Original Article

Causal associations between 45 dietary intake habits and urolithiasis: insights from genetic studies

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Background: Different dietary habits can have varying effects on human health and metabolism, and these can be intervened and regulated. Kidney stones, as a disease caused by multiple factors, are largely attributed to diet and metabolism, but the potential causal relationship with dietary intake habits remains unclear. Therefore, this study aims to link the predicted dietary intake based on 45 genetic factors with urolithiasis and explore the potential causal relationship.

Methods: We extracted complete genome-wide association studies (GWASs) data on 45 dietary intake traits from the UK Biobank study. Data on kidney stones were obtained from the FinnGen database. In both univariable and multivariable Mendelian randomization analyses, we used inverse variance weighted (IVW) as the primary method to calculate P values, odds ratios (ORs), and 95% confidence intervals (CIs). We examined result heterogeneity using Cochran's Q test. We also carefully investigated potential sources of horizontal pleiotropy using the Mendelian randomization (MR)-PRESSO and MR-Egger methods, and conducted linkage disequilibrium score regression (LDSC) analysis on the corrected P values.

Results: Through univariable analysis, we identified 11 dietary habits that potentially causally associate with kidney stones among the 45 examined traits, including 9 protective factors and 2 risk factors. Based on the corrected results with false discovery rate (FDR) and sensitivity analysis, we found one relatively robust evidence. We controlled for common stone risk factors, such as body mass index and smoking, as confounders in multivariable analysis, and no significant results were observed after controlling for these confounders. Based on the LDSC analysis, most of the evidence supports significant genetic correlations with urolithiasis among the 11 traits with potential causal associations.

Conclusions: This study confirms the impact of certain dietary factors on the development of kidney stones. Our findings contribute to providing evidence for dietary adjustments in daily life or dietary guidance specifically targeting kidney stone patients.

Keywords: Diet; dietary habits; FinnGen; urolithiasis; Mendelian randomization (MR)

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Introduction

Urinary stone disease is one of the most common diseases in urology and a challenging global public health issue. Surprisingly, the incidence rate of urolithiasis in Europe has reached as high as 5–9% and continues to rise. On the other hand, the high recurrence rate of stone formers has become a challenging problem that requires expensive medical costs to manage (1,2). Currently, treatment options for urinary stone disease mainly include surgical intervention, ESWL, and medical therapy (3). However, these conventional treatment approaches fail to effectively prevent disease recurrence and pose potential surgical risks, medication side effects, and substantial economic losses. Therefore, it is imperative to focus on disease prevention and intervention for alleviation of the disease recurrence. Renal and ureteral stones, as systemic multifactorial diseases, are closely related to metabolic processes in the body (4), and dietary habits have a significant impact on kidney stones and urine metabolism. Previous studies have found that high sulfur-containing animal proteins, such as beef and pork, generate more acid load, thereby promoting the formation of kidney stones, and have suggested that sufficient dietary intake of fruits and vegetables can reduce the risk of stone recurrence (5,6). They also supported the findings that beverages such as orange juice, alcohol, coffee, and tea are negatively associated with the formation of kidney stones (6). Certainly, besides various dietary habits can interacting with kidney stones in multiple ways, there exist confounding factors beyond diet that can influence the disease. Therefore, it is necessary to further evaluate the relationship between them accurately using scientific methods. In this study, we employed Mendelian randomization (MR) analysis, which naturally eliminates the interference of confounding factors in the environment at the genetic level. Single nucleotide polymorphisms (SNPs) as instrumental variables (IVs) for the exposure (e.g., various dietary habits) are used to estimate whether there is a causal relationship between the exposure and the outcome. Previous studies have utilized MR analysis to investigate the causal associations between coffee, tea, alcohol intake and frequency, fresh fruit consumption, and kidney stones (7-10). However, these studies only focused on a limited part of dietary habits and did not accurately classify different types of alcoholic beverages. Diverse types of alcohol may have different effects on upper urinary tract stones and lower urinary tract stones. For example, punch is positively associated with the formation of urinary stones, while beer has a protective effect against stone formation (11,12). As a result, our study aims to use the MR analysis approach to determine the relationship between dietary habits and urinary stones, which can help in preventing the occurrence of urinary stones effectively through the regulation of modifiable dietary patterns. We present this article in accordance with the STREGA reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-79/rc).

Highlight box

Key findings

- This study identified 11 dietary habits that potentially causally associate with kidney stones, including 9 protective factors and 2 risk factors. Genetic correlations with urolithiasis were found among these traits.

What is known and what is new?

- It is known that diet and metabolism play a role in kidney stone development, but the causal relationship with specific dietary intake habits was unclear.
- This study provides new evidence linking genetic-based dietary intake with urolithiasis.

What is the implication, and what should change now?

- The findings suggest the importance of dietary adjustments in daily life for kidney stone prevention and management. Healthcare providers may consider tailored dietary guidance targeting kidney stone patients based on genetic factors and identified dietary habits.

Methods

Study design and data source

The research workflow framework for analysis is shown in *Figure 1*. In this study, we used 45 dietary habits as exposures, including cereal, bread, fruit and vegetables, meat and fish, dairy products, drinks, salt, and other food intake habits. The relevant genome-wide association studies (GWASs) summary data were obtained from the integrative epidemiology unit (IEU) Open GWAS project, which recruited over 500,000 participants from European populations between 2006 and 2010 (13). The participants' dietary frequency data on common foods and beverages over the past year were collected through touchscreen questionnaires. Smoking and body mass index (BMI) are common risk factors for stone formation (14-16), so we collected data on these risk factors from the

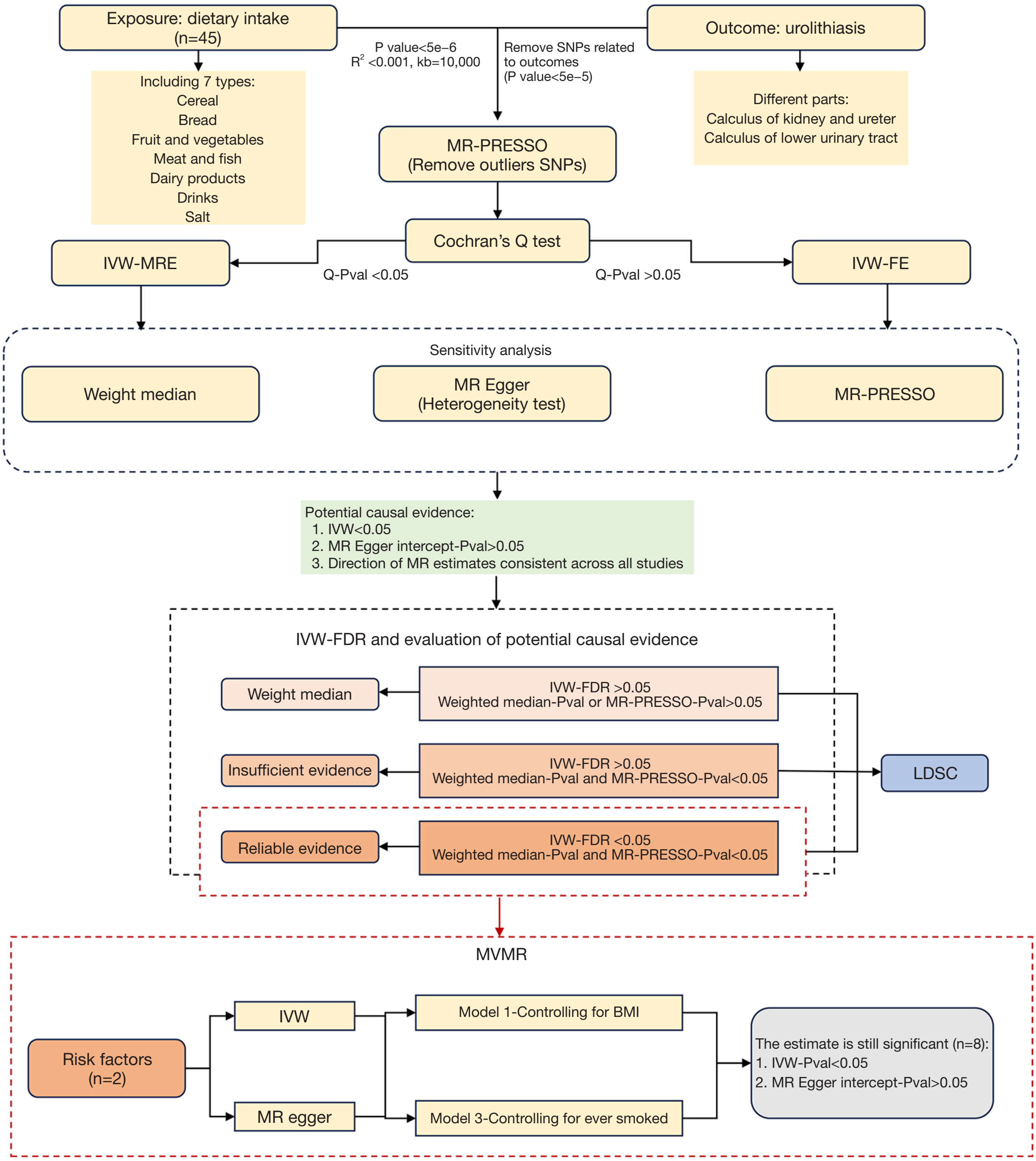

Figure 1 The flowchart of study design. MR, Mendelian randomization; SNPs, single nucleotide polymorphisms; IVW-FE, inverse variance weighted method with fixed effects; MRE, models of random effect; FDR, false discovery rate; LDSC, linkage disequilibrium score regression; MVMR, multivariable MR; BMI, body mass index.

same source. Additionally, to control for these risk factors, they were included in the multivariable analysis together with significant MR results of risk factors. Urinary stone disease was considered as the outcome. Urinary stone disease includes upper urinary tract stones and lower urinary tract stones. However, most studies have only focused on upper urinary tract stones and even consider them as synonymous with urinary stone disease, while neglecting the less common lower urinary tract stones. To comprehensively investigate the causal relationship between dietary habits and urinary stone disease, we have made a more detailed classification of urinary stone

Table 1 Description of GWAS data sources for each phenotype

Dataset type	Variable	GWAS ID	Sample size	Consortium	Journal	Population	Sex
Exposure	Dietary habits	See Table S1		MRC-IEU	*Nature*	European	Males and females
	BMI	ukb-b-19953	461460	MRC-IEU	*Nature*	European	Males and females
	Ever smoked	ukb-b-20261	461066	MRC-IEU	*Nature*	European	Males and females
Outcome	Calculus of kidney and ureter	NA	376406	FinnGen	*Nature*	European	Males and females
	Calculus of lower urinary tract	NA	368091	FinnGen	*Nature*	European	Males and females

GWAS, genome-wide association study; GWAS ID, identity document of GWAS; BMI, body mass index; MRC, the medical research council; IEU, integrative epidemiology unit.

disease. Additionally, clarifying the location of the stone will aid in more subsequent detailed research and clinical recommendations. we obtained GWAS summary data for upper urinary tract stones (kidney and ureter) and lower urinary tract stones from the latest version (version 9) of the FinnGen consortium database (17). The former included 9,713 cases and 366,693 controls based on ICD-10 criteria, and the latter identified 1,398 cases and 366,693 controls based on ICD-10 codes. Detailed information and data sources for the 45 dietary habits and kidney stone outcomes can be found in Table S1 and *Table 1*. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Selection of genetic instrument for diet habits

We applied a parameter threshold of P<5e−6 to filter the SNPs for the IVs representing dietary intake habits. We also employed the linkage disequilibrium (LD) clumping method with parameters r^2=0.001 and kb =10,000 to remove SNPs in linkage disequilibrium. To exclude SNPs that may be associated with the outcome, we set the filtering criteria as P<5e−5. Next, we applied a threshold of F-statistic >10 to exclude weak IVs. MR-PRESSO proves to assess horizontal pleiotropy and identify outliers. After removing the outliers, we proceeded with the final MR analysis using the remaining IVs (18).

Statistical analysis

Statistical analyses in this study were performed using the r4.3.0 software, with the packages "TwoSampleMR" and "MRPRESSO". In the primary univariable and two-sample analyses, the inverse variance weighted (IVW) method was the main statistical approach used to assess the causal relationship between exposure and outcome. Before conducting the analysis, we assessed heterogeneity among the included studies using Cochran's Q test. If heterogeneity was present, the random-effects IVW model was used; otherwise, the fixed-effects IVW model was employed (19). We conducted sensitivity analyses using multiple MR methods, including weighted median, MR Egger, and MR-PRESSO, to examine potential outliers and horizontal pleiotropy issues, thereby enhancing the reliability of the data and results (20-22). Subsequently, we performed false discovery rate (FDR) correction on the significant p-values obtained from the IVW method and integrated the corresponding sensitivity analysis results to further stratify the evidence for potential causal relationships into "reliable", "insufficient", and "weak" levels. The criteria for evaluation were as follows: (I) corrected P value less than 0.05. (II) Significant estimates (P value less than 0.05) from MR-weighted median and MR-PRESSO, respectively. Next, we conducted multivariable MR (MVMR) analysis, which adjusts for the effects of multiple exposures on the outcome and provides direct causal estimates for individual exposures (23). In MVMR, we controlled for BMI and smoking status as covariates and used the IVW method and MR Egger to estimate whether the included models with potential causal associations had positive results and whether there was horizontal pleiotropy after FDR correction. Additionally, we performed MR Steiger analysis to explore the reverse causation of our causal relationships (24). Finally, to address the issue of collinearity among multiple exposure phenotypes, we used the linkage disequilibrium score regression (LDSC) R package to perform LDSC analysis on the FDR-corrected significant results, evaluating the genetic correlation (Rg) between pairs of phenotypes. If the results were not statistically significant, it indicated the absence of collinearity (25).

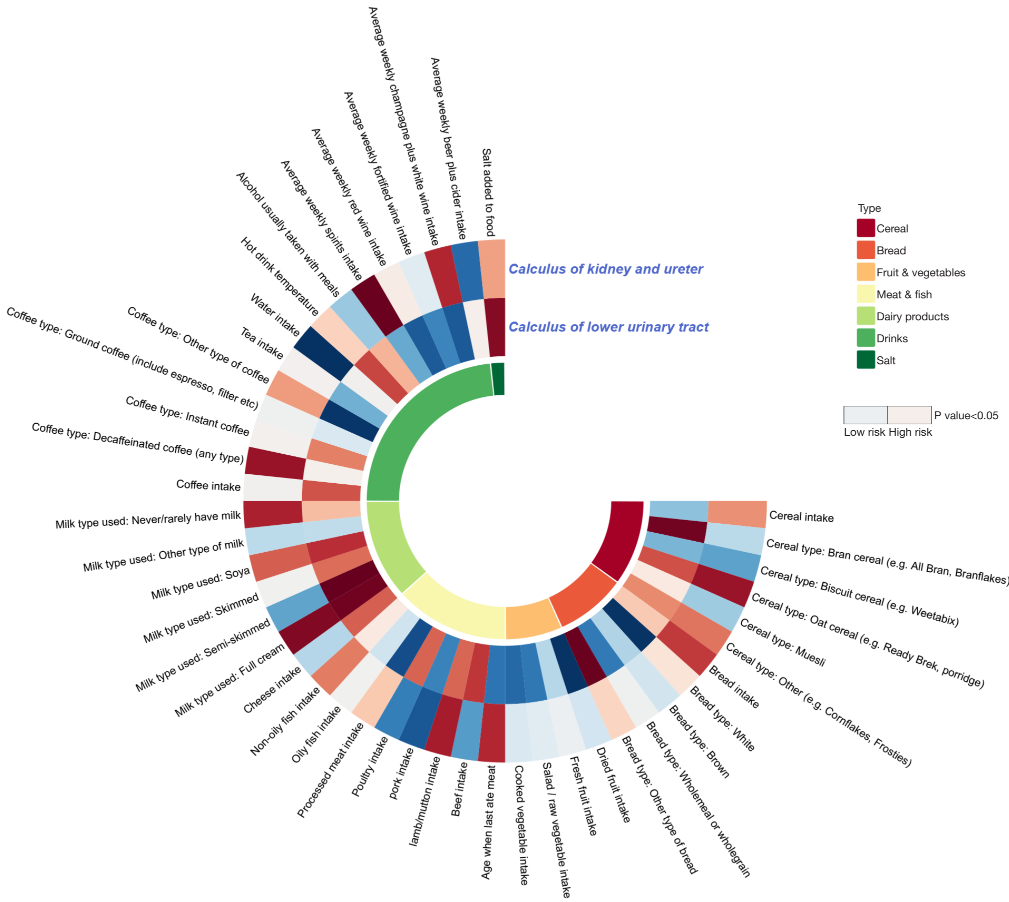

Figure 2 Circle heatmap of Mendelian randomization associations between the 45 dietary intakes and urolithiasis using the IVW method. IVW, inverse variance weighted.

Results

Univariate MR analysis

We conducted various univariable MR analysis methods and FDR correction analysis of P values to examine the associations between 45 dietary habits and different types of urinary stones. The analysis results were then stratified and evaluated based on specific criteria, leading to the identification of 11 potential causal associations, including 1 with reliable evidence, 4 with insufficient evidence, and 6 with weak evidence. The summary results of all univariable IVW analyses and sensitivity analyses can be found in *Figure 2* and Tables S2-S4, while the FDR correction results are presented in Table S5. Among the common dietary habits, tea intake was the only one with reliable causal evidence. Even after FDR correction, it remained significantly associated with a reduced risk of upper urinary stones in the kidney and ureter [odds ratio (OR) =0.516, 95% confidence interval (CI): −0.928 to −0.394, P=1.17E−06, FDR =5.28E-05, weighted median-Pval =1.53E−03, MR-Presso-Pval =6.61E−07]. However, it did not show a significant impact on lower urinary stones (OR =0.818, 95% CI: 0.468 to 1.429, P=4.80E−01, FDR =9.99E−01). Among the associations with insufficient evidence, three dietary habits showed evidence of reducing the risk of upper urinary stones: oily fish (OR =0.71, 97% CI: 0.54 to 0.935, P=0.015, FDR =0.165, weighted median-Pval =2.55E−02, MR-Presso-Pval =1.58E−02), wholemeal or wholegrain bread (OR =0.508, 95% CI: 0.276 to 0.935, P=0.03, FDR =0.212, weighted median-Pval =1.29E−02, MR-Presso-Pval =3.26E−02), and fresh fruit (OR = 0.656, 95% CI: 0.435 to 0.99, P=0.045, FDR =0.252, weighted median-Pval =1.11E−02, MR-Presso-Pval =4.67E−02). However, instant coffee was positively

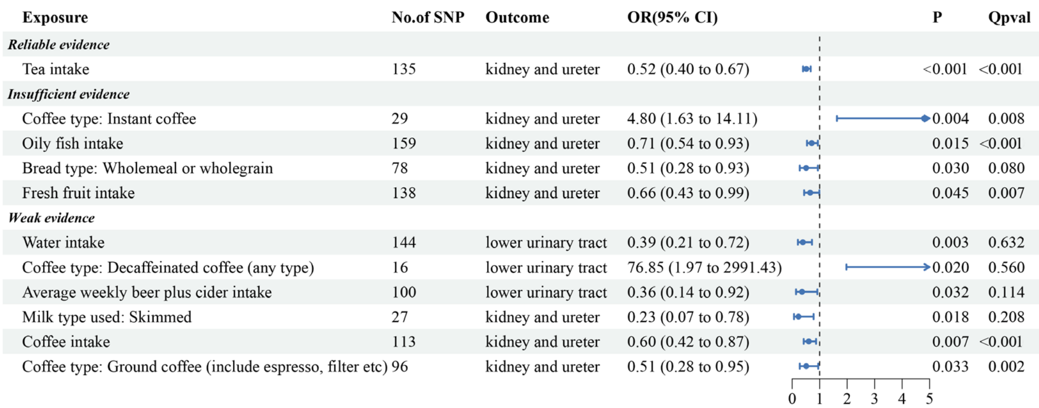

Figure 3 The assessment of the strength of potential causal associations after evaluation by FDR correction and sensitivity analysis, showing the results by the IVW method. SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval; FDR, false discovery rate; IVW, inverse variance weighted.

Table 2 MVMR analysis in two causality evidences

Exposure	Outcome	M1		M2	
		IVW-P value	Egger-P value	IVW-P value	Egger-P value
Coffee type: instant coffee	Calculus of kidney and ureter	1.84E−01	3.21E−10	1.58E−01	7.10E−01
Coffee type: decaffeinated coffee (any type)	Calculus of lower urinary tract	2.63E−01	8.42E−06	4.47E−01	8.99E−01

M1: controlling for BMI; M2: controlling for ever smoked. MVMR, multivariable Mendelian randomization; IVW, inverse variance weighted; BMI, body mass index.

associated with upper urinary stone formation (OR =4.796, 95% CI: 1.63 to 14.113, P=0.004, FDR =0.099, weighted median-Pval =2.40E−02, MR-Presso-Pval =1.41E−02). We found weak evidence for six causal associations: skimmed milk was negatively associated with upper urinary stone risk (OR =0.230, 95% CI: 0.068 to 0.780, P=0.018, FDR =0.165, weighted median-Pval =1.08E-01, MR-Presso-Pval =2.61E−02), while water (OR =0.388, 95% CI: 0.209 to 0.721, P=0.003, FDR =0.124, weighted median-Pval =3.57E−01, MR-Presso-Pval =2.64E−03), average weekly beer plus cider (OR =0.359, 95% CI: 0.141 to 0.916, P=0.032, FDR =0.481, weighted median-Pval =6.86E−02, MR-Presso-Pval =3.45E−02), and decaffeinated coffee (any type) (OR =76.845, 95% CI: 1.974 to 2.99E+03, P=0.020, FDR =0.453, weighted median-Pval =1.97E−01, MR-Presso-Pval =2.73E-02) were associated with lower urinary stones, coffee intake (OR =0.604, 95% CI: 0.42 to 0.869, P=0.007, FDR =0.1, weighted median-Pval =6.19E−02, MR-Presso-Pval =3.86E−03) and ground coffee (OR =0.512, 95% CI: 0.277 to 0.947, P=0.033, FDR =0.212, weighted median-Pval =1.53E−03, MR-Presso-Pval =6.22E−02) might being able to reduce the risk of upper urinary stone. Furthermore, we summarized and evaluated the potential causal associations identified by the IVW method in terms of their strength, as shown in *Figure 3*.

Multivariate MR analysis

Table 2 presents the results of the multivariable analysis after adjusting for confounding factors. In the univariable analysis, we observed that instant coffee was positively associated with the risk of kidney and ureter stones, while decaffeinated coffee was found to increase the risk of lower urinary stones. However, after adjusting for BMI and smoking status, both variables lost their significance in the multivariable analysis, suggesting that these factors may confound the association. Additionally, the MR Egger intercept tests did not indicate significant pleiotropy in the positive results, providing further

Table 3 Results of LDSC for all positive results in univariate analysis

Level of evidence	Phenotype 1	Phenotype 2	Rg	Se	P
Reliable evidence	Tea intake	Calculus of kidney and ureter	−2.29E−01	3.98E−02	8.25E−09
Insufficient evidence	Coffee type: instant coffee	Calculus of kidney and ureter	9.80E−02	6.14E−02	1.10E−01
	Coffee intake	Calculus of kidney and ureter	−7.71E−02	4.73E−02	1.03E−01
	Oily fish intake	Calculus of kidney and ureter	−9.43E−02	4.02E−02	1.91E−02
	Coffee type: ground coffee (include esPRESSO, filter etc.)	Calculus of kidney and ureter	−1.20E−01	4.59E−02	8.87E−03
	Fresh fruit intake	Calculus of kidney and ureter	−1.69E−01	3.89E−02	1.34E−05
Weak evidence	Milk type used: skimmed	Calculus of kidney and ureter	−2.18E−02	6.52E−02	7.39E−01
	Water intake	Calculus of lower urinary tract	−7.46E−02	7.20E−02	3.00E−01
	Coffee type: decaffeinated coffee (any type)	Calculus of lower urinary tract	2.36E−01	1.38E−01	8.74E−02
	Average weekly beer plus cider intake	Calculus of lower urinary tract	−1.73E−01	8.13E−02	3.32E−02

LDSC, linkage disequilibrium score regression; Rg, genetic correlation. Se, standard error.

support for the robustness of the results.

Rg analysis

To further investigate the genetic basis of the identified associations, we conducted the LDSC analysis on all potential causal associations (*Table 3*). The LDSC analysis results revealed that most of the evidence supported significant Rgs with urinary stones. However, in the case of coffee intake, instant coffee, and water, no significant Rgs were observed (P>0.05), indicating that the observed associations may not be driven by underlying genetic factors.

Discussion

We conducted a univariable two-sample MR analysis to examine the overall impact of 45 dietary intake habits on urinary stone risk in different locations. We identified 11 positive evidences of potential causal associations, including 9 protective factors and 2 risk factors. Our findings suggest that the risk of urinary stone formation may be influenced by various dietary factors. These results underscore the importance of further research and contribute to a better understanding of the mechanisms underlying the impact of diet on urinary stone disease.

Comparison of studies

Tea intake, as the only reliable evidence of dietary habits in this study, yielded consistent results with previous research in significantly reducing the risk of urinary stone formation (9,26). A previous study has already established a relationship between fresh fruit consumption and kidney stones, which aligns with our findings (10). However, due to the continuous updates in the FinnGen database, we used the latest nephrolithiasis data that categorized the occurrence of urinary stones into upper and lower urinary tract. Compared to previous literature, our study provided a more detailed analysis of the association between tea and fresh fruit intake with lower urinary tract stones, but no significant correlation was observed. Previous studies on dairy products have been controversial. Coello *et al.* suggested that dairy products may be a risk factor for calcium oxalate stones (27), while Asoudeh *et al.*'s meta-analysis found that higher intake of dairy protein could reduce the risk of kidney stones (28). In our study, we performed a detailed classification and analysis of dairy products and found similar results to the latter study. However, in our results, apart from skim milk which was found to reduce the risk of upper urinary tract stones, there was no significant causal relationship evidence for other types of dairy products. An observational study on diet found a significant correlation between poultry, red meat (pork, beef, lamb, etc.), and the risk of urinary stones, while fish consumption, vegetarianism, and limiting meat intake to less than 50 g/d reduced the risk of urolithiasis by 30% to 50% (29). Our results only supported fish as a protective factor against kidney stone formation. A cross-sectional study based on NHANES found that high water intake (>2.5 L/d) and maintaining a urine volume of 2 L/d could reduce the prevalence of kidney stones (30). However, our study did not find a significant causal relationship between water intake and the formation of stones in the kidneys, ureters, and other parts, but it did reduce the risk of lower urinary tract stones. This may be attributed to the fact that the previous study included stones collected from various locations. There have been many studies on the impact of alcohol on kidney stones, and some have found that alcohol consumption itself is not related to the risk of urolithiasis, but the frequency of alcohol consumption can reduce the risk. Similarly, we found that alcohol did not have a significant impact on kidney and ureteral stones in various alcohol categories, but average weekly beer plus cider intake showed a significant negative correlation with lower urinary tract stone occurrence. The causal relationship between coffee and kidney stones has been reported in relevant literature. Yuan *et al.*'s MR study on coffee, caffeine, and kidney stones showed a negative correlation between coffee and caffeine intake and the risk of kidney stones (7). We also conducted a detailed classification study on different types of coffee. Overall, non-specific coffee intake indeed reduced the risk of kidney stone formation, but different results were observed for other types of coffee: instant coffee showed a significant positive correlation with upper urinary tract stone occurrence, while ground coffee showed a significant negative correlation trend. Decaffeinated coffee showed a significant positive correlation only with the risk of lower urinary tract stone formation.

Mechanism of effects

Research has shown that tea, as a beverage, contains a large amount of flavonoid antioxidants, which can prevent chronic metabolic diseases such as cancer and cardiovascular diseases (31). Our study further confirmed the preventive effect of tea on kidney stones. Fresh fruits contain electrolytes such as potassium, magnesium, and citrate, which effectively reduce the acid load on the kidneys and promote the excretion of urinary calcium and ammonium, thereby increasing the saturation of calcium oxalate crystals in urine and preventing kidney stone formation (32). Wholemeal bread and wholegrain bread are both made from whole grain flour, but they differ slightly in processing methods (33). In our study, we categorized them together. Research has found that dietary fiber in grains contains β-glucans, which are soluble dietary fibers that can slow down the absorption of starch and glucose, and participate in the regulation of metabolic indicators such as blood lipid levels and BMI (34). While regulating metabolism, these whole grain products provide dietary oxalates, which help regulate oxalate metabolism in urine and prevent kidney stone formation (35). The healthy DASH-style diet has been proven to significantly reduce the risk of kidney stone formation (36). Skimmed milk, as part of this diet, is rich in calcium. Dietary calcium in dairy products binds with excessive oxalate in the intestine, reducing the risk of calcium oxalate stone formation (28), as demonstrated in an observational study (37). Unlike regular red meats, fish oil reduces the levels of arachidonic acid (AA) and linoleic acid (LA) in the body, thereby alleviating the production of inflammatory mediators such as prostaglandins. Furthermore, the omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids in fish oil inhibit the fatty acid synthesis pathway, thereby reducing the consumption of citrate in the reaction and increasing the excretion of citrate through the kidneys.

Lower urinary tract stones mainly include bladder stones and urethral stones, with a combined prevalence rate of only 0.5%. Bladder stones are the most common and are mainly caused by urinary tract obstruction due to prostate hyperplasia, neurogenic bladder dysfunction, urinary tract infections, and foreign bodies. In women, bladder stones may be caused by displacement of intrauterine devices. The prevalence rate is higher in economically underdeveloped areas compared to economically developed areas (38-40). In this study, we identified two dietary habits that act as protective factors against lower urinary tract stone formation: water intake and average weekly beer plus cider intake. Many studies have shown that low urine volume is a risk factor for kidney stones, and adequate intake of drinking water can prevent kidney stone formation. A large amount of water intake can dilute the concentration of urine, prevent the formation of crystals of uric acid, oxalate, and other chemical components in urine, and promote their excretion (41-44). However, unexpectedly, the MR analysis in our study did not show a significant association between water intake and kidney or ureteral stones, although water intake was found to reduce the risk of bladder and other lower urinary tract stone formation. Alcohol is also a common beverage, and recent studies on the association between alcohol intake and urolithiasis do not have sufficient evidence to support the causal relationship between the two (8,45-47). The potential causal relationship between alcohol and lower urinary tract stones still needs further experimental research to explore the underlying mechanisms.

Coffee, as a common beverage in this era, comes in various types (48). Caffeine in coffee has been found to be significantly negatively correlated with the risk of kidney stones, as confirmed by relevant cross-sectional and MR studies (7,49). Caffeine can have a diuretic effect and increase the urinary flow rate in patients (50,51). In addition, related *in vitro* studies have found that caffeine can reduce the crystal binding ability of renal tubular epithelial cells and prevent further formation of kidney crystals (52). The negative results of decaffeinated coffee on upper urinary tract stones validate the above points, but research on its positive correlation with the risk of lower urinary tract stones is relatively scarce. The mechanism of instant coffee on kidney stones is not yet clear, but it may contain a large amount of hydrogen peroxide (H_2O_2), which acts by oxidative stress damage to immune cells related to oxalate metabolism (53). After adjusting for two common risk factor variables, BMI and smoking, the significance no longer exists, indicating that BMI and smoking may mediate the effects of these two risk factors mentioned above.

The pros and cons

We differentiated lower urinary tract stones into different locations, which is not commonly done in previous studies on urinary tract stones. Additionally, we utilized the newer version (9th edition) of the FinnGen Consortium database to obtain relevant outcome data. By conducting a causal relationship study between these outcomes and a comprehensive set of 45 common dietary habits, we were able to provide more authoritative evidence on the potential associations and causal directions between diet and urinary tract stone formation, while also minimizing the interference of confounding factors. In the multivariable-adjusted results for the risk factor diet (decaffeinated coffee and instant coffee), we found that BMI and smoking may act as potential mediating factors, offering some revelations for further exploration.

However, there are some limitations in our study. Firstly, the dietary habit data we used were collected through touchscreen questionnaires, which may introduce some subjectivity and potentially impact the accuracy and bias of the data. Secondly, our data did not include subgroup analyses stratified by age and gender, and we did not perform detailed classification and differentiation of stone composition in different locations. Although we performed sensitivity analysis and detected no significant bias in the data, heterogeneity issues inevitably emerged in some of our analysis results, which were not further explored. Additionally, each instrument variable may remain potential issues of pleiotropy, which could impact our research results. Finally, further research is needed to elucidate the mechanisms underlying these associations and validate these findings in larger and more diverse populations.

Conclusions

Our MR study provides scientific genetic evidence for the causal relationship between dietary habits and urinary tract stones. We identified nine dietary habits as protective factors for urinary tract stone formation, while two types of coffee intake were identified as risk factors. The mechanisms of the latter's effects on urinary tract stones may be influenced by BMI and smoking. The significance of our research lies in providing some basis for dietary adjustments in the daily lives of kidney stone patients or dietary guidance specifically targeting stone diseases.

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Footnote

Reporting Checklist: The authors have completed the STREGA reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-79/rc

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-24-79/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-24-79/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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