

News Release

Title

Association of kidney function with cancer incidence and its influence on cancer risk of smoking: the Japan Multi-Institutional Collaborative Cohort Study

Key Points

- In the Japanese population, the association between estimated glomerular filtration rate (eGFR) and cancer incidence was U-shaped, with elevated cancer risk in individuals with moderately low and high eGFRs.
- Cancer risk from smoking increased with lower eGFR.
- These results can help optimize medical care, for example, by identifying populations at high risk of cancer and providing proactive screening tests or by providing focused smoking cessation support for patients with impaired kidney function.

Summary

A research group led by Shimon Kurasawa, Takahiro Imaizumi, and Shoichi Maruyama of the Department of Nephrology, Nagoya University Graduate School of Medicine, has investigated the association of eGFR with cancer incidence and mortality, as well as the differences in cancer risk factors between individuals with and without kidney dysfunction using the follow-up data from the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study. The main findings are as follows: (1) moderately low and high eGFRs were independent cancer risk factors; (2) high eGFR was also associated with a higher risk of cancer mortality; (3) the cancer risk from smoking was higher in patients with lower eGFR. This study was supported by the Platform of Supporting Cohort Study and Biospecimen Analysis (CoBiA) and conducted in collaboration with Dr. Keitaro Matsuo (Chief, Division of Cancer Epidemiology and Prevention, Aichi Cancer Center, Nagoya, Japan), Dr. Kenshi Wakai (Professor, Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan), and other researchers from the J-MICC Study.

Chronic kidney disease (CKD) is one of the major public health problems, affecting approximately one in eight Japanese adults. Several studies have reported the association of reduced kidney function with cancer incidence; however, the results have been inconsistent, with limited data on the Japanese population. In addition, it is unknown whether cancer risk

factors are influenced by kidney function.

The group investigated the association of eGFR with cancer incidence and mortality and the interaction between eGFR and other cancer risk factors regarding cancer incidence by analyzing approximately 55,000 participants of the J-MICC Study with an almost 10-year follow-up period. Compared with eGFR of 60–74 mL/min/1.73 m², moderately low eGFR (30–44 mL/min/1.73 m²) was associated with a 36% higher risk, and high eGFR (≥ 75 mL/min/1.73 m²) with a 9–18% higher risk of cancer incidence; the relationship between eGFR and cancer incidence was U-shaped. Cancer risk from smoking was found to be increased with lower eGFR. These results can be used to optimize medical care, for example, by conducting active screening tests on people at high risk of cancer incidence, or by providing focused smoking cessation support for patients with impaired kidney function.

Research Background

Chronic kidney disease (CKD) is one of the global public health problems, with a prevalence of 9–13% worldwide. The number of patients with CKD in Japan is estimated to be approximately 13 million. Patients with CKD requiring dialysis therapy are known to have a higher risk of cancer incidence due to chronic inflammation, oxidative stress, immunodeficiency, and malnutrition. In several studies, even CKD not requiring dialysis has been reported to be associated with a higher risk of cancer incidence. In addition, patients with kidney failure are also reported to be associated with elevated cancer mortality rates, which may be because of the lack of standard treatment or a higher incidence of adverse events. It is also known that patients with cancer are prone to kidney dysfunction due to the cancer itself or anticancer drugs. In this context, the relationship between cancer and kidney dysfunction is of great importance in clinical practice and has been drawing attention with the new term ‘onco-nephrology.’ However, the results of the association of kidney function with cancer incidence in previous reports are inconsistent; some reports suggest that the lower eGFR, the higher the cancer incidence, and others indicate that not only low eGFR but high eGFR are also associated with a higher risk of cancer incidence. There are racial differences regarding cancer incidence. Additionally, data on the Japanese population are limited. It is also unknown whether other cancer risk factors are affected by kidney function.

Identifying individuals with a higher risk of developing cancer, especially which organs are more prone to cancer, can help optimize medical practice by actively screening high-risk individuals and organs. If there are some cancer risk factors specific to patients with kidney dysfunction,

interventions to improve the factors may prevent cancer. Therefore, the research group investigated the association of kidney function with cancer incidence using the follow-up data from the J-MICC Study and assessed whether there are differences in the cancer risk factors such as smoking, alcohol consumption, dietary habits, and obesity between those with preserved and reduced kidney function.

Research Results

A total of 55,242 individuals aged 35–69 years who participated in the J-MICC Study from 2005 to 2014 and had baseline eGFR and follow-up data were divided into 6 groups according to eGFRs at enrollment of 10–29, 30–44, 45–59, 60–74, 75–89, and ≥ 90 mL/min/1.73 m². Cancer incidence (all cancers and site-specific cancers) and mortality were compared between the groups. After the overall analysis, subgroup analyses of participants with eGFRs ≥ 60 and < 60 mL/min/1.73 m² were conducted to assess whether the kidney function modifies other cancer risk factors.

Association of kidney function and cancer incidence

During a median follow-up period of 9.3 years, 4,278 (7.7%) participants were diagnosed with cancer.

In the multivariable analysis, moderately low and high eGFRs were associated with a higher risk of cancer incidence; compared with eGFR of 60–74 mL/min/1.73 m², the adjusted hazard ratios (95% confidence intervals) for eGFRs of ≥ 90 , 75–89, 45–59, 30–44, and 10–29 mL/min/1.73 m² were 1.18 (1.07–1.29), 1.09 (1.01–1.17), 0.93 (0.83–1.04), 1.36 (1.00–1.84), and 1.12 (0.55–2.26), respectively. Thus, the association between eGFR and cancer incidence was U-shaped. The analyses of site-specific cancers showed trends toward a higher risk of gastric and kidney cancers with lower eGFR; however, these results were not statistically significant due to the limited sample size of lower eGFR groups. On the other hand, the risk of colorectum cancer was similar between the eGFR-based groups.

Association of kidney function and cancer mortality

During the observation period, 1,589 (2.9%) deaths occurred, of which 826 (53%) were due to cancer. High eGFRs were associated with a higher risk of cancer mortality; compared with eGFR of 60–74 mL/min/1.73 m², the adjusted subdistribution hazard ratios (95% confidence intervals) for eGFRs of ≥ 90 , 75–89, 45–59, 30–44, and 10–29 mL/min/1.73 m² were 1.58 (1.29–1.94), 1.27 (1.08–1.50), 0.94 (0.73–1.22), 1.46 (0.79–2.70), and 0.89 (0.20–3.97), respectively. Low eGFR was not statistically associated with cancer mortality;

however, it would not be possible to conclude from this analysis because the statistical power was inadequate due to the relatively small number of individuals with eGFR <45 mL/min/1.73 m². A possible reason for the higher risk of cancer mortality in patients with high eGFR may be that many weakened patients with low muscle mass were included in the high eGFR group. Alternatively, patients with high eGFR may not receive the appropriate dose of chemotherapeutic agents due to the inability to assess accurate kidney function.

Influence of kidney function on cancer risk associated with other factors

The subgroup analyses of participants with eGFRs ≥ 60 and <60 mL/min/1.73 m² showed that the cancer risk of smoking and a family history of cancer was higher in those with eGFR <60 mL/min/1.73 m², with significant interactions. The cancer risk of smoking increased with lower eGFR consistently across the entire eGFR range. One possible reason for this interaction is that carcinogens in cigarettes excreted by the kidneys are prone to accumulate in the body as kidney function declines. The cancer risk of a family history of cancer increased with lower eGFR only in individuals with eGFR <60 mL/min/1.73 m². Common genetic factors for kidney dysfunction and cancer and shared lifestyle and environmental factors among family members might be involved.

Research Summary and Future Perspective

The results of this study provided a basis for greater attention to cancer incidence in individuals with moderately low and high eGFRs. In particular, active screening for gastric and kidney cancers may be beneficial for patients with kidney dysfunction. Further investigation on the association of not only low eGFR but also high eGFR with a higher risk of cancer incidence may deepen medical knowledge on carcinogenesis.

The result that cancer risk from smoking increased with lower eGFR suggests that avoidance of smoking is even more important for cancer prevention in patients with impaired kidney function than in the general population. Therefore, this can give a rationale for providing focused smoking cessation support for patients with reduced kidney function.

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