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Short Communication

Renal Insufficiency According to Time after Cancer Diagnosis: Findings of a Nationwide Cross-Sectional Study

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Abstract

Background: Little is known about the relationship between renal insufficiency and time after cancer diagnosis.

Methods: The data of 71,302 individuals (aged 19 to 79 yr) that participated in the 2007–2019 Korean National Health and Nutrition Examination Surveys were subjected to analysis. Renal insufficiency was defined as an estimated glomerular filtration rate of < 60 ml/min/1.73 m². Odds ratios of renal insufficiency were estimated using multivariate logistic regression models adjusted for potential covariates.

Results: Of the 71,302 study subjects, 3.7% were cancer survivors and 2.2% were long-term (≥ 5 yr) survivors. Renal insufficiency was significantly more prevalent among short-term survivors, but not among long-term survivors, than among subjects without cancer.

Conclusion: A cancer history of ≥ 5 yr is not an independent risk factor of renal insufficiency.

Keyword: Cancer survivors; Long term adverse effects; Renal insufficiency

Introduction

Cancer survivorship has become a critical medico-social issue as numbers of cancer survivors are rapidly increasing (1). Solid evidence has documented cancer survivors are more vulnerable to the development of chronic illnesses than the general population (2), and that diminished renal function has negative impacts on many aspects of cancer patient care. The Renal Insufficiency and Cancer Medications (IRMA) study reported a higher prevalence of chronic kidney disease (CKD) in cancer patients than in the general population and that their survival was poorer than that of cancer patients without kidney disease (3).

The studies on the association between cancers and kidney damage have focused on kidney injuries caused directly during surgery or radiotherapy (4-7). For cancer survivors, only one study has reported a higher risk of CKD (8). Moreover, little is known about the relationship between renal insufficiency development and time after cancer diagnosis. This study aimed to examine the relationship between renal insufficiency and cancer duration using nationwide data.

Methods

Data and participants

Korean National Health and Nutritional Examination Survey (KNHANES) data that collected during the period 2007–2019 was used in the pre-

sent study. KNHANES has a multistage, stratified, complex design that ensures the recruitment of a sample representative of the Korean population and is conducted annually by the Korea Centers for Disease Control and Prevention to assess the health and nutritional status of the noninstitutionalized Korean civilian population. Detailed information on KNHANES has been described elsewhere (9).

Initially, we identified 78,886 subjects aged 19 to 79 yr old (age at cancer diagnosis was not specified for individuals ≥ 80 yr old). Times from cancer diagnoses were calculated by subtracting ages at diagnoses from ages at survey completion. For the analysis, subjects were dichotomized about 5 yr post-diagnosis into short- and long-term cancer survivors groups. After excluding 7,292 subjects with missing or erroneous (>200 $ml/min/1.73m^2$) glomerular filtration rate (GFR) data and 292 patients with a history of renal insufficiency, 71,302 subjects (68,685 subjects without cancer, 1,018 short-term cancer survivors, and 1,599 long-term cancer survivors) were included in the analysis.

Data collection

The primary outcome was renal insufficiency, which was defined as and GFR of <60 $ml/min/1.73m^2$ as determined using the equation derived in the Modification of Diet in Renal Disease (MDRD) study: $186.3\times(\text{serum creatinine}^{-1.154})\times(\text{age}^{-0.203})\times0.742$ (if female). Data on following covariates were collected: demographics (age, sex, economic status, and highest education level), health related habits (smoking status and drinking frequency), and comorbidities (obesity, hypertension, type 2 diabetes, and cardiovascular diseases such as angina pectoris, myocardial infarction, and stroke). Economic status was classified by median household income. Educational level was categorized as "middle school or lower" and "high school or beyond". Those that drank more than twice per week were defined as frequent drinkers, and obesity was defined as a body mass index of ≥ 25 kg/m^2, according to the WHO recommendation for Asians.

Statistical Analysis

Means ± standard deviations or numbers (percentages) were used to describe subject characteristics. The significances of intergroup differences were determined by one-way ANOVA or the Chi-square test, as appropriate. Multivariate logistic regression models adjusted for potential covariates, were used to determine the odds ratios of renal insufficiency. The analysis was performed using STATA MP Software, version 17.0 (STATA Corp., College Station, TX), and *P* values of less than 0.05 were considered statistically significant.

Results

Subject characteristics are presented in Table 1. Cancer survivors were more likely to be older, female, and have a poorer socioeconomic state and more comorbidities, and these differences tended to be greater for long-term survivors. U-shaped time-related patterns were observed for relations between health-related habits and the development of renal insufficiency. In addition, renal insufficiency was more prevalent among cancer survivors than among subjects without cancer, and temporal patterns of renal insufficiency development were similar for short- and long-term survivors.

Table 2 shows odds ratios of renal insufficiency at different times after cancer diagnosis. The prevalence of renal insufficiency was significantly greater among short-term cancer survivors than those without cancer even after adjusting for potential confounders, but not among long-term cancer survivors after adjusting for age.

Discussion

Kidney disease and cancer may constitute a vicious circle because kidney disease interrupts the bioavailability and/or safety profiles of chemoregimens, leads to suboptimal responses, increases the risk for drug-induced kidney injury, and aggravates kidney disease (10).

Table 1: Subject characteristics according to time after cancer diagnosis

Variable	*Cancer Survivors*			
	Subjects without cancer	<5 year after cancer	≥5 years after cancer	*P* Value
Numbers	68,685	1,018	1,599	
Demographics				
Age (years)	48.9±15.8	58.1±12.5	62.0±11.2	<0.001
Female gender	38,509 (56.1)	617 (60.6)	1,045 (65.4)	<0.001
Low education level	21,082 (32.0)	451 (44.4)	828 (52.1)	<0.001
Low-income level	29,142 (42.9)	464 (46.1)	886 (55.9)	<0.001
Health-related habits				
Current smoker	13,825 (20.6)	79 (7.8)	138 (8.7)	<0.001
Frequent drinker	14,968 (25.2)	112 (13.1)	229 (18.1)	<0.001
Comorbidities				
Obesity	22,992 (33.5)	308 (30.3)	502 (31.4)	0.023
Hypertension	13,783 (20.2)	322 (31.6)	537 (33.6)	<0.001
Type 2 diabetes	5,329 (7.8)	133 (13.1)	255 (16.0)	<0.001
Cardiovascular disease[a]	2,688 (3.9)	45 (4.4)	133 (8.3)	<0.001
GFR<60 ml/min/1.73m^2	1,654 (2.4)	58 (5.7)	91 (5.7)	<0.001

GFR, glomerular filtration rate.
Data are presented as means ± standard deviations or numbers (percentages); [a] includes angina pectoris, myocardial infarction, and stroke

Table 2: Odds ratios of renal dysfunction according to time after a diagnosis of cancer with respect to subjects without cancer

Variable	*Unadjusted*		*Age adjusted*		*Multivariate[a] adjusted*	
	OR (95% CI)	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Within 5 yr of cancer diagnosis	2.45 (1.87–3.21)	<0.001	1.51 (1.15–2.00)	0.004	1.53 (1.10–2.12)	0.012
≥ 5 yr after cancer diagnosis	1.56 (1.40–1.74)	<0.001	1.07 (0.95–1.19)	0.262	1.10 (0.96–1.26)	0.185

OR, odds ratio; CI, confidence interval
[a]Includes age, sex, education level, economic status, current smoking, frequent drinking, obesity, hypertension, type 2 diabetes, and cardiovascular disease (angina pectoris, myocardial infarction, or stroke)

However, while kidney disease is known to adversely affect cancer outcomes, it is not clear whether cancer increases the risk of kidney disease. As expected, our analysis indicates that short-term survivors are at high risk of renal insufficiency. During the trajectories of treatments, cancer patients are at high risk of kidney injury (11), which can cause hypertension and atherosclerosis indirectly, and thus, affect the development of renal insufficiency. Furthermore, cancer patients are at risk of conditions, such as cachexia, hypercalcemia, and paraneoplastic kidney injury (12, 13).

It is noteworthy that, in the current study, long-term survivorship was not associated with renal insufficiency. Until now, only one study (8) has reported a higher risk of CKD among cancer survivors, however, they did not consider time after cancer diagnosis. The risk of renal insufficiency is problematic during the acute treatment phase, but that risk may not be long-lasting over 5 yr after cancer diagnosis. Our study suggested that the vulnerability to renal insufficiency should not be exaggerated for long-term cancer survivors.

Our study has several limitations that require consideration. First, the cross-sectional nature of KNHANES precludes inferences regarding caus-

al and temporal relationships. Second, our definition of renal insufficiency was based on a single measurement, and thus, did not reflect changes in estimated GFRs over time. Third, our findings are subjected to residual confounding, for example, by clinical variables, such as risk factors prediagnoses, cancer types, and treatment modalities.

Conclusion

This is the first study to examine the temporal nature of renal insufficiency development in Korean cancer survivors. Interestingly, our findings indicated long-term adult cancer survivors do not have higher renal insufficiency rates than members of the general population without a cancer history. A prospective longitudinal study that includes other ethnicities is needed to confirm our findings.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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