Self-Fluid Management in Prevention of Kidney Stones: A PRISMA-Compliant Systematic Review and Dose–Response Meta-Analysis of Observational Studies

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Abstract: Epidemiologic studies have suggested that daily fluid intake that achieves at least 2.5 L of urine output per day is protective against kidney stones. However, the precise quantitative nature of the association between fluid intake and kidney stone risk, as well as the effect of specific types of fluids on such risk, are not entirely clear.

We conducted a systematic review and dose–response meta-analysis to quantitatively assess the association between fluid intake and kidney stone risk. Based on a literature search of the PubMed, Embase, and Cochrane Library databases, 15 relevant studies (10 cohort and 5 case–control studies) were selected for inclusion in the meta-analysis with 9601 cases and 351,081 total participants.

In the dose–response meta-analysis, we found that each 500 mL increase in water intake was associated with a significantly reduced risk of kidney stone formation (relative risk (RR) = 0.93; 95% CI: 0.87, 0.98; P < 0.01). Protective associations were also found for an increasing intake of tea (RR = 0.96; 95% CI: 0.93, 0.99; P = 0.02) and alcohol (RR = 0.80, 95% CI: 0.75, 0.85; P < 0.01). A borderline reverse association was observed on coffee intake and risk of kidney stone (RR = 0.88, 95% CI: 0.76, 1.00; P = 0.05). The risk of kidney stones was not significantly related to intake of juice (RR = 1.02, 95% CI: 0.95, 1.10; P = 0.64), soda (RR = 1.03; 95% CI: 0.90, 1.17; P = 0.65), or milk (RR = 0.96; 95% CI: 0.88, 1.03; P = 0.21). Subgroup analysis and sensitivity analyses showed inconsistent results on coffee, alcohol, and juice intake.

Increased water intake is associated with a reduced risk of kidney stones; increased consumption of tea and alcohol may reduce kidney stone risk. An average daily water intake was recommended for kidney stone prevention.

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INTRODUCTION

Kidney stone is a common disease that has become increasingly prevalent over the past 2 decades. Currently, the kidney stone prevalence rate worldwide is approximately 1.7% to 8.8%. It is more likely for men aged 60 to 69 to develop a kidney stone. Kidney stones can have serious clinical and economic consequences. Indeed, patients who suffer from large stones usually need surgical treatment, and in the year 2000, the cost of kidney stones was approximately $2.81 billion in the United States alone.

Increased fluid intake may help prevent the formation of stones by diluting urine concentration, decreasing urine acidity, and by taking away excess salt. These beneficial effects, however, may be offset by the tendency of increased fluid intake to dilute stone inhibitors such as magnesium, pyrophosphate, and glycosaminoglycan. A recent meta-analysis, based on the results of 2 randomized trials, concluded that high water intake decreased the long-term risk of kidney stone recurrence by approximately 60%. However, pooled evidence from only 2 studies is not conclusive. Additionally, data on the association between specific beverage types and risk of stone formation are sparse.

Accordingly, this study conducted a more extensive systematic review and meta-analysis of the quantitative relationship between fluid intake and risk of kidney stones, with a particular emphasis on examining the linear or nonlinear trends of the association. This study also examined the association of specific beverage types with kidney stone risk.

MATERIALS AND METHODS

This systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (PRISMA). There are no ethical issues involved in our study for our data were based on published studies.

Search Strategy

Eligible studies were identified by searching the PubMed, Embase, and Cochrane Library databases for relevant studies of the association between fluid intake and risk of kidney stones. The search included studies that were published through February 15, 2015. A manual search of the references of the retrieved articles and relevant reviews was also conducted. In order to identify studies with relevant information on the exposure of interest (fluid intake), databases were searched...
using the following terms: “water,” “fluid,” “liquid,” “beverage,” “tea,” “alcohol,” “wine,” “beer,” “drink,” “soda,” “milk,” “diet,” “coffee,” “juice.” For the outcome of interest (kidney stone), search terms included: “kidney stone,” “kidney calculi,” “kidney calculus,” “renal stone,” “renal calculi,” “renal calculus,” and “nephrolithiasis.” The term “Humans” was used to limit the search results. No languages were limited during the search.

Study Inclusion and Exclusion Criteria

Studies were included in the meta-analysis if they: based on a cohort, case–control, or nested case–control design; defined kidney stone cases as patients diagnosed for the first time with a kidney stone without obvious bone disease; contained exposure information on at least one of the fluids of interest (water, coffee, tea, alcohol, juice, soda, milk); and had a sufficient data information. Additionally, to be included in the dose–response analyses, relevant studies were required to contain information on quantitative serving size with at least 3 quantitative categories. We excluded cross sectional studies, grey literature, and conference abstract. Studies which reported 24-hour urine biochemical changes after fluid intake were also excluded.

Data Extraction

Two reviewers conducted data extraction independent of one another. A standardized data collection form was used which extracted the following information: first author’s name, publication year, country of study, follow-up, study design, sex, age range, number of cases, the total sample size or person-years of follow-up, quantitative serving size, effect size (odds ratio, relative risk, hazard ratio) with confidence intervals (CI), and control variables. When a given study presented models that adjusted for different numbers of control variables, data were extracted from the model that adjusted for the largest number of variables. Unadjusted results were extracted only when no other results were presented. When there was no information on serving size in an article, an assumption was made that a serving size of 1 cup (or glass) was equal to 150 mL. As for alcohol, 15.2 mL of alcohol, 120 mL wine, or 240 mL beer were assumed to contain approximately 12 g alcohol (1 standard drink). Different periods of study (Stage I or Stage II) were regarded as 2 different studies. If multiple publications from the same data set or study were detected, we only included the publication with the longer follow-up period. Potential errors were checked by a third-party author and any divergences were resolved by discussion.

Statistical Analysis

The term “water,” “total fluids” were regarded as water intake in this article. The relative risk (RR) was used to measure the association between beverage intake and risk of kidney stones. Odds ratios and hazard ratios were regarded to be approximately equal to the RR, since the prevalence of kidney stones in the selected studies was approximately 10% or less. For dose–response analyses, we fitted both linear and nonlinear models to the data (n ≥ 3). More specifically, we first estimated the RR of kidney stones per unit increment (500 mL for water, 110 mL for coffee and tea, 150 for juice, and 10 g for alcohol) of exposure within each study by generalized least-squares regression models. From these models, the regression coefficients were combined in a random-effects model, with fluid intake modeled as a continuous, linear variable. Then, to model possible nonlinear exposure-outcome associations, we ran models in which the exposure was modeled as a restricted cubic spline with 3 fixed knots at 10th, 50th, and 90th percentile of the exposure distribution. The median values or middle point of each serving size were assigned to the corresponding relative risk for each study. When there were open-ended categories, we assumed the length of the open ended interval to be the same as that of the adjacent interval. When the lowest category was not analyzed as reference category (such as), the method of Hamling et al was used to convert the results. If a study reported incomplete data, we used the method of Bekerking et al to evaluate the missing data. In the dose–response analyses, non-linearity was assessed by assuming that the regression coefficient of the second spline equaled zero, which is the Wald test.

Not all studies reported dose–response information for specific fluids. Thus, we conducted analyses which analyzed the association of specific fluid intake modeled as a dichotomous variable (intake of 1–2 servings, or about 110–240 mL vs. no intake) with kidney stone risk. If a given study did not contain dose information at the 1 to 2 serving level, the results of the category nearest to that level was used in the pooled analysis. Further sensitivity analyses were conducted to evaluate whether this influenced the results. The I² statistics, which varied from 0% to 100%, were used to test heterogeneity, and were categorized as low (0–40%), moderate (30–60%), substantial (50–90%), and considerable (75–100%). A fixed-effects model was applied until slight heterogeneity (I² < 30%) was detected; or a random-effect model was used. When the value of I² was >75%, the combination would be terminated. When studies reported results separately by sex or other subtypes, the RRs were pooled using a fixed-effects model before adding the RRs to the overall meta-analysis. The inverse variance method was used to calculate the weight of each RR. Egger’s regression test was used to detect potential publication bias. Subgroup analyses were used to detect possible sources of heterogeneity and potential difference among subgroups. Sensitivity analyses were also used to detect whether results were influenced by transformation of the data, the quality of included studies, and potential confounding factors. All P-values were 2-sided.

RESULTS

Search Results and Study Characteristics

An initial literature search identified 2739 studies. After removing duplicate and unrelated studies, 2 cross-sectional studies and 1 case–control study that included kidney stone cases with bone disease, 15 studies remained for the meta-analysis. A flow diagram illustrating how studies were selected is shown in Figure 1.

Among the included 15 studies, 10 were cohort studies, and 5 were case–control studies. The 15 studies combined had 9601 cases and 351,081 total participants (duplicate data from different studies were not counted). Three of the case–control studies described matching information that was utilized in matching controls to cases, while the other 2 case–control studies did not report such information. For cohort studies, the follow-up period ranged from 4 to 20 years. Nine of the studies were conducted in the United States, while 4 were conducted in China, 1 in Finland, and 1 in the United Kingdom.

Assessment of study quality was conducted according to the Newcastle Ottowa-Scale (NOS). The scale contains 9 items, and each item accounts for 1 point. Among the included studies, quality scores ranged from 3 to 8 points, with a mean
were identified as the same publication of study.\textsuperscript{38} After excluding multiple publications, 3 studies reported dose–response information.\textsuperscript{30,38,39} The meta-analysis showed that, compared to no tea consumption, those who consumed 1 to 2 cups of tea per day had a RR of kidney stones of 1.06 (95% CI: 0.94, 1.20; \(P = 0.32; I^2 = 45.5\%\); Figure 4). When modeled as a continuous variable, each 110 mL/day increase in tea consumption was associated with a kidney stone RR of 0.96 (95% CI: 0.93, 0.99; \(P = 0.02\)), and there was some evidence this relationship was borderline nonlinear (\(P = 0.07\) for nonlinearity test). The protective effect of tea consumption appeared to begin at an intake level of approximately 250 mL/day. Compared to the reference dose (0 mL), those whose daily tea intake was 102, 204, 257, 525, and 825 mL had a RR of kidney stones of 1.02 (95% CI:0.95, 1.09), 0.97 (95% CI: 0.90, 1.04), 0.91 (95% CI: 0.86, 0.99), 0.59 (95% CI: 0.39, 0.89), and 0.33 (95% CI:0.13, 0.84), respectively.

### Alcohol Intake and Risk of Kidney Stones

Nine studies\textsuperscript{6,18,27,29,30,36,38–40} reported on the association between alcohol intake and risk of kidney stones. Of these studies\textsuperscript{6,40} reported dose–response information. Studies\textsuperscript{6,40} were identified as the same publication of study.\textsuperscript{38} The meta-analysis showed that, compared to those who did not drink alcohol, those who drank about 1 standard drink (12 g) of alcohol per day had a RR of kidney stones of 0.80 (95% CI: 0.63, 1.01; \(P = 0.06; I^2 = 67.1\%\); Figure 5). When modeled as a continuous variable, each 10 g/day increase in alcohol consumption was associated with a kidney stone RR of 0.80 (95% CI: 0.75, 0.85; \(P < 0.01\)), and there was no significant evidence that this association was nonlinear (\(P = 0.73\) for nonlinearity test).

### Other Beverages and Risk of Kidney Stones

After excluding multiple publications, 3 studies\textsuperscript{30,36,38} reported on the association between juice intake and risk of kidney stones, 4 studies\textsuperscript{29,30,36,38} reported on the association between soda intake and risk of kidney stones, and 5 studies\textsuperscript{30,31,36,38,39} reported on the association between milk consumption and kidney stone risk. Limited studies reported data that could be used for dose–response analyses. The overall meta-analysis showed that, compared to those with no juice consumption, those with 1 to 2 cups per day of juice intake had a RR of kidney stones of 1.02 (95% CI: 0.95, 1.10; \(P = 0.64; I^2 = 0\%\); compared to those with no soda intake, those with 1 to 2 cups per day of soda intake had a RR of kidney stones of 1.03 (95% CI: 0.90, 1.17; \(P = 0.65; I^2 = 42.6\%\)). Additionally, compared to those with no milk consumption, those who consumed 1 to 2 cups of milk per day had a kidney stone RR of 0.96 (95% CI: 0.88, 1.03; \(P = 0.21; I^2 = 0\%) (see Figure 6).

### Subgroup Analysis and Sensitivity Analysis

Subgroup analyses were conducted on country, study design, and other subtypes (if reported, such as sex). Apart from coffee and alcohol, no substantial changes of the results were found between subgroups (Table 2).

For coffee intake, the kidney stone RR associated with 1 to 2 servings of coffee per day was not significant in the subgroup of case–control studies (RR = 0.85, 95% CI: 0.64, 1.13; \(P = 0.26; I^2 = 41.7\%\)). A subgroup analysis showed that alcohol intake was not associated with a lower risk of kidney stones (RR = 0.76, 95% CI: 0.46, 1.25; \(P = 0.28; I^2 = 86.6\%\) in case–

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**FIGURE 1.** The flow diagram of study inclusion.
| Author            | Country   | Research                          | Describe                                                                 | Types of Beverages                              | Main Findings                                                                 | Adjusted Item                                                                 | Quality Score |
|-------------------|-----------|-----------------------------------|---------------------------------------------------------------------------|-----------------------------------------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------|---------------|
| Curhan33          | America   | Nurses' Health Study I            | Cohort study; 4 year follow-up (1986–1990); mean age were 40–75; use semi-quantitative frequency questionnaire with 131 items | Total fluids intake                           | RR of highest vs. lowest levels of water intake was 0.71 (0.52, 0.97) | Age, profession, use of thiazide diuretics, alcohol, dietary intake of calcium, animal protein, potassium, and total fluid | 7             |
| Curhan4          | America   | Nurses' Health Study II           | Cohort study; 8 year follow-up (1991–1999); mean age were 40–75; use self-reported frequency questionnaire        | Total fluids intake | RR of highest vs. lowest levels of water intake was 0.68 (0.56, 0.83) | Age, body mass index, family history, and intake of supplemental calcium, dietary calcium, animal protein, potassium, sodium, sucrose, phyte, and fluid | 7             |
| Curhan10         | America   | Health Professionals Follow-up Study | Cohort study; cases were men; 6 year follow-up; mean age were 40–75; use semi-quantitative frequency questionnaire | Alcohol, milk, juice, soda, coffee, tea | RRs were 0.54 (95% CI: 0.38, 0.75) for caffeinated coffee, 0.77 (95% CI: 0.50, 1.19) for decaffeinated coffee, 0.53 (95% CI: 0.23, 1.19) for highest vs. lowest tea intake | Age, profession, geographic region, thiazide, diuretics, dietary intake of calcium, protein, potassium, and all 21 beverages | 8             |
| Curhan6          | America   | Nurses' Health Study             | Cohort study; cases were women, 8 year follow-up; mean age were 40–75; use self-reported frequency questionnaire | Alcohol, milk, juice, soda, coffee, tea      | RRs were 0.67 (95% CI: 0.50, 0.93) for caffeinated coffee, 0.83 (95% CI: 0.55, 1.25) for decaffeinated coffee, 0.78 (95% CI: 0.60, 1.10) for highest vs. lowest tea intake | Age, dietary intake of calcium, animal protein, potassium, sodium, and sucrose; intake of supplemental calcium, and 17 beverages | 7             |
| Dai70            | China     | China’s area study               | Case–control study; hospital-based controls without description of match; use interviewer administered questionnaire suit for China | Water, alcohol, coffee, tea, juice, milk, soft drink | RRs of highest vs. lowest levels of water intake were 0.53 (0.31, 0.90) and 0.72 (0.36, 1.43) for men and women | Age, BMI, blood pressure, education, and history of hypertension | 5             |
| Ferraro28        | America   | Health Professionals Follow-Up and Nurses’ Health Study | Cohort study; 8 years follow-up; participants were health male aged 40–75; use self-reported FFQs with 130 items | Water, alcohol, coffee, tea, juice, milk, soft drink | RRs of highest vs. lowest levels of water intake were 0.90 (0.81, 1.00) and 0.89 (0.82, 0.97) respectively | Age, race, region, body mass index, use of furosemide, thiazides, high BP, diabetes, BMI, intake of calcium, potassium, phytate, animal protein, vitamin C, total calories, profession, all the beverages | 8             |
| Goldfarb99       | America   | Vietnam Era Twin (VET) Registry  | Case–cohort study; cases and controls were twins aged from 34 to 50 years; matched with age, sex, age | Alcohol, coffee, tea, milk | RR of current drinkers was 1.6 (0.6, 4.4); RRs of highest vs. lowest levels of tea, coffee intake were 1.2 (0.4, 3.2) and 0.4 (0.2, 0.8) | Age, body mass index, hypertension, and smoking; N = 251 pairs with complete information on all covariates | 6             |
| Hirvonon30       | Finland   | National Public Health Institute | Cohort study; mean 6.1 years of follow-up (1985–1995); participants were male smokers aged 50–69, use self-administered diet questionnaire with 768 items | Water, alcohol, coffee, tea, juice, milk, soft drink | RRs of highest vs. lowest levels of water, alcohol intake were 0.95 (0.67, 1.35) and 0.51 (0.36, 0.72) respectively | Age, supplementation group, vocational training, marital status, and intake of magnesium, fiber, and alcohol | 7             |
| Krieger29        | Puget Sound | Group Health Cooperative        | Case–control study; Group Health Cooperative-based controls matched with age | Beer, coffee, tea, soda | RR was 0.44 (95% CI: 0.31, 0.63) and 0.71 (95% CI: 0.49, 1.02) for beer and coffee intake | Age, sex | 4             |
| Lin77            | China     | China’s area study               | Case–control study; sex- and age-matched hospital-based controls; use structured questionnaire by interviewers | Total fluids and alcohol intake | RRs of highest vs. lowest levels of water, alcohol intake were 0.90 (0.81, 1.00) and 0.89 (0.82, 0.97) respectively | Age, sex | 4             |
| Sorensen37       | America   | Women’s Health Initiative        | Cohort study; mean follow-up was 8 year (from 1993); participants were woman aged 50–79, use self-reported WHI food questionnaire | Total water intake | RR of highest vs. lowest levels of water intake was 0.80 (0.66, 0.96) | Adjusted for age, race/ethnicity, education, geographic region, calcium supplementation, and current estrogen use | 8             |
| Taylor15         | America   | Nurses’ Health Study I and II     | Cohort study; 14 years follow-up (1986–1999); mean age were 40–75; use self-reported frequency questionnaire with 131 items | Total fluids intake | RR of highest vs. lowest levels of water intake was 0.71 (0.59, 0.85) | Age, body mass index, use of thiazide diuretics, fluid intake, alcohol use, calcium supplement use, dietary intake of animal protein, calcium, potassium, sodium, vitamin C, and magnesium | 7             |
European Prospective Investigation into Cancer and Nutrition
Cohort study; participants aged from 20 to 90 years; follow-up 20 years (1997–2007); self-reported
Alcohol
RR was 0.65 (95% CI 0.47, 0.91) for highest vs. lowest alcohol intake
Sex, method of recruitment, region of residence and long-term medical treatment and adjusted for smoking, alcohol consumption, BMI, self-reported prior diabetes, and energy intake
8

China’s area study
Case–control study; hospital-based controls matched with age and sex; use interviewer administered questionnaire
Constantly drinking tea
RR was 1.46 (1.03, 1.07) for constantly drinking tea vs. none
Adjusted for age, sex, labor intensity, source of tap water and boiled water, drinking habit, fresh vegetables, family history
3

China’s area study
Case–control study; controls are volunteers had annual routine physical examinations without description of match
Total fluids, tea, milk
RRs of highest vs. lowest levels of fluid, tea, milk were 0.60 (0.30, 0.90), 1.3 (1.0, 1.8), 0.9 (0.6, 1.6) for women
Fluid intake, smoking status, gender, bladder management, race, neurologic level
5

CI, confidence interval; RR, relative risk.
control studies. Variation among other subgroups could not be assessed reliably due to small numbers.

As to heterogeneity of results, in most cases, the case–control studies showed a greater heterogeneity than cohort studies. Additionally, studies conducted in the United States showed mild heterogeneity, while considerably greater degrees of heterogeneity were observed in studies conducted in other countries (Finland, British).

Sensitivity analyses were conducted by omitting 1 study at a time to see whether the omission of the study influenced the overall results. We found that, for alcohol intake (about 12 g), 2 studies\(^\text{27,39}\) substantially influenced the results, as omitting either study led the results to become statistically significant (RR\(_\text{omit}\)\(^27 \approx 0.78, 95\% \text{CI} : 0.61, 0.99; \text{RR}\(_\text{omit}\)\(^39 \approx 0.77, 95\% \text{CI} : 0.61, 0.97). \) For milk intake, when omitting study,\(^30\) the results reached to statistical significant (RR = 0.90, 95% CI: 0.82, 0.98). Other fluids showed robust results.

### Publication Bias

The meta-analysis results for water, tea, and alcohol intake were examined for publication bias (there were not enough studies to conduct publication bias analyses for other beverages). Egger’s regression test of publication bias did not show strong evidence of publication bias \((P = 0.92, P = 0.55, P = 0.76).\)

### DISCUSSION

This is the first meta-analysis to have investigated the association of different types of beverages with risk of kidney stones. The meta-analysis confirmed that water intake was associated with a reduced risk of kidney stones. It also found that coffee, tea, and alcohol intake may reduce the risk of kidney stones. In contrast, juice, soda, and milk intake were not associated with kidney stone risk. Further subgroup analyses and sensitivity analyses showed unstable results for coffee and alcohol.

By increasing urine volume, increased water intake can dilute urine concentration, reduce CaOx super saturation, decrease urine acid, and remove salt.\(^6,41\) The European Association of Urology guidelines\(^42\) suggest that daily water intake should achieve at least 2.5 L of urine volume in order to prevent kidney stones. The present meta-analysis found no obvious threshold at which water intake began to be associated with reduced kidney stone risk. Instead, any increase in water intake, even at low levels of intake, was associated with reduced kidney stone risk. Thus, an average daily water intake should be recommended. The results of the present meta-analysis are partly consistent with a previous meta-analysis,\(^43\) which found that increased fluid intake (>2000 mL/day) was associated with a 61% reduction in the risk of kidney stones. Another conference abstract\(^43\) comparing the highest versus lowest level of total fluid intake, observed a 60–80% deceased risk of kidney stone in the highest level group. In our meta-analysis, greater than 2000 mL of water intake per day reduced the risk of first kidney stone occurrence risk by at least 8% compared to 1500 mL daily intake, and the highest (3100 mL) category showed a 26% reduction of kidney stone risk compared to the reference category (1500 mL). Compared to the earlier meta-analysis, our meta-analysis quantitatively evaluated the effects of different doses of water intake and thus provides more refined information.

Caffeine, which is present in both in coffee and tea, is a potential risk factor for kidney stones because it may increase the urinary calcium/creatinine ratio.\(^34\) In our study, coffee and tea intake were associated with a reduced risk of kidney stones when modeled as a continuous variable but not as a dichotomous variable. This may suggest a dose-dependent relationship between coffee (and tea) intake in prevention of stones. It is possible that some beneficial substances in coffee and tea (such as calcium)\(^35\) offset the influence of caffeine. But this result may be influenced by the inconsistency between different study designs. Further studies, especially based on cohort design, were needed.

Tea consumption appeared to show a borderline nonlinear relationship with kidney stone risk, with a reduction in risk seen mostly at intake levels above 250 mL/day. Animal experiments support this result.\(^45,46\) In rats, green tea consumption significantly decreased urinary oxalate excretion and calcium oxalate deposit formation, possibly by the antioxidative action of epigallocatechin gallate and the activity of superoxide dismutase.\(^45,46\) However, it is difficult to explain why a reduction in kidney stone risk would only occur above a certain threshold of tea consumption, though increased consumption of water might partially explain such a threshold effect.

Our meta-analysis on alcohol consumption showed inconsistent results. Although 12 g of alcohol intake showed no
TABLE 2. Results of Subgroup Analysis

| Subgroup Analysis | Case–Control | Cohort | Study Type | Country | Other Subtypes |
|-------------------|--------------|--------|------------|---------|---------------|
|                   |              |        |            |         |               |
| Water             |              |        |            |         |               |
| Study number      | 4            | 3      |            |         |               |
| RR (95% CI)       | 0.90 (0.85, 0.96) | 0.96 (0.92, 0.99) | 0.94 (0.93, 0.96) | 0.89 (0.84, 0.95) | 1.00 (0.96, 1.05) |               |
| P-value           | <0.01        | 0.02   | <0.01      | <0.01   | 1             |               |
| Heterogeneity (I²)| 38.50%       | 74.50% |            | 0.00%   | 38.50%        |               |
|                   |              |        |            |         |               |
| Tea               |              |        |            |         |               |
| Study number      | 2            | 3      |            |         |               |
| RR (95% CI)       | 0.85 (0.64, 1.13) | 0.90 (0.82, 0.98) | 0.75 (0.60, 0.93) | 0.93 (0.77, 1.12) | 0.97 (0.93, 1.12) | 0.84 (0.77, 0.91) | 0.74 (0.69, 0.80) |               |
| P-value           | 0.26         | 0.01   | <0.01      | 0.43    | 0             |               |
| Heterogeneity (I²)| 41.70%       | 51.20% |            | 51.40%  |               |               |
|                   |              |        |            |         |               |
| Alcohol           |              |        |            |         |               |
| Study number      | 3            | 4      |            |         |               |
| RR (95% CI)       | 0.76 (0.46, 1.25) | 0.80 (0.71, 0.91) | 0.79 (0.65, 0.96) | 0.67 (0.45, 1.01) | 0.96 (0.77, 1.19) | 0.64 (0.31, 1.30) | 0.78 (0.63, 0.96) |               |
| P-value           | 0.28         | <0.01  | 0.02       | 0.7     | 0             | 0.57           | 0.07           |               |
| Heterogeneity (I²)| 86.6%        | 5.30%  |            | 36.00%  | 15.60%        | 77.10%         | 89.60%         |               |
|                   |              |        |            |         |               |
| Soda              |              |        |            |         |               |
| Study number      | 2            | 2      |            |         |               |
| RR (95% CI)       | 0.97 (0.73, 1.28) | 1.07 (0.91, 1.26) | 1.02 (0.91, 1.05) | 0.86 (0.68, 1.08) | 1.17 (1.00, 1.37) | 1.15 (0.95, 1.17) | 0.98 (0.92, 1.04) |               |
| P-value           | 0.83         | 0.41   | 0.76       | 0.18    | 0             |               |               |               |
| Heterogeneity (I²)| 54.00%       | 52.40% |            | 0.00%   |               |               |               |               |
|                   |              |        |            |         |               |
| Milk              |              |        |            |         |               |
| Study number      | 2            | 3      |            |         |               |
| RR (95% CI)       | 1.02 (0.60, 1.73) | 0.94 (0.86, 1.04) | 0.89 (0.77, 1.03) | 1.02 (0.60, 1.73) | 1.00 (0.94, 1.07) | 0.96 (0.91, 1.01) | 0.98 (0.93, 1.04) |               |
| P-value           | 0.94         | 0.23   | 0.11       | 0.94    | 1             | 0.14           | 0.52           |               |
| Heterogeneity (I²)| 74.10%       | 55.10% |            | 34.30%  | 74.10%        | 0.00%          | 2.70%          |               |

CI, confidence interval; RR, relative risk.

1 RR was the results of linearity dose–response meta-analysis of water intake.
2 RR was the results of about 1 to 2 servings of beverages intake.
3 Indicated considerable heterogeneity (>75%).
Strength and Limitations

The present study’s comprehensive literature search, and strict study design, lends credibility to the study’s results. Linear and nonlinear dose–response meta-analysis quantitatively evaluated the association of different levels of beverages intake on kidney stone risk, providing a more refined analysis than some prior studies. Additionally, subgroup and sensitivity analyses suggested that our study’s results were robust in most cases, which strengthens the conclusions of our study.

This present study had some limitations. One limitation was that our evaluation and transformation of the raw data was fairly crude. A second limitation was that there were limited numbers of cohort studies focusing on the association between fluid intake and the risk of kidney stones. This small number of cohort studies is potentially problematic, since some research indicates that random errors induced by a small numbers of trials may cause bias in the results of meta-analyses. A third limitation was that different categories of fluid intake among studies made it difficult to pool results across studies. Indeed, some studies only reported the effect of any versus no fluid intake, or high versus no intake, while others reported 110 mL versus no intake of fluids. Although dose–response meta-analysis was used to overcome this problem, for soda and milk, there were limited studies reporting relevant data that could be used in a dose–response analysis. Furthermore, differences in how studies categorized fluid intake may have contributed to some of the heterogeneity we observed in our results, especially for juice intake. A fourth limitation was that, in our meta-analysis, most of the studies were conducted in the United States and China, and may not be generalizable to other countries. Fifth, we did not examine interactions among subgroups because the subgroup sample sizes were too small for such analyses to produce statistically reliable results.

CONCLUSIONS

Increased water is associated with a reduced risk of developing kidney stones, increased intake of coffee, tea, and alcohol showed potential benefits on stones prevention, but needs to be confirmed further. Soda and milk intake appeared to be unrelated to stone risk. Current evidence is insufficient for definitively determining the relationship between juice intake and risk of kidney stones.

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