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Correcting for Attrition Bias Reveals Renal Impairment as a Strong Independent Risk Factor for Incident Cancer: A National Cohort Study

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Luning Dong[1]*, Shanshan Liu[2]*, Tingting Liu[1]#

[1]Department of Nursing, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China.

[2]Department of Burn and Plastic, Jinling Hospital & Affiliated Hospital of Medical School, Nanjing, China.

#: Correspondence: Tingting Liu (tingtingliu2025@126.com)

*These authors contributed equally: Luning Dong and Shanshan Liu.

Abstract

Objective: The co-morbidity of chronic kidney disease (CKD) and cancer complicates nursing management. This study aimed to investigate the association between renal impairment and 4-year cancer incidence in a large, nationally representative cohort, while methodologically correcting for attrition bias and rare event outcomes.

Methods: This prospective cohort study used data from 6,307 participants in the China Health and Retirement Longitudinal Study (CHARLS). Analysis utilized Firth's penalized logistic regression for rare cancer events (n=32) and Inverse Probability Weighting (IPW) to correct for significant attrition bias (39.1% loss to follow-up).

Results: After IPW correction, the risk landscape was fundamentally altered. Renal impairment emerged as a strong, independent risk factor for incident cancer (OR=4.70, 95% CI: 1.35–16.38). This correction also rectified other associations, notably reversing dyslipidemia from a protective to a risk factor.

Conclusion: Renal impairment is a significant cancer risk factor. Rigorous statistical methods to correct for attrition bias are essential for valid longitudinal results. These findings support enhanced, nurse-led cancer surveillance for patients with CKD and the development of integrated onco-nephrology care models.

Keywords

Renal Impairment, Cancer Incidence, Oncology, Attrition Bias, Prospective Cohort Study

1. Introduction

The intersection of chronic kidney disease (CKD) and cancer presents a growing global

health challenge (1). CKD is increasingly recognized as a risk factor for incident cancer (2), likely driven by shared mechanisms such as chronic inflammation and immune dysregulation (3). This association creates complex care needs, posing significant challenges to nursing practice. Nurses are pivotal in managing CKD (4), yet require a robust evidence base to shift from reactive care to proactive cancer surveillance for this high-risk group.

Unfortunately, longitudinal studies quantifying this risk are often compromised by methodological challenges. High attrition rates can introduce significant selection bias, while rare event outcomes, like cancer incidence, challenge standard statistical models (5). Failing to address these issues leads to unreliable conclusions.

Therefore, this study investigated the association between renal impairment and 4-year cancer incidence in a large, nationally representative Chinese cohort. Our objective was to provide reliable, clinically meaningful evidence by explicitly addressing the dual methodological challenges of rare events and attrition bias, thereby informing targeted screening protocols.

2. Methods

2.1. Study Design, Population, and Variables

This prospective cohort study utilized data from the China Health and Retirement Longitudinal Study (CHARLS) (6), a nationally representative sample of Chinese residents aged ≥45. We included 6,307 participants from the 2011 baseline (with biomarker data) who were free of cancer, with follow-up in 2015.

The primary exposure was renal impairment, defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation incorporating serum creatinine and cystatin C (7). The primary outcome was incident cancer at the 2015 follow-up, identified via self-report of a physician's diagnosis.

Baseline (2011) covariates included sociodemographics (age, gender, education), lifestyle factors (smoking, drinking), clinical measures (body mass index, BMI; C-reactive protein, CRP), self-reported comorbidities (hypertension, diabetes, dyslipidemia), and depressive symptoms (Center for Epidemiologic Studies Depression Scale 10-item, CES-D-10) (8).

2.2. Statistical Analysis

Baseline characteristics were summarized (t-tests, χ^2 tests), revealing significant attrition bias between retained and lost participants. To simultaneously address this selection bias and the rare cancer outcome (n=32), which can cause estimation instability, our primary analysis employed a weighted Firth's penalized logistic regression. This approach incorporated Inverse Probability Weights (IPW) to account for selection bias. These weights were derived from a logistic model predicting the probability of retention based on all baseline characteristics. Concurrently, the Firth's penalization method provided stable and unbiased estimates despite the low event count. The final model included key covariates (e.g., renal impairment, age, sex, smoking) to estimate adjusted odds ratios (ORs) and 95% CIs. Given the substantial corrections

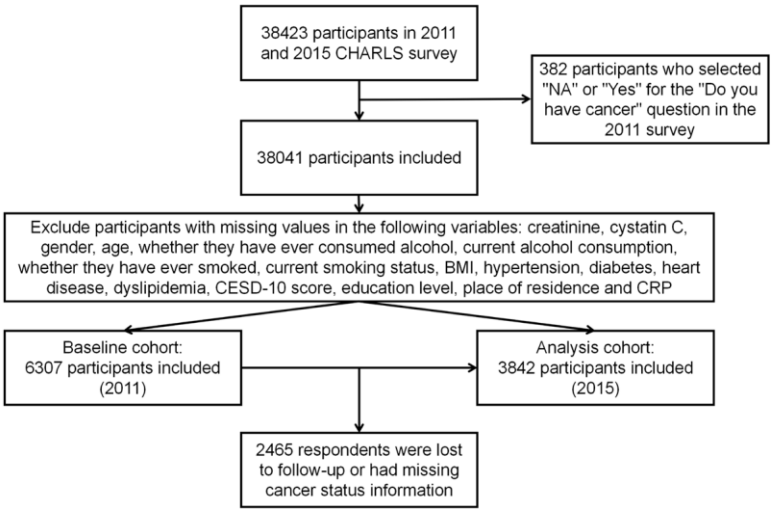
observed, these IPW-weighted results were considered the primary and most reliable findings. All analyses used Stata 17.0 ($p < 0.05$).

3. Results

3.1. Cohort Characteristics and Attrition

From an initial 6,307 participants at baseline, 2,465 (39.1%) were lost to follow-up by 2015. The final analytical cohort included 3,842 participants, among whom 32 incident cancer cases were identified over the 4-year period (Figure 1).

Figure 1. Flowchart of Study Participant Selection.



Baseline characteristics of the full cohort (N=6,307) are detailed in Table 1. The 528 participants (8.4%) with renal impairment (eGFRcr-cys < 60 mL/min/1.73 m²) were significantly older (72.2 vs. 58.8 years, $P < 0.01$) and had a higher prevalence of comorbidities, including hypertension (37.3% vs. 23.5%, $P < 0.01$), diabetes (8.7% vs. 5.5%, $P < 0.01$), and heart disease (14.4% vs. 11.2%, P=0.03). This group also exhibited significantly higher C-reactive protein (CRP) levels ($P < 0.01$).

Significant attrition bias was detected; participants lost to follow-up were systematically different from those retained. They were younger, had higher baseline kidney function, and had a lower prevalence of comorbidities like hypertension and heart disease (all $P < 0.01$). This confirmed the necessity of correcting for selection bias.

Table 1: Baseline Characteristics of 6307 Participants.

Characteristics	Total (N=6307)	eGFRcr-cys ≥ 60 (N=5779)	eGFRcr-cys < 60 (N=528)	P
Age (years), (Mean±SD)	59.9 ± 10.2	58.8 ± 9.5	72.2 ± 9.0	＜0.01
Gender, n (%)				0.02
Male	2892 (45.9)	2623 (45.3)	269(50.9)	
Female	3415 (54.1)	3156 (54.7)	259 (49.1)	
Smoking Status, n (%)				0.01
Never Smoker	3869 (61.3)	3569 (61.8)	300 (56.8)	
Ever Smoker	532 (8.4)	471(8.2)	61 (11.6)	
Current Smoker	1906 (30.2)	1739 (30.1)	167 (31.6)	

Drinking Status, n (%)				＜0.01
Never Drinker	3765 (59.7)	3430 (59.4)	335 (63.4)	
Ever Drinker	529 (8.4)	456 (7.9)	73 (13.8)	
Current Drinker	2013 (31.9)	1893 (32.8)	120 (22.7)	
BMI (kg/m²), (Mean±SD)	23.5 ± 4.2	23.6 ± 4.3	23.8 ± 3.3	0.30
Baseline Illnesses, n (%)				
Hypertension	1555 (24.7)	1358 (23.5)	197 (37.3)	＜0.01
Diabetes	366 (5.8)	320 (5.5)	46 (8.7)	＜0.01
Heart Disease	726 (11.5)	650 (11.2)	76 (14.4)	0.03
Dyslipidemia	522 (8.3)	485 (8.4)	37 (7.0)	0.32
CESD-10 Score, median (Q1,Q3)	7 (3, 12)	7 (3, 12)	8 (4, 13)	0.16
CRP (mg/L), median (Q1,Q3)	1 (0.5, 2)	1 (0.5, 1.8)	1.6 (1.3, 5.4)	＜0.01
Educational level, n (%)				＜0.01
Below Primary School	3119(49.5)	2775(48.0)	344(65.2)	
Primary School	1398(22.2)	1295(22.4)	103(19.5)	
Middle School	1191(18.9)	1138(19.7)	53(10.0)	
Above Middle School	599(9.5)	571(9.9)	28(5.3)	
Area of Residence, n (%)				0.37
Urban	2211(35.1)	2016(34.9)	195(36.9)	
Rural	4096(64.9)	3763(65.1)	333(63.1)	

3.2. Impact of Attrition Bias Correction on Risk Estimates

Initial, unweighted regression analyses on the complete-case cohort (N=3,842) failed to show a significant association between renal impairment and cancer (P=0.150). Moreover, this model produced clinically implausible results, suggesting dyslipidemia (OR=0.30, 95% CI: 0.098–0.932) and current smoking (OR=0.33, 95% CI: 0.156–0.707) were protective (Table 2).

Table 2. Comparison of Unweighted (Complete-Case) and IPW-Weighted Logistic Regression Models for Incident Cancer.

Variable	Unweighted Model		IPW-weighted Model	
	OR (95% CI)	P	OR (95% CI)	P
eGFRcr-cys	2.387 (0.730-7.800)	0.150	4.70 (1.35 – 16.38)	0.015
Heart Disease	2.416 (1.124-5.193)	0.024	2.63 (1.15 – 6.01)	0.021
Dyslipidemia	0.302 (0.098-0.932)	0.037	3.46 (1.21 – 9.91)	0.021
Hypertension	2.329 (1.069-5.072)	0.033	1.07 (0.44 – 2.59)	0.883
Diabetes	1.821 (0.696-4.767)	0.222	0.76 (0.17 – 3.30)	0.713
Smoking Status (Current vs. Not)	0.332 (0.156-0.707)	0.004	0.14 (0.03 – 0.62)	0.010
Drinking Status (Current vs. Not)	0.996 (0.624-1.591)	0.988	0.72 (0.26 – 1.98)	0.519
Age	0.99 (0.948-1.033)	0.634	0.98 (0.92 – 1.04)	0.461
Gender (Female vs. Male)	1.665 (0.602-4.610)	0.326	1.57 (0.61 – 4.01)	0.349
Educational Level	1.372 (0.948-1.986)	0.093	2.51 (0.79 – 8.02)	0.120
Area of Residence	0.622 (0.295-1.314)	0.213	0.65 (0.30 – 1.41)	0.271
CES-D-10 Score	1.05 (0.99 – 1.11)	0.079	1.06 (0.99 – 1.13)	0.118
BMI	1.00 (0.93 – 1.07)	0.947	0.99 (0.90 – 1.10)	0.913

To correct for the significant attrition bias, an IPW model was applied. This correction fundamentally altered the risk landscape, revealing clinically coherent associations. In the final IPW-weighted model, renal impairment emerged as a strong and independent

risk factor for incident cancer (OR=4.70, 95% CI: 1.35–16.38, P=0.015).
The corrective power of the IPW model was further evidenced by the reversal of the dyslipidemia association, which became a significant risk factor (OR=3.46, 95% CI: 1.21–9.91). Conversely, the previously significant association for hypertension was nullified (P=0.883), indicating the initial finding was an artifact of bias. In the final weighted model, heart disease remained a significant risk factor (OR=2.63), while current smoking showed an even stronger, albeit counterintuitive, protective association (OR=0.14). These IPW-adjusted results are considered the primary, most reliable findings of the study.

4. Discussion

In this prospective cohort study of middle-aged and older Chinese adults, our primary and most robust finding, derived from an IPW-adjusted model, demonstrates that renal impairment is a strong and independent risk factor for incident cancer (OR=4.70). This study underscores the critical importance of rigorous methodology, as initial uncorrected analyses produced misleading results. Our principal finding aligns with growing evidence linking CKD to elevated cancer risk (9). The biological mechanisms are likely multifactorial. Our baseline data showed renal impairment was associated with higher C-reactive protein, a marker of systemic inflammation, which is a well-established driver of carcinogenesis (10). Furthermore, the uremic state itself may increase susceptibility by causing an accumulation of potential carcinogens, oxidative stress, and profound immune system dysregulation (11). This inflammation-driven pathway is mirrored in other conditions like severe burns, which also induce systemic inflammation and known malignancies (e.g., Marjolin's ulcers) (12).
A central narrative of this study is the methodical correction of severe bias. Initial logistic regression models failed to detect the risk from renal impairment and produced counterintuitive results, such as a "protective" effect for dyslipidemia and smoking. These paradoxes highlighted significant underlying bias from rare events (n=32) and high attrition (39.1%). While Firth’s penalized regression offered a partial correction for rare events, it could not address the selection bias. The pivotal contribution was the IPW analysis. The dramatic reversal of the dyslipidemia association from protective to a significant risk factor, and the nullification of the hypertension risk, demonstrated the extent to which attrition bias distorted the findings. Our final IPW-weighted model provides a clinically more coherent and plausible risk profile compared to unadjusted models, underscoring that such adjustments are essential for the validity of longitudinal studies with high attrition.
A critical, counterintuitive finding was the strong inverse association for current smoking (IPW-adjusted OR=0.14), a paradox that persisted despite IPW adjustment, contradicting its known carcinogenic role. While IPW corrected other biases (e.g., dyslipidemia), its failure here warrants caution. This anomaly may stem from residual confounding by unmeasured factors (like health-seeking behavior) or unaddressed selection bias, such as competing risks where smokers died from other causes first (a "healthy-survivor" effect). Additionally, the rare outcome (n=32) may have caused model instability, highlighting the complex limitations of IPW in observational cohorts.

These findings have significant implications for oncology nursing. Nurses should advocate for enhanced cancer screening in CKD patients. Post-diagnosis, complex management is required, from meticulous chemotherapy dose adjustments to disentangling overlapping symptoms (e.g., uremic vs. treatment fatigue) (13). The dual burden also demands nursing research into targeted symptom and psychosocial support models (14). From a health systems perspective, this study strongly supports the development of integrated onco-nephrology care pathways, potentially led by nurse navigators, to guide this high-risk population across the care continuum (15).

This study has limitations. Cancer ascertainment was based on self-report, which is subject to recall bias. The 4-year follow-up is relatively short for cancer development, contributing to the rare event count. Lastly, while our model adjusted for many covariates, residual confounding from unmeasured variables is possible, and IPW cannot correct for unobserved factors influencing attrition.

5. Conclusion

Our rigorous analysis, correcting for severe bias, identifies renal impairment as an independent cancer risk factor. This finding underscores the need for cancer surveillance in CKD patients.

Declarations

Ethical Approval and Consent to participate

The National School of Development at Peking University provided the data sets in the CHARLS. The original CHARLS study was approved by the Institutional Review Board (IRB) of Peking University (approval number: IRB00001052-11015 for the household survey and IRB00001052-11014 for blood samples). All participants provided written informed consent.

Human Ethics

This study does not involve human clinical trials.

Consent for publication

All authors have read and agreed to the published version of the manuscript.

Availability of supporting data

The author confirms that all data generated or analysed during this study are included in this published article.

Competing interests

The authors have no conflicts of interest to declare.

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Authors' contributions

Conceptualization, L.D.; methodology, L.D.; software, L.D.; validation, L.D., S.L. and T.L.; formal analysis, T.L.; investigation, L.D.; resources, L.D.; data curation, L.D.; writing — original draft preparation, L.D.; writing — review and editing, T.L.; visualization, S.L.; supervision, T.L.; project administration, T.L.; funding acquisition, T.L.

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