous metastasis (13). The renal metastases from NSCLC are diagnosed at autopsy, because renal metastases are often clinically asymptomatic (14). In a study, when the aMDRD formula was used, the incidence of renal insufficiency varied between cancer types, ranging from 50.8% of breast cancer patients to 56.0% of lung cancer patients (6). Kidney metastasis can be detected by magnetic resonance imaging (MRI), ultrasonography, abdominal computerized tomography (CT) scans and positron emission tomography (PET). Kidney metastasis can be categorized as a bilateral, exophytic, small, multiple or wedge-shaped within the renal capsule (15). The most common primary solid tumor that is responsible for renal metastasis is pulmonary carcinoma, followed by thyroid, gastric, soft tissue, and breast carcinomas (16-19). Renal metastatic tumors often occur in the cortical area near the glomerular vasculature (20).

The spectrum of renal disease induced by lung cancer includes acute kidney injury (AKI), chronic kidney disease (CKD), proteinuria, nephrotic syndrome, and electrolyte disorders. In patients with lung cancer, the most common renal complication is AKI.

The manifestations include pre-renal injury due to volume depletion, intra-renal by nephrotoxic chemotherapeutic agents (such as cisplatin-based), tumor lysis syndrome, metastatic kidney infiltrations, or post-renal obstruction (21). Currently, AKI also is reported among hospitalized coronavirus disease 2019

(COVID-19) patients, a critical group to consider among cancer patients who had been infected simultaneously (22-24). CKD is common in patients with lung cancer, especially in the elderly (25). In both, patients with early-stage and advanced lung cancer, CKD affects survival and the treatment regimen (26,27). The incidence of lung cancer induced AKI among males was almost three times higher than females (14). Although the paraneoplastic nephrotic syndrome is not common, it may appear in patients with lung cancer (28). Renal paraneoplastic syndrome symptoms may range from asymptomatic proteinuria to severe nephrotic syndrome. In 1% to 3% of patients with primary lung cancer, nephrotic syndrome caused by membrane glomerulonephritis (MGN) has been reported. There are 49 cases of tumor-related MGN in the literature, including nine cases of SCLC (29). One study reported a case of SCLC without metastases discovered by a paraneoplastic nephrotic syndrome (30). The complete remission of cancer was achieved by chemotherapy and radiotherapy with the resolution of nephrotic syndrome, while tumor progression occurred at the same time with fatal renal failure (30). It was also detected in one case of isolated unilateral renal metastases which was induced by lung cancer (31). Jørgensen et al suggested that the albumin-to-creatinine ratio (ACR) can predict malignancy in certain tissues (32). ACR was assessed in 5425 patients for 10.3 years at the time of the first diagnosis of cancer. They found a significant association between ACR and lung cancer (32). A study investigated patients with newly diagnosed SCLC from 2004 to 2011 in Taiwan. This study showed that SCLC patients with significant proteinuria were associated with poor nutritional status and more severe renal insufficiency (33). In a European case-control study, results of dipstick urinalysis check were collected from 1026 patients with primary lung cancer. Proteinuria was significantly more common in patients with lung cancer as compared to the control group (30.1% versus 8.8%; $P < 0.05$). The incidence of proteinuria was significantly associated with the more progressive disease stage. Additionally, the incidence of proteinuria was significantly higher in patients with SCLC (37.5%) than NSCLC (28%) (34).

Materials and Methods

Articles related to this topic were searched in Embase, Scopus, Web of Science, PubMed and the directory of open access journals (DOAJ), using specific combination of keywords. The keywords used are; cancer, kidney injury, lung cancer, acute kidney injury, chronic kidney disease, metastasis, nephrotic syndrome, immune checkpoint inhibitors, glomerular damage, epidermal growth factor receptor, renal metastasis and pulmonary carcinoma.

Mechanism of association of renal disease with lung cancer

Various tumors can cause renal disease through different mechanisms like paraneoplastic effect, obstruction, direct infiltration, distant metastasis from the tumor and secretory diarrhea (caused by hormone secretion). A study by Wen et al suggested that tumor infiltration of the kidneys in patients with SCLC may be considered as a mechanism of AKI (35). Numerous cases of AKI arising from solid tumor infiltration, usually with widespread parenchymal replacement, have been described (36). A case report by Dobkin et al suggested that the lung metastases-induced progressive renal failure occurs mainly by parenchymal distortion and tubular damage by tumor cells. However, the renal injury may be due to sloughed parenchyma or lymphatic obstruction, vascular invasion, thrombosis, and tumor infiltration of the renal parenchyma (37,38).

Lung cancer drugs

Cisplatin, a commonly used chemotherapeutic agent for lung cancer, is found to be nephrotoxic (39). Almost 20% of patients with high-dose cisplatin therapy developed AKI (40). Pemetrexed, a folate metabolism blockade, is currently used in combination with cisplatin for metastatic NSCLC and malignant mesothelioma (41). A study reported a patient with metastatic NSCLC who developed renal failure and tubular cell apoptosis accompanied with nephrogenic diabetes insipidus and distal renal tubular acidosis after consecutive treatment with pemetrexed (42). Therefore, it is necessary to adjust the dosage of anticancer drugs, such as platinum salts, and dose according to the level of renal function and by suitable, validated methods to prevent drug accumulation and decrease associated adverse events. For this purpose, several guidelines, publications, and handbooks are available for clinicians for dosage adjustment of anticancer drugs in patients with renal failure (43). However, some important anticancer drugs, such as gemcitabine, are not nephrotoxic, therefore, it is not necessary to reduce the dosages (7).

The spectrum of cancer-associated renal diseases has changed over the past 20 years due to the use of newer chemotherapeutic regimens including immune checkpoint inhibitors (ICPIs) and epidermal growth factor receptor (5). Immune checkpoint inhibitors target the programmed death 1 (PD-1) signaling pathway and have recently been approved for use in progressive pretreated NSCLC and melanoma. Evidence suggests that immune checkpoint inhibitors are associated with increased risk of AKI, glomerular damage, and electrolyte disturbances (44). A study reported six cases of AKI in patients with lung cancer treated with ICPIs, with each case showing evidence of acute interstitial nephritis on kidney biopsy (45,46). By analyzing randomized clinical trials (RCT)

data from 3695 patients, Cortazar et al reported an overall incidence of almost 2.2% for ICPI-associated AKI (47). In 2018, a meta-analysis of 48 RCTs including 11 845 patients treated with immune checkpoint inhibitors had a 4.2-fold higher risk of AKI against controls taking non-nephrotoxic agents (48). A study examined cancer patients treated with immune checkpoint inhibitors from 2008 to 2018 who then underwent a kidney biopsy with reported nephrotoxicity associated with ICPIs incidence as low as 2% when nivolumab was used alone; in contrast to 4.5% when nivolumab and ipilimumab were used as a combination.

In other studies, immune checkpoint inhibitors were shown to cause acute tubulointerstitial nephritis, thrombotic microangiopathy, nephrotic syndrome (focal segmental glomerulosclerosis, minimal-change disease (MCD), membranous nephropathy, pauci-immune glomerulonephritis, and immunoglobulin A (IgA) nephropathy (49). Proposed mechanisms include direct lymphocytic cellular infiltration of the renal interstitium, immune complex-mediated renal injury, vasculopathy, and release of cytokines causing podocyte foot process effacement (49).

Anticancer therapeutics targeted against epidermal growth factor receptor includes gefitinib and erlotinib for lung cancer. Gefitinib was used in the treatment of pulmonary malignancies associated with MCD in a single case report (50). Another case report study showed an individual with anaplastic lymphoma kinase-positive advanced non-small cell pulmonary carcinoma who detected complex kidney cyst during crizotinib therapy. (51). Epidermal growth factor receptor can be bound by ligands that regulate renal inflammation, cell growth, and fibrosis, potentially leading to kidney damage, as summarized by Rayego-Mateos et al (52).

Chronic kidney disease (CKD) and dialysis

It is well-known that CKD has a relative prevalence in cancer patients, unrelated to the malignancy type (3). The causes of CKD in cancer consist of the effects of nephrotoxicity of some anticancer drugs and the glomerular diseases associated with the cancer (53).

While there are a few reports (54,55) regarding patients with CKD following treatment of pulmonary malignancy, chronic renal failure may harmfully impact the survival rate of patients with pulmonary malignancy. After adjusting for numerous contradictory factors, Wei et al revealed that CKD increases the risk of mortality and is a potential risk factor for lung cancer patients (56).

Yamamoto et al retrospectively analyzed data of patients who suffered surgery for NSCLC between 2007 and 2014, of the 671 patients, 55 had CKD (57). Furthermore, among patients who underwent pulmonary tumor

surgery, chronic renal failure was accompanied with poor overall survival (57). Squamous cell carcinoma was more frequently diagnosed in patients with CKD as compared to patients without it. The 5-year disease-free and 5-year overall survival rates in patients with CKD were 60.0% and 68.9%, respectively, and for patients without CKD were 69.7% and 80.0%, respectively. While CKD patients have restriction in their choice of systemic treatment, surgery remains the main support for the treatment of pulmonary tumor in this group (57). As CKD individuals tend to have a poor respiratory function, cardiothoracic surgeons should cautiously choose the type of resection to attain equilibrium between the therapeutic benefit and harm in lung cancer patients. Few studies are available on the perioperative morbidity of lung surgery in lung cancer patients on dialysis (58,59). For instance, a retrospective review of seven patients on dialysis undergoing lung surgery was performed. In these patients, there was a high occurrence of respiratory problems as well as hyperkalemia, hemodynamic instability, and a tendency for postoperative bleeding (60).

Risk of lung cancer in patients with CKD or renal cancer

Reduced kidney function may be an independent risk factor for cancer in older men and this risk increases when glomerular filtration rate falls to approximately 40 ml/min, as well as in patients on dialysis or transplant recipients (61). Therefore, CKD prevention may be a new and valuable approach for decreasing cancer risk in the general population (61).

The detection of primary lung cancer is difficult when kidney cancer spreads primarily to the lungs. Bowman and colleagues identified 151 patients undergoing systemic targeted therapy for metastatic renal cell carcinoma (RCC) from 2006 to 2013, and reported the proportion and incidence rate for developing NSCLC with previous metastatic RCC (62). The incidence rate for the progress of NSCLC in patients with metastatic RCC was 0.87 per 100 person-years (62). Lung cancer is more prevalent after kidney transplant (63). Therefore, vigilant attention should be paid to transplant candidates noting; age, smoking and medical history of cancers- especially lung cancer (64).

Treatment of renal metastasis

Renal biopsy is an essential diagnostic technique in diagnosing kidney disease in individuals with confirmed malignant disease (35). The techniques to treat metastatic kidney disease are broad, especially based on the type of metastatic renal disease. A study of two cases with paraneoplastic nephrotic syndrome induced by advanced SCLC concluded that if the primary tumor is unresectable,

irradiation can be the first choice in the treatment of nephrotic syndrome (28). Verma et al reported 4 cases of solitary kidney metastasis in individuals with pulmonary malignancy that experienced stereotactic body radiation therapy (SBRT) and concluded that SBRT for mitigation of renal metastases from NSCLC is a safe and effective treatment (65). Nephrectomy may also be a beneficial choice in the treatment of solitary kidney metastasis in individuals with NSCLC (66). In this regard, Adamy et al examined the effect of nephrectomy in patients with solitary renal metastatic tumors and suggested that surgical resection may be an appropriate approach with a positive effect on the patients' survival rate (67). In highly selected cases, patients with metastatic NSCLC, have surgical resection of extrathoracic metastasis to reduce symptoms and increase disease-free time (68). In addition, a case report by Degen et al examined whether the minimally invasive procedure of cryoablation was a possible treatment in the control of solitary kidney metastasis from pulmonary malignancy (69). While this treatment is not the standard of care, this case report revealed the ongoing and new advancements in onco-nephrology and therapy of metastatic lung cancer to the kidneys.

Conclusion

Lung cancer is recognized as the second most common cancer and the leading cause of cancer-related deaths worldwide. Lung cancer is also the most common primary cancer leading to recognized soft tissue metastasis. Kidneys receive about 25% of the cardiac output making them susceptible to hematogenous metastasis. The most common primary solid tumor responsible for renal metastasis is pulmonary carcinoma. In this review, we found that CKD harmfully affects the survival of individuals with pulmonary malignancy and the reduced kidney function may be a potential risk factor for cancer. Additionally, we found that the renal disease has arisen from lung cancer or its treatments such as immune checkpoint inhibitors. Future observational and RCT studies are warranted to comprehensively investigate the impacts of lung cancer on renal function and structure to better guide the clinicians in treating patients and saving lives.

Authors' contribution

Primary draft by AHA and MA_s. MEK, BP, RT and AT completed and extended the manuscript. MK and MA_b edited the paper. RT and AHA finalized the paper. All authors read and signed the final manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data accuracy, duplicate publication) have been ultimately obeyed by the authors.

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References

1. Yuichiro K, Matsubara T, Yanagita M. Onco-nephrology: current concepts and future perspectives. *Jpn J Clin Oncol.* 2015;45(7):617-628.
2. Arrieta O, Michel Ortega RM, Villanueva-Rodríguez G, et al. Association of nutritional status and serum albumin levels with development of toxicity in patients with advanced non-small cell lung cancer treated with paclitaxel-cisplatin chemotherapy: a prospective study. *BMC Cancer.* 2010;10:50. doi: 10.1186/1471-2407-10-50.
3. Stengel B. Chronic kidney disease and cancer: a troubling connection. *J Nephrol.* 2010;23(3):253-262.
4. Mazouz A, Amaadour L, Souaf I, Fatemi HE, Amarti A, Erraïsse MA, et al. Synchronous malignant renal mass in patient with a Lung cancer: case report and literature review. *Pan Afr Med J.* 2015;20:22. doi: 10.11604/pamj.2015.20.22.5541.
5. Humphreys BD, Soiffer RJ, Magee CC. Renal failure associated with cancer and its treatment: An update *J Am Soc Nephrol.* 2005;16(1):151-61. doi: 10.1681/ASN.2004100843.
6. Launay-Vacher V, Oudard S, Janus N, Gligorov J, Pourrat X, Rixe O, et al. Prevalence of renal insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. *Cancer.* 2007;110(6):1376-84. doi: 10.1002/cncr.22904.
7. Launay-Vacher V, Eteessami R, Janus N, Spano JP, Ray-Coquard I, Oudard S, et al. Lung cancer and renal insufficiency: prevalence and anticancer drug issues. *Lung.* 2009;187(1):69-74. doi: 10.1007/s00408-008-9123-5.
8. Ephraïm RKD, Mantey R, Atombo S, Sakyi SA, Fondjo LA, Tashie W, et al. Chronic kidney disease in type 2 diabetes mellitus patients: Comparison of KDIGO and KDOQI guidelines. *Alexandria Journal of Medicine.* 2018;54(4):445-9.
9. Cancer. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>.
10. Blandin Knight S, Crosbie PA, Balata H, Chudziak J, Hussell T, Dive C. Progress and prospects of early detection in lung cancer. *Open Biol.* 2017;7(9):170070. doi:10.1098/rsob.170070
11. Watmough PJ, Canty SJ, Higgins G, Paul AS. Soft tissue metastases from malignant tumours. *J Bone Joint Surg Br* 2005; 87: 2-3.
12. Perisano C, Spinelli MS, Graci C, Scaramuzza L, Marzetti E, Barone C, et al. Soft tissue metastases in lung cancer: A review of the literature. *Eur Rev Med Pharmacol Sci.* 2012;16(14):1908-14.
13. Kaufman DP, Basit H, Knohl SJ. *Physiology, Glomerular Filtration Rate (GFR)*. I Treasure Island (FL): StatPearls Publishing; 2020.
14. Tomita M, Ayabe T, Chosa E, Nakamura K. Isolated renal metastasis from non-small-cell lung cancer: Report of 2 cases. *Case Rep Surg.* 2015;2015:357481. doi:10.1155/2015/357481.
15. Honda H, Coffman CE, Berbaum KS, Barloon TJ, Masuda K. CT analysis of metastatic neoplasms of the kidney. Comparison with primary renal cell carcinoma. *Acta Radiol.* 1992;33(1):39-44.
16. Zhou C, Urbauer DL, Fellman BM, Tamboli P, Zhang M, Matin SF et al. Metastases to the kidney: a comprehensive analysis of 151 patients from a tertiary referral center. *BJU Int* 2016;117:775-82. doi: 10.1111/bju.13194.
17. Wagle DG, Moore RH, Murphy GP: Secondary carcinomas of the kidney. *J Urol.* 1975 ;114(1):30-32. doi: 10.1016/s0022-5347(17)66935-0.
18. Barry-Brooks M, Yoo DC, Chaump M, Noto RB. Non-small cell lung cancer with unsuspected distant metastasis to the kidney seen on PET/CT. *Med Health R I* 2012;95:144-6.
19. Agrawal V, Ye J, McCann J, Hehn B, Freeman J, Allen S, et al. Progressive renal failure in a patient with lung adenocarcinoma. *NDT Plus.* 2010;3:461-4. doi: 10.1093/ndtplus/sfq09.
20. Matson MA, Cohen EP. Acquired cystic kidney disease: occurrence, prevalence, and renal cancers. *Medicine.* 1990 Jul;69(4):217-226. doi: 10.1097/00005792-199007000-00003.
21. Lam AQ, Humphreys BD. Onco-nephrology: AKI in the cancer patient. *Clin J Am Soc Nephrol.* 2012;7(10):1692-700. doi: 10.2215/CJN.03140312.
22. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary Pathology of Early-Phase 2019 Novel Coronavirus (COVID-19) Pneumonia in Two Patients With Lung Cancer. *J Thorac Oncol.* 2020;15(5):700-704. doi:10.1016/j.jtho.2020.02.010
23. Luo J, Rizvi H, Preeshagul IR, et al. COVID-19 in patients with lung cancer. *Ann Oncol.* 2020;S0923-7534(20)39894-X. doi: 10.1016/j.annonc.2020.06.007
24. Adapa S, Chenna A, Balla M, Merugu GP, Koduri NM, Daggubati SR, et al. COVID-19 Pandemic Causing Acute Kidney Injury and Impact on Patients With Chronic Kidney Disease and Renal Transplantation. *J Clin Med Res.* 2020;12(6):352-361. doi: 10.14740/jocmr4200
25. Owonikoko TK1, Ragin CC, Belani CP, Oton AB, Gooding WE, Taioli E, Ramalingam SS. Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. *J Clin Oncol* 2007;25:5570-7. doi: 10.1200/JCO.2007.12.5435.
26. Islam KM, Jiang X, Anggondowati T, Lin G, Ganti AK. Comorbidity and survival in lung cancer patients. *Cancer Epidemiol Biomarkers Prev.* 2015;24(7):1079-85. doi: 10.1158/1055-9965.EPI-15-0036.
27. Leduc C, Antoni D, Charloux A, Falcoz PE, Quoix E. Comorbidities in the management of patients with

- lung cancer. *Eur Respir J*. 2017;49(3):1601721. doi: 10.1183/13993003.01721-2016.
28. Shikata Y, Hayashi Y, Yamazaki H, Shikata K, Makino H. Effectiveness of radiation therapy in nephrotic syndrome associated with advanced lung cancer. *Nephron*. 1999;83(2):160-4.
 29. Grivaux M, Renault D, Gallois JC, Barbanel C, Blanchon F. Small cell lung cancer revealed by extramembranous glomerulonephritis. *Rev Mal Respir*. 2001;18(2):197-9.
 30. Yangui I, Msaad S, Smaoui M, Makni S, Kammoun K, Khébir A, et al. Small-cell lung cancer and rapidly fatal nephritic syndrome. *Rev Pneumol Clin*. 2007;63(5 Pt 1):331-4. doi: 10.1016/s0761-8417(07)74212-8.
 31. Cai J, Liang G, Cai Z, Yang T, Li S, Yang J. Isolated renal metastasis from squamous cell lung cancer. *Multidiscip Respir Med*. 2013;8:2. doi: 10.1186/2049-6958-8-2.
 32. Jørgensen L, Heuch I, Jenssen T, Jacobsen BK. Association of albuminuria and cancer incidence. *J Am Soc Nephrol*. 2008;19(5):992-8. doi: 10.1681/ASN.2007060712.
 33. Hsu SN, Hsu YJ, Lin C, Su SL, Lin SH. Proteinuria: Associated with poor outcome in patients with small cell lung cancer. *J Cancer Res Ther*. 2018;14(Suppl):S688-93. doi: 10.4103/0973-1482.191037.
 34. Pedersen LM, Milman N. Prevalence and prognostic significance of proteinuria in patients with lung cancer. *Acta Oncol*. 1996;35(6):691-5. doi: 10.3109/02841869609084000.
 35. Wen YK, Chen ML. Acute renal failure secondary to small cell lung cancer with tumor infiltration of the kidneys. *Ren Fail* 2006; 28: 261-264. doi: 10.1080/08860220600580423.
 36. Manning EC, Belenko MI, Frauenhoffer EE, Ahsan N. Acute renal failure secondary to solid tumor renal metastases. Case report and review of the literature. *Am J Kidney Dis*. 1996;27(2):284-91. doi: 10.1016/s0272-6386(96)90555-7.
 37. Dobkin SF, Brem AS, Caldamone AA. Primary renal lymphoma. *J Urol*. 1991;146:1588-1590.
 38. Arranz Arijia JA, Carrion JR, Garcia FR, Tejedor A, Perez-Manga G, Tardio J, Menarguez FJ. Primary renal lymphoma: report of 3 cases and review of the literature. *Am J Nephrol*. 1994;14:148-153. doi: 10.1159/000168705.
 39. Pignon JP, Tribodet H, Scagliotti GV, et al. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. *J Clin Oncol*. 2008;26(21):3552-3559. doi: 10.1200/JCO.2007.13.9030.
 40. Assayag M, Rouvier P, Gauthier M, Costel G, Cluzel P, Mercadal L, et al. Renal failure during chemotherapy: renal biopsy for assessing subacute nephrotoxicity of pemetrexed. *BMC Cancer*. 2017;17(1):770. doi: 10.1186/s12885-017-3705-7.
 41. Scagliotti GV, Parikh P, von Pawel J, Biesma B, Vansteenkiste J, Manegold C, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol*. 2008;26(21):3543-51. doi: 10.1200/JCO.2007.15.0375.
 42. Vootukuru V, Liew YP, Nally JV Jr. Pemetrexed-induced acute renal failure, nephrogenic diabetes insipidus, and renal tubular acidosis in a patient with non-small cell lung cancer. *Med Oncol*. 2006;23(3):419-22. doi: 10.1385/MO:23:3:419.
 43. Launay-Vacher V, Janus N, Deray G. Renal insufficiency and cancer treatments. *ESMO Open*. 2016;1(4):e000091. doi: 10.1136/esmoopen-2016-000091.
 44. Manohar S, Kompotiatis P, Thongprayoon C, Cheungpasitporn W, Herrmann J, Herrmann SM. Programmed cell death protein 1 inhibitor treatment is associated with acute kidney injury and hypocalcemia: meta-analysis. *Nephrol Dial Transplant*. 2019;34(1):108-117. doi: 10.1093/ndt/gfy105.
 45. Shirali AC, Perazella MA, Gettinger S. Association of acute interstitial nephritis with programmed cell death 1 inhibitor therapy in lung cancer patients. *Am J Kidney Dis*. 2016;68(2):287-91. doi: 10.1053/j.ajkd.2016.02.057.
 46. Wanchoo R, Karam S, Uppal NN, Barta VS, Deray G, Devoe C, Launay-Vacher V, Jhaveri KD. Adverse renal effects of immune checkpoint inhibitors: A narrative review. *Am J Nephrol*. 2017;45(2):160-9. doi: 10.1159/000455014.
 47. Cortazar FB, Marrone KA, Troxell ML, Ralto KM, Hoenig MP, Brahmer JR et al. Clinicopathological features of acute kidney injury associated with immune checkpoint inhibitors. *Kidney Int*. 2016;90(3):638-47. doi: 10.1016/j.kint.2016.04.008.
 48. Manohar S, Kompotiatis P, Thongprayoon C, Cheungpasitporn W, Herrmann J, Herrmann SM. Programmed cell death protein 1 inhibitor treatment is associated with acute kidney injury and hypocalcemia: meta-analysis. *Nephrol Dial Transplant*. 2019;34(1):108-17. doi: 10.1093/ndt/gfy105.
 49. Mamlouk O, Selamet U, Machado S, Abdelrahim M, Glass WF, Tchakarov A, et al. Nephrotoxicity of immune checkpoint inhibitors beyond tubulointerstitial nephritis: single-center experience. *J Immunother Cancer*. 2019;7(1):2. doi: 10.1186/s40425-018-0478-8.
 50. Kumasaka R, Nakamura N, Shirato K, Osawa H, Takanashi S, Hasegawa Y, et al. Side effects of the therapy: case 1. Nephrotic syndrome associated with gefitinib therapy. *J Clin Oncol* 2004;22:2504-5.
 51. Chan WY, Ang MK, Tan DS, Koh WL, Kwek JW. Imaging features of renal complications after crizotinib treatment for non-small-cell lung cancer: a case report. *Radiol Case Rep*. 2016;11(3):245-7. doi: 10.1016/j.radcr.2016.04.010.
 52. Rayego-Mateos S, Rodrigues-Diez R, Morgado-Pascual JL, Valentijn F, Valdivielso JM, Goldschmeding R, Ruiz-Ortega M. Role of epidermal growth factor receptor (EGFR) and its ligands in kidney inflammation and damage. *Mediators Inflamm*. 2018;2018:8739473. doi:10.1155/2018/8739473.
 53. Selamet U, Abudayyeh A. Chronic kidney disease as a complication of cancer. *Journal of Onco-Nephrology* 2017, 1:74-80. doi: 10.5301/jo-n.5000010.
 54. Lu MS, Chen MF, Lin CC, Tseng YH, Huang YK, Liu HP, Tsai YH. Is chronic kidney disease an adverse factor in lung cancer clinical outcome? A propensity score matching study. *Thorac Cancer*. 2017;8(2):106-113. doi: 10.1111/1759-7714.12414.
 55. Visser S, Huisbrink J, Veer NE van 't, Toor JJ van, Boxem

- AJM van, Walree NC van, Stricker BH, Aerts JGJV. Renal impairment during pemetrexed maintenance in patients with advanced non-small cell lung cancer: a cohort study. *Eur Respir J* 2018;52(4):1800884. doi: 10.1183/13993003.00884-2018.
56. Wei YF, Chen JY, Lee HS, Wu JT, Hsu CK, Hsu YC. Association of chronic kidney disease with mortality risk in patients with lung cancer: a nationwide Taiwan population-based cohort study. *BMJ Open*. 2018;8(1):e019661. doi: 10.1136/bmjopen-2017-019661.
 57. Yamamoto Y, Kanzaki R, Kanou T, Ose N, Funaki S, Minami M, Shintani Y. Long-term outcomes of pulmonary resection for lung cancer patients with chronic kidney disease. *World J Surg*. 2019;43(12):3249-58. doi: 10.1007/s00268-019-05143-3.
 58. Yamamoto Y, Kanzaki R, Ose N, Funakoshi Y, Ikeda N, Takami K, Iwasaki T, Iwazawa T, et al. Lung cancer surgery for patients on hemodialysis: a decade of experience at multicenter institutions. *Ann Thorac Surg*. 2020;109:1558-65. Doi: 10.1016/j.athoracsur.2019.11.044.
 59. Park BJ, Shin S, Kim HK, Choi YS, Kim J, Shim YM, Surgical treatment for Non-Small Cell Lung cancer in patients on hemodialysis due to chronic kidney disease: clinical outcome and intermediate-term results. *Korean J Thorac Cardiovasc Surg*. 2015;48(3):193-8. doi: 10.5090/kjtcs.2015.48.3.193.
 60. Tsuchida M, Yamato Y, Aoki T, Watanabe T, Hashimoto T, Shinohara H, Hayashi J. Complications associated with pulmonary resection in lung cancer patients on dialysis. *Ann Thorac Surg*. 2001;71(2):435-8. doi: 10.1016/s0003-4975(00)02226-8.
 61. Wong G, Hayen A, Chapman JR, Webster AC, Wang JJ, Mitchell P, Craig JC. Association of CKD and cancer risk in older people. *J Am Soc Nephrol*. 2009;20(6):1341-50. doi: 10.1681/ASN.2008090998.
 62. Bowman IA, Pedrosa I, Kapur P, Brugarolas J. Renal cell carcinoma with pulmonary metastasis and metachronous non-small cell lung cancer. *Clin Genitourin Cancer*. 2017;15(4):e675-80. doi: 10.1016/j.clgc.2017.01.026.
 63. Sprangers B, Nair V, Launay-Vacher V, Riella LV, Jhaveri KD. Risk factors associated with post-kidney transplant malignancies: an article from the Cancer-Kidney International Network. *Clin Kidney J*. 2018;11(3):315-29. doi:10.1093/ckj/sfx122.
 64. Guo Y, Ng T, Morrissey P. Lung cancer following kidney transplant: incidence, risk factors, and outcomes. *Am J Transplant*. 2013;13(suppl 5).
 65. Verma V. Stereotactic body radiation therapy for metastases to the kidney in patients with non-small cell lung cancer: a new treatment paradigm for durable palliation. *Ann Palliat Med*. 2017;6:96-103.
 66. Wang J, Wang L, Long L, Tao Q, Xu F, Luo F. Solitary renal metastasis from squamous cell carcinoma of the lung. A case report. *Medicine (Baltimore)*. 2019;98(5):e14310. doi: 10.1097/MD.00000000000014310.
 67. Adamy A, Von Bodman C, Ghoneim T, Favaretto RL, Bernstein M, Russo P. Solitary, isolated metastatic disease to the kidney: memorial Sloan-Kettering cancer center experience. *BJU Int*. 2011;108:338-42.
 68. Karagkiouzis G, Koulaxouzidis G, Tomos P, Spartalis ED, Konstantinou F, Charpidou A, Syrigos KN. Solitary metastasectomy in non-small cell lung cancer. *J BUON* 2012;17:712-8.
 69. Degn S, Davidsen JR, Graumann O. Cryoablation: a potential treatment option for renal metastasis from lung cancer? *BMJ Case Rep*. 2018;2018. pii: bcr-2018-225841. doi: 10.1136/bcr-2018-225841.

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