

COMMENTARY

Possible combinatorial effects of current smoking and alcohol intake on chronic kidney disease in a Japanese nationwide cross-sectional survey

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Chronic kidney disease (CKD) affects more than 200 million people worldwide and over 13 million adults in Japan.¹ Although CKD can occur at any age, it becomes more common in aging populations, and its prevalence is increasing. Importantly, CKD can be both a cause and a consequence of cardiovascular disease (CVD) and is presently a critical worldwide healthcare issue that represents a large and growing unmet medical need. Unfortunately, there is no definitive, curative treatment to block the process of CKD progression, with the exception of kidney transplantation, and CKD is closely associated with poor health outcomes, including CVD complications and increased mortality.¹ CKD is a risk factor for CVD morbidity and mortality, and several established cardiovascular risk factors, including diabetes, hypertension, dyslipidemia, hyperuricemia and visceral obesity, are also risk factors for CKD.^{1,2}

In addition to the established risk factors for the development of CKD, several modifiable lifestyle factors, including physical activity, smoking and diet factors such as alcohol intake, are associated with the development of obesity and obesity-related disease and may also be associated with the development of CKD, at least partially via obesity-related pathways.³ Thus, it is plausible that CKD is also closely associated with lifestyle, and several previous studies have investigated

the association between lifestyle factors and the development of CKD.^{3–8} Cigarette smoking is reportedly associated with an increased risk of CKD.⁴ Alcohol may have both positive and negative effects.⁴ Although moderate alcohol consumption is associated with a decreased risk, heavy alcohol consumption is associated with an increased risk of CKD.⁴ However, because CKD would be closely associated with a combination of lifestyle modifications rather than with changes in each factor individually,⁴ the results for several lifestyle factors are inconsistent, and few studies have investigated the impact of overall dietary patterns on CKD.^{3,5–8} A combination of healthy lifestyle factors, such as abstaining from smoking, preventing obesity, consuming alcohol moderately, exercising regularly and having a healthy diet, reportedly reduces CVD risk significantly, and a linear relationship was observed between CVD risk reduction and the number of healthy lifestyle factors displayed in each study.⁴ This observation suggests that an analysis using a combination of lifestyle factors may capture the influence of multiple health behaviors better than an analysis based on a single health behavior because health behaviors are complex and consist of multiple dimensions.⁴

Interestingly, to examine whether current smoking is an effective modifier of the association between CKD and alcohol consumption, Matsumoto *et al.*⁹ performed a related cross-sectional study on a population of people who presented for a health checkup under a program that targets the insured population aged ≥ 40 years using data from the Specific Health Check and Guidance in Japan. Of the 506 807 participants aged 40 years or older, 292 013 (57.6%) were included

in their analysis, and outcomes were kidney dysfunction, indicated by an estimated glomerular filtration rate (eGFR) less than $60 \text{ ml min}^{-1} \text{ per } 1.73 \text{ m}^2$, and proteinuria.⁹

In their analysis, the authors calculated the odds ratio of each drink score using univariate and multivariate logistic regression models, excluded people with a past medical history of CVD and CKD, divided participants into current smoking and non-current smoking groups and used the presence of proteinuria as the dependent variable.⁹ In addition, the authors calculated the odds ratio of each drink score using univariate and multivariate logistic regression models, excluded people with a past medical history of CVD and CKD, divided participants into current smoking and non-current smoking groups, and used the presence of $\text{eGFR} < 60 \text{ (ml min}^{-1} \text{ per } 1.73 \text{ m}^2)$ as the dependent variable.⁹

In the results of their study, drinking a small amount of alcohol was associated with a lower prevalence of proteinuria in non-current smokers.⁹ However, in current smokers in the same study, the association between alcohol and proteinuria was not observed.⁹ In addition, the analysis using $\text{eGFR} < 60 \text{ ml min}^{-1} \text{ per } 1.73 \text{ m}^2$ revealed that in both smokers and non-current smokers, alcohol consumption was inversely associated with the risk of CKD.⁹ Therefore, in this large-scale, cross-sectional study, the authors examined the association between alcohol and current smoking and CKD in a Japanese population and concluded that mild-to-moderate alcohol consumption is associated with a lower risk of CKD (proteinuria and eGFR), especially among non-smokers.⁹ These results are interesting and important for understanding the pathogenesis of CKD.

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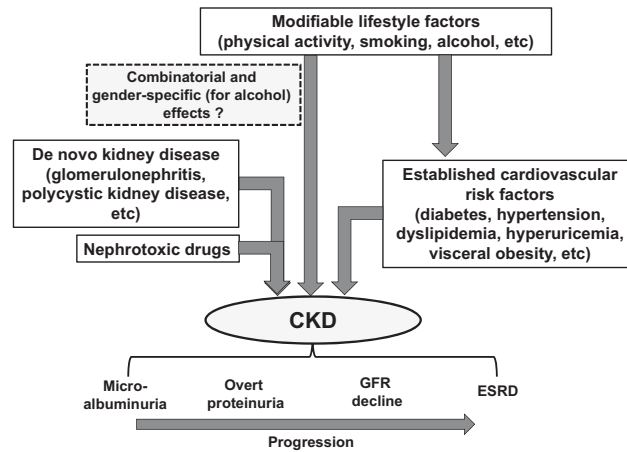


Figure 1 Schema of the possible combinatorial effects of current smoking and alcohol intake on chronic kidney disease. CKD, chronic kidney disease; ESRD, end-stage renal disease; GFR, glomerular filtration rate.

Several results presented in the study by Matsumoto *et al.*⁹ need further explanation. In male non-current smokers, a drink score of either 2 (= <19 g per day) or 3 (20–39 g per day) was significantly associated with lower prevalence of proteinuria, but there was no significant reduction of proteinuria with a drink score of 1 (occasionally), as shown in Table 3 of their manuscript.⁹ On the other hand, in female non-smokers, a drink score of either 2 (= <19 g per day) or 3 (20–39 g per day) was not significantly associated with a lower prevalence of proteinuria, but there was a significant reduction in proteinuria with a drink score of 1 (occasionally), as shown in Table 4 of their manuscript.⁹ How do the authors explain these inconsistent results? According to the author’s discussion, there are gender-specific differences related to the intensity of the effects of the alcohol intake (Figure 1). Smoking status and alcohol intake reportedly increase the likelihood of fibrosis and cirrhosis and the risk of hepatic carcinoma and upper gastrointestinal tract malignancy in women with chronic liver disease more than in men.¹⁰ Although the relevant mechanisms of these gender effects are unknown, they might help explain the differences in the effects on men and women based on the quantity of alcohol consumed.⁹

Although this is a large-scale study, the nature of the study is cross-sectional. Therefore, the authors should be cautious when making conclusions about causal relationships from the results of the present study, even if they seem to be theoretically plausible. Nevertheless, mild-to-moderate alcohol consumption might be associated with a lower risk of CKD (proteinuria and eGFR), especially among non-current smokers, because current smoking could modify the potential benefits of mild-to-moderate alcohol consumption and inhibit CKD progression. Further longitudinal studies are needed to examine the causal relationships related to the findings obtained in the present study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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