

Original Article

Association between chronic kidney disease and cancer including the mortality of cancer patients: national health and nutrition examination survey 1999-2014

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Abstract: Purpose: This study aimed to investigate the association between chronic kidney disease (CKD) and different types of cancer and the effect of CKD on mortality among types of cancer. Methods: 30559 participants from NHANES 1999-2014 were included in our analysis, which had 2824 participants with cancer. Subgroups were grouped by cancer location. The association of different types of cancer with CKD was assessed using logistic regression models. Kaplan-Meier estimates and Cox proportional hazards models were used to evaluate the correlation between CKD and all-cause mortality in different cancer groups. Results: Age, gender, race, education level, income level, hypertension, diabetes, smoking status, alcohol consumption, TG, HDL-C, UA and eGFR were significantly different between the cancer and non-cancer group. The three cancers with highest prevalence of CKD were kidney cancer (72.3%), bladder cancer (54.7%), and colon cancer (43.0%) in this study. The prevalence of CKD was higher in cancer patients compared to non-cancer ones. Only genitourinary cancer showed a positive association with CKD (OR=1.23, 95% CI: 1.05-1.44) after adjusting for confounding factors. However, CKD was an independent risk factor for mortality from cancer regardless of the type of cancer. Conclusion: CKD is significantly associated only with genitourinary cancer among different types of cancer. CKD is an independent risk factor for survival in cancer patients, regardless of the type of cancer. Monitoring and maintaining the renal function of cancer patients is essential for prolonging their life.

Keywords: Chronic kidney disease, genitourinary cancer, cancer, prevalence, mortality, NHANES

Introduction

Cancer causes a significant clinical, social, and economic burden, and there were 18.1 million new cases of cancer and 9.6 million deaths globally from cancer in 2018 [1, 2]. CKD (chronic kidney disease, CKD) is one of the most critical complications of cancer, and CKD is related to cancer in many ways [3]. Some studies have reported that the prevalence of CKD in cancer patients was higher than in cancer-free patients, and CKD could worsen the prognosis of cancer patients [4-6]. However, it remains unclear whether the association of CKD and cancer and the effect of CKD on cancer mortality differ among different types of cancer.

Patients with cancer have a higher prevalence of kidney disease. The causes of CKD in cancer

patients can be roughly divided into two categories. The first category is direct renal involvement, which includes primary renal tumor, metastatic infiltration, obstruction of vessels or urinary tract, and paraneoplastic glomerulopathies; the second category is complications of therapy, which includes tumor lysis syndrome, nephrotoxic medications, nephrectomy, and bone marrow transplant nephropathies [3]. Acute kidney injury, electrolyte imbalances, and acidbase disturbances also play a role in the development of CKD in cancer patients [7].

The coexistence of CKD and cancer is common. There is a new interdisciplinary field called onconeurology focusing on the complex relationships between the kidneys and cancer [8]. This relationship has been described as 'circular'. On the one hand, cancers or their treat-

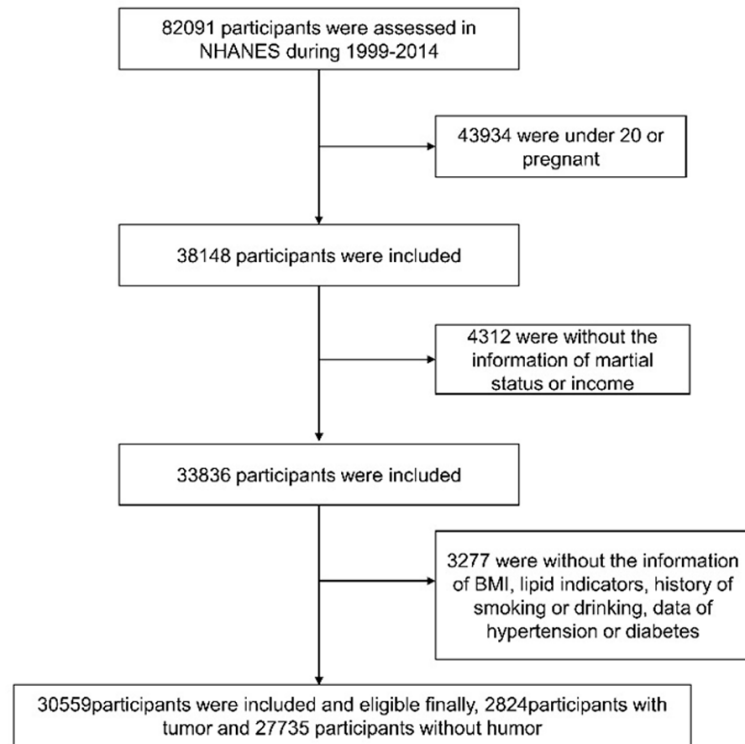


Figure 1. The screening process in this study. BMI: body mass index.

ment may impair renal function directly or indirectly [9, 10]. On the other hand, poor kidney function in cancer patients may decrease the safety of anti-cancer agents, further worsening the prognosis and increasing mortality [11, 12].

We not only compared the differences of cancer patients and non-cancer patients, but also studied the association between CKD and different types of cancer, and the effect of CKD on mortality among different types of cancer. Types of cancer included digestive cancer, genitourinary cancer, breast cancer, skin cancer, and other cancer, according to the location of cancer and the number of patients with different cancers in our study.

The number of cancer patients with CKD is rapidly increasing, but there are few studies on these patients. Our study focused on the relationship between CKD and different types of cancer and the effect of CKD on the prognosis of patients with different types of cancer, using big data from NHANES (National Health and Nutrition Examination Survey, NHANES).

Methods

Participants

We used the NHANES database to analyze in this study. National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) conducted this survey [13]. Moreover, written informed consent was provided to all participants in NHANES, and this survey was approved and reviewed by the NCHS Research Ethics Review Board. Data from 1999 to 2014 (82,091 subjects) was used in this study. Non-pregnant individuals >20 years of age (38,148 subjects) were selected, and we included participants with the demographic characteristics (33,836 subjects). We excluded participants without an answer to the question “Ever been told you had cancer or malignancy?” in

the NHANES medical conditions section (MCQ) questionnaire or with incomplete information on hypertension, diabetes, history of smoking and drinking, body mass index, or lipid markers (30,650 subjects). Participants without the data on mortality were excluded, and our study finally included 30,559 participants, of whom 2,824 participants had cancer. See **Figure 1** for detailed information.

Measures

Information of cancer of participants: The answer to the question “Ever been told you had cancer or malignancy?” on the MCQ questionnaire was used for learning whether the participants had cancer or malignancy. The answer to the question “What kind of cancer was it?” gave the location of cancer [13]. We classified cancer into five types based on the location and the number of patients with cancer (total number >100): digestive cancer, genitourinary cancer, skin cancer, breast cancer, and others. Digestive cancer included the cancer of the colon, esophagus, gallbladder, liver, pancreas (pancreatic), rectum (rectal), and stomach. Genitourinary cancer contained the cancer of

the bladder, cervix, kidney, ovary (ovarian), prostate, testis (testicular), and uterus (uterine). Skin cancer consisted of melanoma and other skin cancer. Breast cancer had a relationship only with the cancer of the breast. Others included all kinds of cancer not mentioned before, with a total number <100.

CKD: Participants with an eGFR (estimated glomerular filtration rate, eGFR) <60 mL/min/1.73 m², which was calculated by the Chronic Kidney Disease Epidemiology Collaboration equation, and/or with urinary albumin creatinine ratio >30 mg/g were considered to have CKD [14].

Covariates: The adjusted analyses included many covariates, such as sex, age, races (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other), status of marriage (married, widowed, divorced, separated, never married, living with a partner), different education levels (college and higher, less than high school, high school graduate) and income (high, middle, low), hypertension (yes, no), diabetes (yes, no), the status of alcohol drinking (never drinker, current drinker or past drinker), smoking status (former smoker, never smoker or current smoker), BMI, and eGFR (mL/min/1.73 m²). Moreover, high-density lipoprotein cholesterol (HDL-c) (mmol/L), uric acid (UA) (mmol/L), total cholesterol (TC) (mmol/L) and triglycerides (TG) (mmol/L) were included.

The family monthly poverty level index was used to classify the income level of participants, in which the low income means the value ≤1.30, the middle level of income means the value is between 1.30 to 1.85, and high level of income means >1.85. Participants with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or who used antihypertensive medications before the measurement were considered to have hypertension. Moreover, if the value of fasting blood glucose concentration was greater than 7 mmol/L, or the patient used any oral hypoglycemic agent or insulin, then the patient was considered to have diabetes.

Mortality: Time to death was the primary outcome. NHANES-linked National Death Index public access files provided the cause of death and vital status of participants until 31 December 2015 [15].

Statistical analysis

The CDC analytic recommendations provided a guideline for analyzing the database of NHANES. Standard descriptive statistics were reported for cancer and non-cancer groups. Since the data distribution was non-normal, the quartile and median values were calculated in this study for numerical variables. In addition, the percent (n) for categorical variables was calculated. Subgroups were grouped by cancer location. The associations of different cancers with CKD were assessed using logistic regression. Three models were calculated. No adjustments were done in Model 1. Model 2 was adjusted for age, sex, and demographic variables, including marital status, race, income, and education level. Variables mentioned before were adjusted in Model 3 and we further adjusted the status of diabetes, hypertension, alcohol consumption, smoking or not, TC, HDL-c, TG, uric acid, and BMI in this model. The effect of the different cancer groups was presented compared to the non-cancer group. We calculated the odds ratios of CKD with a 95% confidence interval. Moreover, we established three Cox proportional hazards models to assess the correlation between CKD and all-cause mortality of cancer group. There was no adjustment in Model 1, and age, sex, and demographic variables were adjusted in Model 2, the demographic variables including marital status, race, the level of education and income. Model 3 further adjusted the status of diabetes and hypertension, plus the status of alcohol consumption and smoking, TG, TC, HDL-c, uric acid, eGFR, and BMI. We calculated the hazard ratios of death with a 95% confidence interval. Statistically significant was considered as a two-sided *P*-value <0.05. SPSS software (version 26.0 for Windows; SPSS, Chicago, IL, USA) was used to perform the analyses. GraphPad Prism 6 was used to draw the graphs of this work and the survival curve of cancer patients.

Result

Description of participants

Participants' median age was 45 (quartile 35-64) years old in this study, and 50.6% were male. 49% of participants were non-Hispanic white, and more than half were married. 73.8% of them are at the educational level of college

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Table 1. Baseline characteristics of the population according to cancer status

| | All participants | | | p-value |
|---|---------------------|---------------------|---------------------|---------|
| | Total | Cancer, N=2824 | No-cancer, N=27735 | |
| Age, years | 49 (35-64) | 69 (57-77) | 47 (34-62) | <0.001 |
| Gender | | | | 0.002 |
| Man, No (%) | 15464 (50.6%) | 1352 (47.9%) | 14112 (50.9%) | |
| Women, No (%) | 15095 (49.4%) | 1472 (52.1%) | 13623 (49.1%) | |
| Race/ethnicity | | | | <0.001 |
| Mexican American, No (%) | 5209 (17%) | 177 (6.3%) | 5032 (18.1%) | |
| Other Hispanic, No (%) | 2237 (7.3%) | 111 (3.9%) | 2126 (7.7%) | |
| Non-Hispanic White, No (%) | 14986 (49%) | 2111 (74.8%) | 12875 (46.4%) | |
| Non-Hispanic Black, No (%) | 6089 (19.9%) | 349 (12.4%) | 5740 (20.7%) | |
| Other Race-Including Multi-Racial, No (%) | 2038 (6.7%) | 76 (2.7%) | 1962 (7.1%) | |
| Marital status | | | | <0.001 |
| Married | 16485 (53.9%) | 1706 (60.4%) | 14779 (53.3%) | |
| Widowed | 2585 (8.5%) | 486 (17.2%) | 2099 (7.6%) | |
| Divorced | 3223 (10.5%) | 333 (11.8%) | 2890 (10.4%) | |
| Separated | 976 (3.2%) | 72 (2.5%) | 904 (3.3%) | |
| Never married | 5161 (16.9%) | 143 (5.1%) | 5018 (18.1%) | |
| Living with partner | 2129 (7.0%) | 84 (3%) | 2045 (7.4%) | |
| Education | | | | <0.001 |
| Less than high school, No (%) | 3426 (11.2%) | 282 (10.0%) | 3144 (11.3%) | |
| High school graduate, No (%) | 4584 (15.0%) | 340 (12.0%) | 4244 (15.3%) | |
| College and higher, No (%) | 22549 (73.8%) | 2202 (78.0%) | 20347 (73.4%) | |
| Category of income | | | | <0.001 |
| Low, No (%) | 9379 (31.1%) | 665 (23.5%) | 8712 (31.4%) | |
| Middle, No (%) | 4074 (13.3%) | 355 (11.9%) | 3719 (13.4%) | |
| High, No (%) | 16324 (53.4%) | 1723 (61.0%) | 14601 (52.6%) | |
| Hypertension | | | | <0.001 |
| Yes, No (%) | 12868 (42.1%) | 1788 (63.3%) | 11080 (39.9%) | |
| No, No (%) | 17688 (57.9%) | 1036 (36.7%) | 16652 (60%) | |
| Diabetes | | | | <0.001 |
| Yes, No (%) | 4162 (13.6%) | 594 (21.0%) | 3577 (12.9%) | |
| No, No (%) | 26285 (86%) | 2230 (79.0%) | 24154 (87.6%) | |
| Alcohol consumption | | | | 0.001 |
| Current drinker, No (%) | 18630 (61.0%) | 1615 (57.2%) | 17015 (61.3%) | |
| Past drinker, No (%) | 5055 (16.5%) | 659 (23.3%) | 6150 (22.2%) | |
| Never, No (%) | 6809 (22.3%) | 548 (19.4%) | 4507 (16.3%) | |
| Smoking status | | | | <0.001 |
| Current smoker, No (%) | 6692 (21.9%) | 426 (15.1%) | 6266 (22.6%) | |
| Past smoker, No (%) | 11160 (36.5%) | 1243 (44%) | 11458 (41.3%) | |
| Never, No (%) | 12701 (41.6%) | 1154 (40.9%) | 10006 (36.1%) | |
| Body mass index (kg/m ²) | 27.8 (24.2-32.1) | 27.6 (24.3-31.7) | 27.8 (24.2-32.1) | 0.392 |
| HDL-c (mmol/l) | 1.3 (1.1-1.6) | 1.3 (1.1-1.6) | 1.3 (1.1-1.6) | <0.001 |
| TC (mmol/l) | 5.0 (4.3-5.7) | 5.0 (4.3-5.7) | 5.0 (4.3-5.7) | 0.748 |
| TG (mmol/l) | 1.3 (0.9-2.1) | 1.5 (1.0-2.1) | 1.3 (0.9-2.1) | <0.001 |
| Uric acid (mmol/L) | 321.2 (267.7-380.7) | 327.1 (273.6-386.6) | 321.2 (261.7-380.7) | <0.001 |
| eGFR (mL/min/1.73 m ²) | 91.4 (74.8-107.2) | 75.2 (60.6-90.4) | 92.9 (76.7-108.6) | <0.001 |
| CKD, No (%) | 5593 (18.3%) | 916/2824 (32.4%) | 4677/27735 (16.9%) | <0.001 |
| Death number, No (%) | 3386 (11.1%) | 725 (25.7%) | 2661 (9.6%) | <0.001 |

Values for categorical variables are given as count (percentage); values for continuous variables are given as median (interquartile range). HDL-c, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease.

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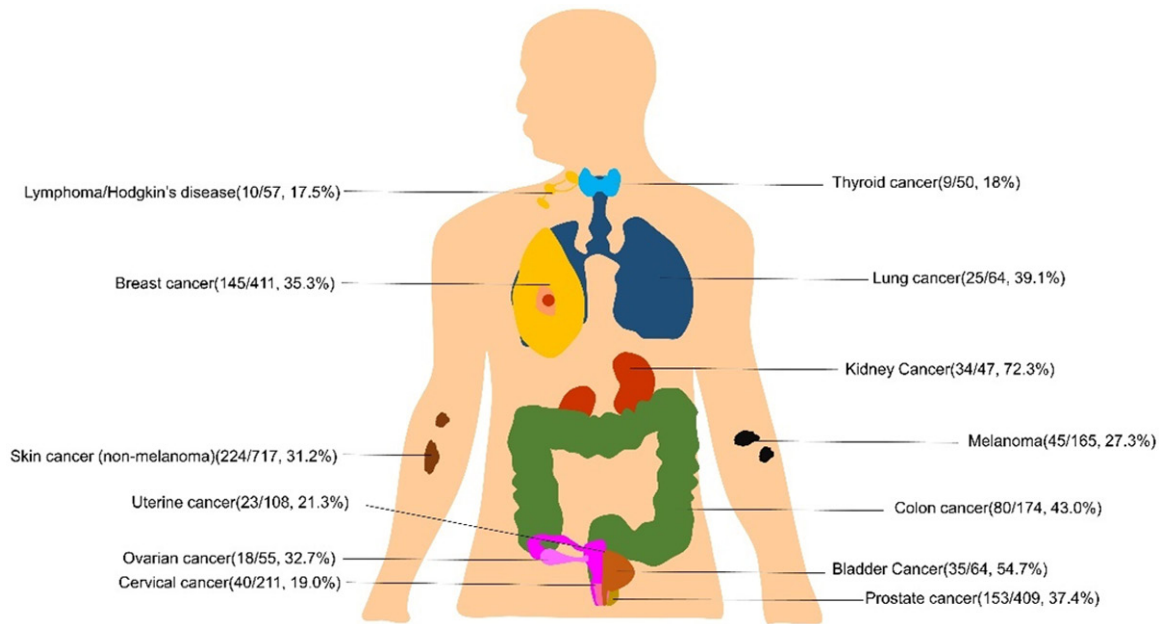


Figure 2. The body map of the incidence of CKD among different tumor patients. CKD: chronic kidney disease.

and higher. Almost 70% of participants had middle or high income. There was a total of 2824 participants with cancer. Compared to non-cancer ones, participants with cancer were more likely to be female, aged, non-Hispanic white, of higher educational level, higher income, hypertensive, diabetic, non-alcohol drinker, and non-smoker. Patients with cancer showed less favorable TG, HDL-C, and UC, lower value of eGFR compared with cancer-free ones (**Table 1**).

Body map of the prevalence of CKD among different types of cancer

The body map of the prevalence of CKD among different cancers with more than 50 subjects is shown in **Figure 2**. Since kidney cancer is deeply associated with kidney function, we demonstrated the prevalence of CKD among kidney cancer as well. The three types of cancer with the top 3 prevalences of CKD were kidney cancer (72.3%), bladder cancer (54.7%), and colon cancer (43.0%). The details of the prevalence of CKD among other cancers are shown in **Figure 2**.

Correlation of CKD with cancer

The prevalence of CKD among cancer patients was higher than in cancer-free ones regardless

of the type of cancer as shown in **Table 2**. **Table 2** shows the logistic models between CKD and different types of cancer. Among all participants, genitourinary cancer patients were most likely to have CKD compared with cancer-free ones, with an odds ratio for having CKD of 1.23 (95% CI: 1.05-1.44). However, there was no significant relationship between CKD and other types of cancer or total cancer.

CKD and mortality in cancer patients

The baseline clinical characteristics of CKD and non-CKD cancer patients are shown in **Table S1**. Age, gender, race/ethnicity, marital status, education level, the prevalence of hypertension, the prevalence of diabetes, alcohol consumption status, smoking status, HDL-c, TC, TG, Uric acid, eGFR, and mortality were different in cancer patients with or without CKD. The different mortality of cancer patients with CKD or without CKD is shown in **Figure 3A**; and the hazard ratio and 95% confidence intervals (95% CIs) of death with CKD among patients with different types of cancer and all patients with cancer are shown in **Figure 3B**. There was a meaningful correlation between mortality from all causes in cancer patients with CKD. Cancer patients who had CKD had a worse mortality rate compared to non-CKD patients, as shown in **Figure 3A** regardless of the type of

Table 2. Prevalence of CKD among cancer patients and the odds ratios (ORs) and 95% confidence intervals (95% CIs) of having CKD among cancer patients

| | CKD/total number (%) | p-value | Model 1 | | Model 2 | | Model 3 | |
|----------------------|----------------------|---------|------------------|---------|------------------|---------|------------------|---------|
| | | | OR | p-value | OR | p-value | OR | p-value |
| No-cancer | 4677/27735 (16.9%) | Ref | Ref | | Ref | | Ref | |
| Digestive cancer | 98/230 (42.6%) | <0.001 | 3.66 (2.81-4.76) | <0.001 | 1.32 (0.99-1.74) | 0.055 | 1.23 (0.91-1.65) | 0.173 |
| Genitourinary cancer | 306/911 (33.6%) | <0.001 | 2.49 (2.17-2.87) | <0.001 | 1.21 (1.04-1.41) | 0.016 | 1.23 (1.05-1.44) | 0.013 |
| Skin cancer | 269/882 (30.5%) | <0.001 | 2.16 (1.87-2.51) | <0.001 | 0.97 (0.82-1.14) | 0.698 | 0.94 (0.79-1.12) | 0.483 |
| Breast cancer | 145/411 (35.3%) | <0.001 | 2.69 (2.19-3.30) | <0.001 | 0.97 (0.78-1.22) | 0.805 | 0.89 (0.70-1.13) | 0.351 |
| Others | 51/212 (24.1%) | 0.006 | 1.56 (1.14-2.14) | 0.006 | 0.91 (0.64-1.28) | 0.581 | 0.83 (0.58-1.20) | 0.324 |
| Total cancer | 916/2824 (32.4%) | <0.001 | 2.37 (2.17-2.58) | <0.001 | 1.07 (0.97-1.18) | 0.184 | 1.04 (0.94-1.15) | 0.419 |

Model 1: Unadjusted; Model 2: Adjusted for age, sex, marital status, race/ethnicity, education level, and category of income; Model 3: Additional adjusted for hypertension, diabetes, alcohol consumption, smoking status, body mass index, high-density lipoprotein cholesterol, total cholesterol, triglyceride, and uric acid. CKD: chronic kidney disease.

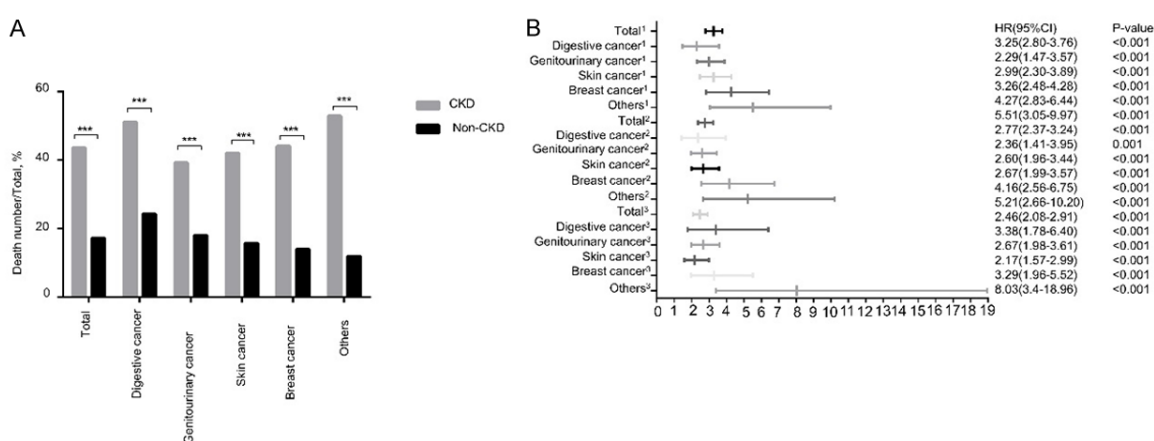


Figure 3. A: The different mortality of cancer patients with or without CKD. B: The hazard ratio and 95% confidence intervals (95% CIs) of hazard of death with CKD among patients with different types of cancer and all patients. ¹Non-adjusted; ²Adjusted for age, sex, race/ethnicity, education level, and category of income; ³Additionally adjusted for hypertension, diabetes, alcohol consumption, smoking status, body mass index, estimated glomerular filtration rate, high-density lipoprotein cholesterol, total cholesterol, triglyceride, and uric acid; CKD: chronic kidney disease; ***: P<0.001.

cancer. Moreover, the hazard ratio and 95% CIs demonstrated a higher mortality risk in cancer patients with CKD compared to cancer patients without CKD. This was independent of the type of cancer. The survival curve of all cancer patients and different types of cancer groups were shown in **Figure 4**.

Discussion

Our study found that patients with cancer had a higher prevalence of CKD compared with cancer-free ones. The effects of CKD for patients with digestive cancer, genitourinary cancer, skin cancer, and breast cancer were studied separately because these cancers represented a considerable number of patients. Only patients with genitourinary cancer were more

likely to have CKD than individuals without cancer. Cancer patients with CKD had a higher risk of death than cancer patients without CKD regardless of the type of cancer.

In the present study, compared with cancer-free participants, those with cancer were more likely to be female, aged, non-Hispanic white, non-alcohol drinkers, and non-smokers; and had a higher educational level and a higher income; and were more likely to have hypertension and diabetes. Cancer patients showed less favorable TG, HDL-C, UA, and eGFR compared with those who were cancer-free. It is well known that age is an independent risk factor for cancer [16]. Patients with breast cancer accounted for 14.6% of cancer participants in this study, which may explain that cancer

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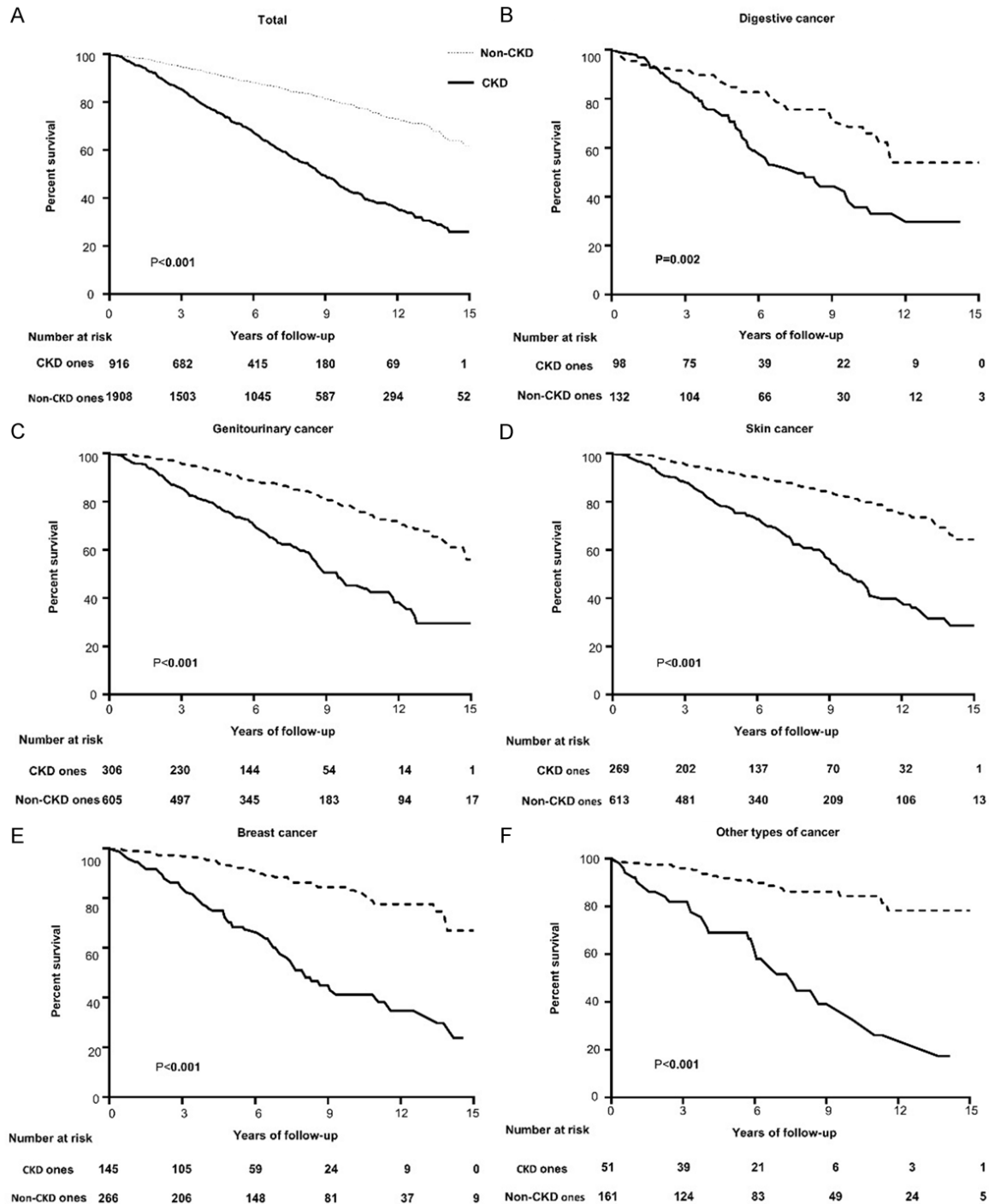


Figure 4. Mortality is related to CKD status among all cancer patients and different cancer types. CKD: chronic kidney disease.

patients are more likely to be female. Cancer patients were more likely to be non-Hispanic white and had a higher educational level and income, possibly since people with these characteristics were more active in seeking medical treatment and screening to detect cancer.

There were more females, and only a few lung cancers and liver cancers in our cancer patients, which may partially explain why cancer patients in our study were more likely to be non-alcohol drinkers and non-smokers. Cancer patients were more likely to have hypertension,

diabetes, dyslipidemia, and renal dysfunction, consistent with prior studies [17-19].

Participants in this study were grouped as non-cancer, digestive cancer, genitourinary cancer, skin cancer, breast cancer, and other types of cancer, and the non-cancer group was the reference group. We found that in these different types of cancer, only genitourinary cancer was positively associated with CKD compared with the non-cancer group. These results revealed that only genitourinary cancer was directly associated with CKD. CKD and genitourinary cancer were independent risk factors for each other [20-23]. For other types of cancer, it was not the cancer itself, but anti-cancer treatment and complications that were a direct risk factor for CKD [23, 24].

CKD was associated with an increased risk of death in cancer patients, which is in line with other studies [6]. CKD was a risk factor for death not only in genitourinary cancer patients, but also in digestive cancer, genitourinary cancer, skin cancer, breast cancer, and other types of cancer patients. CKD is the final result of cancer-associated kidney complications, such as paraneoplastic glomerulopathies and chemotherapy-associated kidney diseases [25, 26]. Paraneoplastic glomerulopathies are induced by abnormal immune responses caused by cancer, which include membranous nephropathy, minimal change disease, IgA nephropathy, membranoproliferative glomerulonephritis, and extracapillary glomerulonephritis [27]. Moreover, some treatments for cancers such as surgery, chemotherapy, and radiotherapy may also result in the decline of renal function [28, 29]. The spread and growth of cancer of the genitourinary system often directly damage renal tissue or block the ureters, eventually leading to impaired renal function [30, 31]. The frequent use of contrast media by cancer patients due to examination can also affect renal function [32].

The treatment of cancer has both positive and negative effects on the prognosis of cancer patients. The use of anti-cancer agents and some surgeries may result in the decline of renal function. Conversely, kidney problems will worsen the prognosis of cancer patients by reducing the adequacy of anti-cancer treatment [33]. Cancer patients with CKD are usually classified as excluded from the study of

new anti-cancer drugs and new anti-cancer therapies. Patients with kidney disease are more likely to be frail. This frail state may result from the dysregulation of energy input and output, making them progressively weaker [34].

The nephrotoxicity of chemotherapy drugs is a crucial reason for the decline of renal function in patients with cancer. For example, cisplatin is a representative chemotherapy drug with nephrotoxicity and is widely used to treat solid tumors, such as ovarian, head and neck, and testicular germ cells. Cisplatin can induce AKI (acute kidney injury, AKI) and then develop into CKD. Some studies have proven that the pathophysiology of cisplatin-induced AKI includes 4 major mechanisms: proximal tubular injury, oxidative stress, inflammation, and vascular injury in the kidney [35]. Apoptosis, autophagy, dysregulation of cell-cycle proteins, DNA damage, mitochondrial dysfunction, direct toxicity to renal tubular epithelial cells, and activation of the MAPK (mitogen-activated protein kinase, MAPK) signaling pathways are the mechanisms of proximal tubular injury [36-41]. According to the pathophysiologic mechanisms of injury motioned above, therapies for cisplatin-induced AKI include erythropoietin (inhibits tubular apoptosis), mesenchymal stem cells, cytokine inhibitors (TNF- α or IL33 inhibitors), inhibitors of oxidant stress, anti-inflammatory agents, and inhibitors of the MAPK pathway that can reduce CD4⁺ T cells.

Since our study is a retrospective study based on a public database called NHANES, some limitations are present. First, the number of patients with some types of cancer is very small, even with a high global prevalence, such as lung cancer. These surveys spanned from 1999 to 2014, and each happened in only one region of the USA. Therefore, there may be differences in the prevalence of different types of cancer between this database and all over the world. Secondly, there was no specific laboratory or pathologic indicator for cancer diagnosis, and some important risk factors for the mortality of cancer, such as cancer stage, treatment, and ECOG (Eastern Cooperative Oncology Group, ECOG) PS (performance status, PS), were not included in this study. NHANES is not a professional cancer patient database and cancer patients and their cancer types were confirmed by a questionnaire survey. Thirdly, the eGFR and urine protein were cross-section-

al data that cannot reflect the renal function of the cancer patient changing with time, and we cannot distinguish whether the CKD is primary or secondary. Finally, retrospective studies may have memory bias.

Conclusion

The prevalence of CKD in different types of cancer patients is higher than that in non-cancer patients. Still, only genitourinary cancer was positively associated with CKD among different types of cancer in this study. CKD was an independent risk factor for death for different types of cancer patients. Medical staff should pay more attention to cancer-associated kidney disease to prolong the life of cancer patients. Given that the number of cancer patients with renal dysfunction is increasing, clinical research on them is of great significance.

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Disclosure of conflict of interest

None.

Abbreviations

AKI, Acute Kidney Injury; BMI, Body Mass Index; CD, Cluster of Differentiation; CDC, Centers for Disease Control and Prevention; CI, Confidence Interval; CKD, Chronic Kidney Diseases; DNA, Deoxyribonucleic Acid; ECOG, Eastern Cooperative Oncology Group; eGFR, Estimated Glomerular Filtration Rate; HDL-c, High-Density Lipoprotein Cholesterol; IL, Interleukin; MAPK, Mitogen-Activated Protein Kinase; MCQ, Medi-

cal Conditions Section; NCHS, National Center for Health Statistics; NHANES, National Health and Nutrition Examination Survey; PS, Performance Status; TC, Total Cholesterol; TG, Triglyceride; TNF, Tumor Necrosis Factor; UC, Uric Acid.

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Chronic kidney disease and cancer

Table S1. Baseline characteristics of cancer patients according to whether they have CKD

| | All cancer patients | | | p-value |
|---|---------------------|---------------------|---------------------|---------|
| | Total | CKD, N=916 | No-CKD, N=1908 | |
| Age, years | 69 (57-77) | 70 (68-77) | 64 (53-73) | <0.001 |
| Gender | | | | 0.003 |
| Men, No (%) | 1352 (47.9%) | 475 (51.9%) | 877 (46.0%) | |
| Women, No (%) | 1472 (52.1%) | 441 (48.1%) | 1031 (54.0%) | |
| Race/ethnicity | | | | 0.025 |
| Mexican American, No (%) | 177 (6.3%) | 42 (4.6%) | 135 (7.1%) | |
| Other Hispanic, No (%) | 111 (3.9%) | 44 (2.4%) | 89 (4.7%) | |
| Non-Hispanic White, No (%) | 2111 (74.8%) | 712 (77.7%) | 1399 (73.3%) | |
| Non-Hispanic Black, No (%) | 349 (12.4%) | 122 (13.3%) | 227 (11.9%) | |
| Other Race-Including Multi-Racial, No (%) | 76 (2.7%) | 18 (2%) | 58 (3.0%) | |
| Marital status | | | | 0.003 |
| Married | 1706 (60.4%) | 520 (56.8%) | 1186 (62.2%) | |
| Widowed | 486 (17.2%) | 249 (27.2%) | 237 (12.4%) | |
| Divorced | 333 (11.8%) | 84 (9.2%) | 249 (13.1%) | |
| Separated | 72 (2.5%) | 18 (2.0%) | 54 (2.8%) | |
| Never married | 143 (5.1%) | 29 (3.2%) | 114 (6.0%) | |
| Living with partner | 84 (3%) | 16 (1.7%) | 68 (3.6%) | |
| Education | | | | <0.001 |
| Less than high school, No (%) | 282 (10.0%) | 125 (13.6%) | 157 (8.2%) | |
| High school graduate, No (%) | 340 (12.0%) | 137 (15.0%) | 203 (10.6%) | |
| College and higher, No (%) | 2202 (78.0%) | 654 (71.4%) | 1548 (81.1%) | |
| Category of income | | | | 0.118 |
| Low, No (%) | 665 (23.5%) | 229 (25.7%) | 438 (23.2%) | |
| Middle, No (%) | 355 (11.9%) | 137 (15.4%) | 218 (11.4%) | |
| High, No (%) | 1723 (61.0%) | 514 (57.6%) | 1209 (63.4%) | |
| Hypertension | | | | <0.001 |
| Yes, No (%) | 1788 (63.3%) | 726 (79.3%) | 1062 (55.7%) | |
| No, No (%) | 1036 (36.7%) | 190 (20.7%) | 846 (44.3%) | |
| Diabetes | | | | <0.001 |
| Yes, No (%) | 594 (21.0%) | 270 (29.5%) | 315 (16.5%) | |
| No, No (%) | 2230 (79.0%) | 644 (70.3%) | 1586 (83.1%) | |
| Alcohol consumption | | | | 0.022 |
| Current drinker, No (%) | 1615 (57.2%) | 480 (52.4%) | 1135 (59.5%) | |
| Past drinker, No (%) | 659 (23.3%) | 219 (23.9%) | 329 (17.2%) | |
| Never, No (%) | 548 (19.4%) | 217 (23.7%) | 442 (23.2%) | |
| Smoking status | | | | 0.001 |
| Current smoker, No (%) | 426 (15.1%) | 93 (10.2%) | 333 (17.5%) | |
| Past smoker, No (%) | 1243 (44%) | 404 (44.1%) | 750 (39.3%) | |
| Never, No (%) | 1154 (40.9%) | 419 (45.7%) | 824 (43.2%) | |
| Body mass index (kg/m ²) | 27.6 (24.3-31.7) | 27.7 (24.7-31.6) | 27.5 (24.1-31.7) | 0.718 |
| HDL-c (mmol/l) | 1.3 (1.1-1.6) | 1.3 (1.1-1.6) | 1.3 (1.1-1.6) | 0.002 |
| TC (mmol/l) | 5.0 (4.3-5.7) | 4.8 (4.1-5.6) | 5.1 (4.4-5.8) | <0.001 |
| TG (mmol/l) | 1.5 (1.0-2.1) | 1.5 (1.1-2.3) | 1.4 (1.0-2.0) | <0.001 |
| Uric acid (mmol/l) | 327.1 (273.6-386.6) | 362.8 (303.3-434.2) | 315.2 (261.7-362.8) | <0.001 |
| eGFR (mL/min/1.73 m ²) | 75.2 (60.6-90.4) | 54.3 (45.6-62.9) | 82.7 (71.8-95.1) | <0.001 |
| Death number, No (%) | 725 (25.7%) | 339 (43.6%) | 326 (17.1%) | <0.001 |

Values for categorical variables are given as count (percentage); values for continuous variables are given as median (interquartile range). HDL-c, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease.