Published in final edited form as:

J Urol. 2011 May ; 185(5): 1775–1780. doi:10.1016/j.juro.2011.01.003.

Caffeine intake and risk of stress, urgency, and mixed urinary incontinence

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Abstract

Purpose—Although caffeine consumption is common, and is generally believed to affect bladder function, little is known regarding caffeine intake and incident urinary incontinence.

Materials and Methods—We conducted a prospective cohort study of 65,176 women without incontinence, aged 37–79 years, in the Nurses' Health Studies. Incident incontinence was identified from questionnaires, during 4 years of follow-up. Caffeine intake was measured using food frequency questionnaires administered prior to incontinence development. Multivariable-adjusted relative risks for the relation between caffeine intake and incontinence risk were calculated, as well as attributable risks.

Results—Caffeine was not associated with incontinence monthly or more, but there was a modest, significantly increased risk of incontinence at least weekly among women with the highest versus the lowest intake (RR 1.19, 95% CI 1.06–1.34, comparing >450 vs. <150 mg/day) and a significant trend of increasing risk with increasing intake (p-value for trend=0.01). This risk appeared focused in incident urgency incontinence (RR 1.34, 95% CI 1.00–1.80 comparing >450 vs. <150 mg/day, p-value for trend=0.05), but not stress or mixed incontinence (p-values for trend=0.75 and 0.19, respectively). The attributable risk for urgency incontinence associated with high caffeine intake was 25%.

Conclusions—Our findings suggest that high caffeine intake, but not lower levels, is associated with a modest increase in incidence of frequent urgency incontinence; one-quarter of these cases among women with the highest level of caffeine consumption might be eliminated if high caffeine intake was eliminated. Confirmation of these findings in other studies is needed before recommendations can be made.

Keywords

urinary incontinence; caffeine; epidemiology

INTRODUCTION

Caffeine is consumed regularly by >85% of adults in the United States¹ and has long been described in the lay literature as a bladder irritant.² Yet, there are limited scientific data regarding the relation between caffeine intake and incident urinary incontinence (UI). Previous epidemiologic studies have largely been cross-sectional^{3–5}; although their findings generally do not support caffeine as a risk factor for UI, the cross-sectional design could lead to biased results if women with UI reduce caffeine consumption to improve their symptoms. In addition, the majority of previous studies focused on consumption of specific beverages rather than total caffeine, which would underestimate an individual's total exposure to caffeine from a variety of beverages and food. Finally, few studies have examined associations separately by UI type, which could be important if caffeine primarily increases risk of urgency UI.

Therefore, we prospectively investigated the association between total caffeine intake and incident UI, including stress, urgency, and mixed UI, over four years of follow-up in 65,176 women enrolled in the Nurses' Health Study (NHS) and NHSII.

MATERIALS AND METHODS

Study population

In 1976, the NHS was initiated when 121,700 female nurses, aged 30–55 years, returned a mailed questionnaire about their health and lifestyle. The NHSII was initiated in 1989 when 116,430 female nurses aged 25–42 years returned a similar questionnaire. Updated information has been collected using biennial questionnaires. UI questions were included on the 2000, 2002, and 2004 NHS questionnaires and the 2001, 2003, and 2005 NHSII questionnaires. The Institutional Review Board of Brigham and Women's Hospital approved these studies. Participants provided informed consent by returning their questionnaires.

For these analyses, we defined baseline as 2000 (NHS) and 2001 (NHSII). Of the women who responded to the UI questions at baseline, 93% (NHS: 78,197/83,997; NHSII: 79,684/85,507) provided UI information on at least one follow-up questionnaire. Importantly, responders and non-responders were highly similar in mean caffeine intake, thus there is unlikely any meaningful bias due to the small loss to follow-up.

Among participants with baseline UI data, we excluded 40,807 NHS and 43,926 NHSII participants with prevalent UI, defined as UI at least once per month or UI less than once per month of quantities at least enough to wet the underwear. In addition, at the beginning of each 2-year follow-up period, we excluded women missing data on UI incidence, caffeine intake, or important potential confounding factors (BMI or parity). We also excluded women with major neurologic conditions (stroke, multiple sclerosis, Parkinson's disease, or amyotrophic lateral sclerosis) or functional limitations (defined as difficulty climbing a flight of stairs, walking 1 block, bathing, or dressing), which might be related to UI. Thus, 65,176 women (34,148 NHS; 31,028 NHSII) were included in analyses.

Measurement of UI

Participants were asked, "During the last 12 months, how often have you leaked or lost control of your urine?" Response options were never, less than once per month, 2–3 times per month, about once per week, and almost every day. Women who reported UI were then asked, "When you lose your urine, how much usually leaks?" Response options were a few drops, enough to wet your underwear, enough to wet your outer clothing, and enough to wet the floor. A reliability study among 200 participants demonstrated high reproducibility of responses to these questions.⁶

Incident cases were defined as those reporting UI at least once per month on any follow-up questionnaire. Among incident cases, frequent incontinence was UI at least once per week.

At the first follow-up, we assessed incontinence type using a supplementary questionnaire⁷ mailed only to women with frequent incontinence because we believed that they would report precipitating circumstances of their incontinence more accurately than women with less frequent incontinence. In the NHS, due to the large number of women with incident frequent UI, the supplementary questionnaire was mailed to a random sample of 80% of the cases (n=2,183) and completed by 84%. In the NHSII, the supplementary questionnaire was mailed to 98% of incident cases with frequent UI (n=1,224; 19 women identified after the supplementary questionnaire mailing was complete did not receive a mailing) and completed by 79%. For the second follow-up period, data on incontinence type were collected directly from the main questionnaire; thus, information on incontinence type was available from 99% of cases with frequent incontinence.

Stress UI was defined as leaking primarily with coughing, sneezing, lifting things, laughing, or exercise. Urgency UI was defined as primarily leaking accompanied by an urge to urinate or a sudden feeling of bladder fullness. UI type was classified as mixed when stress and urgency UI symptoms were equally common. In additional analyses, we combined urgency and mixed UI to examine any urgency UI. Cases of frequent UI that did not meet any of these definitions were excluded from analyses (n=187).

Measurement of caffeine consumption

Dietary data were collected approximately every four years since 1980 in the NHS and every four years starting in 1991 in the NHSII with validated semi-quantitative food frequency questionnaires (FFQs). Participants were asked how often on average during the previous year they consumed specific items, including coffee with caffeine ("1 cup"), tea with caffeine ("1 cup"), caffeinated soda ("1 glass, bottle or can"), and chocolate (e.g., "bar or packet"). There were 9 response options ranging from "none or less than 1/month" to "6+/day". Using U.S. Department of Agriculture food composition data supplemented with other sources, estimated caffeine contents were 137 mg per cup of coffee, 47 mg per cup of tea, 46 mg per can/bottle of cola beverage, and 7 mg per serving of chocolate.⁸ We calculated total caffeine intake by summing the caffeine content for specific items multiplied by weights proportional to the frequency of use of each item.

The reproducibility and validity of the FFQs have been reported previously.⁹ In an NHS validation study, there were high correlations between intakes assessed with the FFQ and four 1-week diet records completed over a 1-year period; correlations were 0.78 for coffee, 0.93 for tea and 0.84 for cola drinks.¹⁰

Statistical analysis

Since the commonly hypothesized mechanisms for caffeine's effects on the bladder act acutely, for the primary analyses, we determined women's exposure to caffeine using the most recently reported caffeine intake prior to incontinence development. We categorized caffeine intake as 0–149, 150–299, 300–449, or 450–1352 mg per day, approximately corresponding to the amount of caffeine in 1, 2, 3, or ≥ 4 cups of coffee.

Cox proportional hazards models stratified by age in months and 2-year time periods were used to calculate multivariable-adjusted RRs, estimated by hazard ratios, and their 95% CIs for each case definition. Covariates in the models were potential UI risk factors identified from the literature, including parity, BMI, cigarette smoking, race, diabetes, total fluid intake, and physical activity. Total fluid intake included milk, juice, tea, coffee, soda, punch, alcohol, and water. Covariate status was updated at the beginning of each follow-up cycle.

We conducted analyses in each cohort separately as well as after pooling the data from the two cohorts. Before combining data, we tested whether the association between caffeine and UI varied between cohorts by using an interaction term in the Cox proportional hazards models. For each outcome, the interaction term was not significant (all p-values for interaction ≥ 0.21), thus we present only results from pooled analyses. Pooled analyses were adjusted for study cohort.

We conducted several secondary analyses to further explore the association between caffeine and incident incontinence. First, we repeated the analyses using the average of the two most recent reports of caffeine intake to address concerns that some women may have reduced their intake in response to very early urinary symptoms. In addition, since coffee was the primary source of caffeine in our population, we conducted separate analyses of caffeinated and decaffeinated coffee intake to consider the direct effects of caffeine versus lifestyle factors that may be associated with coffee drinking. Finally, to estimate the absolute effect of caffeine on incontinence incidence, we calculated the attributable risk, an estimate of the percentage of incident UI among those with high caffeine intake in our cohort that could be prevented by reducing caffeine intake.

For all analyses, two-tailed p-values < 0.05 were considered statistically significant. Data were analyzed using SAS 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

At baseline, NHS participants were 54–79 years old and NHSII participants were 37–54 years old. The largest contributor to total caffeine intake was coffee (76%), followed by soda (11%) and tea (11%). Nearly half (49%) of the women were in the lowest category of caffeine intake; few women (9%) reported consuming ≥ 450 mg of caffeine per day. Women who consumed more caffeine had higher mean daily fluid intake and were more likely to be current cigarette smokers (table 1). These variables were included in adjusted analyses.

Among women with daily caffeine intakes of 0–149, 150–299, 300–449, and ≥ 450 mg, the incidence rates for frequent UI were 1.9, 1.6, 2.5, and 2.7 cases per 100 person-years, respectively. After adjusting for potential confounding factors, there was a significantly increased risk of incident frequent UI in the highest versus the lowest category of caffeine intake (RR 1.19, 95% CI 1.06–1.34) (table 2), and there was a significant trend of steadily increasing risk with increasing caffeine intake (p for trend=0.01).

When we examined the risk of specific UI types (table 3), the highest versus the lowest category of caffeine intake was associated with a borderline significant increased risk of urgency UI (RR 1.34, 95% CI 1.00–1.83, $p=0.05$) and there was a borderline significant trend of increasing risk of urgency UI with increasing caffeine intake (p for trend=0.05). In additional analyses of urgency UI with or without stress UI (data not shown in tables), the highest versus the lowest category of caffeine intake was significantly associated with increased risk (RR 1.26, 95% CI 1.03–1.55; p for trend=0.03). Caffeine intake was not associated with risks of incident stress or mixed UI.

We conducted several additional analyses to further explore the relation between caffeine and UI risk (data not shown in tables). First, in analyses using average caffeine intake from the two most recent questionnaires, rather than the most recent report of caffeine intake, results were similar to those reported above. Second, we analyzed the specific relations between UI and caffeinated and decaffeinated coffee. Higher daily intake of caffeinated coffee was associated with significantly increased risks of frequent UI (RR 1.17, 95% CI 1.02–1.34, comparing ≥ 4 vs. 0 cups, p for trend=0.03) and urgency UI (RR 1.42 95% CI 1.04–1.95, p for trend=0.02). In contrast, no significant associations were seen between

decaffeinated coffee and UI (RR= 0.97, 95% CI 0.74–1.26 for frequent UI, ≥ 4 vs. 0 cups/day), indicating that relations observed between caffeine and UI were likely due to caffeine, rather than to other components of coffee or to lifestyle factors related to coffee drinking.

To assess the absolute effect of high caffeine intake on UI risk, we calculated attributable risks. We found that, among women who consumed ≥ 450 mg of caffeine per day, 16% of frequent UI and 25% of urgency UI could be avoided by reducing caffeine intake to 0–149 mg/day.

DISCUSSION

In this analysis, we observed no association between caffeine intake and UI overall, but a modest increased risk of frequent UI among women in the highest level of daily caffeine intake (≥ 450 mg). This increased risk appeared to be primarily explained by a higher risk of urgency UI. If women who consumed higher levels of caffeine reduced their intake, one-quarter of urgency UI might be eliminated. We found no increase in UI with lower levels of caffeine consumption.

Several potential biological mechanisms support our finding of an association between caffeine and urgency UI. For example, caffeine may promote incontinence through its diuretic effect, especially among people with underlying detrusor overactivity.¹¹ In addition, laboratory studies have shown that low doses of caffeine can increase the velocity of muscle contractions in bladder smooth muscle through increased release of intracellular calcium from intracellular storage sites.¹² Finally, a case-control study in humans found an association between high caffeine intake and detrusor instability (OR 2.4, 95% CI 1.1–6.5 comparing >400 mg/day to <100 mg/day).¹³

In another prospective study, Dalloso et al. found no association between daily tea or coffee consumption and stress UI or overactive bladder syndrome, defined as urgency and/or urgency UI, among 6,424 women aged ≥ 40 years.¹⁴ However, the follow-up period was 1 year versus 4 years in our study, the endpoint of overactive bladder syndrome was less specific than our urgency UI endpoint, and they did not distinguish decaffeinated from caffeinated coffee or tea, or evaluate total caffeine intake, all of which may have resulted in bias to the null.

Some limitations of our study should be considered. All information on UI and caffeine intake was self reported. However, previous studies have established the reliability and validity of self-reported UI data.^{6,15} In addition, previous findings indicate that self-reported UI type is highly specific, which is most important to achieve valid results in prospective studies.¹⁷ Additionally, we only evaluated UI type in those with frequent UI, which may improve sensitivity. Furthermore, our caffeine data were derived from well-validated FFQs.^{9,10}

In an observational study, confounding cannot be ruled out as a potential explanation for the observed results. However, in secondary analyses, caffeinated but not decaffeinated coffee was significantly associated with risks of frequent UI and urgency UI, providing some reassurance that caffeine, rather than lifestyle factors associated with drinking coffee which were unaccounted for in our models, was responsible for our significant findings. Substantial confounding by lifestyle factors associated with drinking soda is less likely, since soda contributed to 11% of caffeine intake and we adjusted for many factors associated with soda consumption, such as BMI, physical activity, and diabetes. Furthermore, as part of other research, we found that soda intake was not associated with UI after adjustment for caffeine, indicating that soda intake (or lifestyle factors related to soda

consumption) is not an important confounder.[Townsend MK, Jura YH, Curhan GC, et al. Fluid intake and risk of incident stress, urgency, and mixed incontinence; submitted]

In addition, our FFQ could not distinguish women who consumed large quantities of caffeine at once versus spread throughout the day. Thus, we cannot examine whether different consumption patterns might result in different risks of UI.

Finally, because >95% of our study participants are white, our findings may not be generalizable to non-white women, in whom incidence and type of incontinence tend to be different than in white women.

CONCLUSIONS

In conclusion, our findings suggest that higher daily caffeine intake (roughly equivalent to ≥ 4 cups of coffee or ≥ 10 cups/cans of caffeinated tea or soda per day), but not lower levels, is associated with a modest increased risk of frequent urgency UI in women. Among women with high caffeine intake in our population, 25% of incident urgency incontinence may be attributable to caffeine consumption. Thus, if our findings are confirmed in future studies, self-monitoring and counseling to reduce caffeine intake might be considered to reduce the burden of incident UI in women.

Acknowledgments

FUNDING/SUPPORT: This study was funded by grants DK62438, CA87969, and CA50385 from the National Institutes of Health. Dr. Townsend is supported by the Yerby Postdoctoral Fellowship Program at Harvard School of Public Health.

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Table 1
Characteristics of study participants in each cohort according to caffeine intake at baseline*

Characteristic [†]	Caffeine intake (mg/day)							
	Nurses' Health Study				Nurses' Health Study II			
	0-149 (n=16211)	150-299 (n=4524)	300-449 (n=9245)	≥ 450 (n=2681)	0-149 (n=14180)	150-299 (n=5108)	300-449 (n=7712)	≥ 450 (n=2654)
Mean age, years (SD)	65.9 (7.0)	65.0 (7.0)	65.1 (6.9)	64.2 (6.6)	45.8 (4.8)	45.9 (4.7)	46.4 (4.6)	46.5 (4.4)
Mean BMI, kg/m ² (SD)	25.9 (4.8)	26.0 (4.7)	25.6 (4.5)	25.6 (4.7)	25.5 (5.6)	25.7 (5.5)	25.2 (4.9)	25.6 (5.2)
Mean physical activity, metabolic equivalent-hrs/wk (SD)	19.3 (17.3)	18.6 (16.9)	19.3 (16.9)	18.8 (17.0)	22.7 (22.0)	22.5 (21.4)	23.3 (22.3)	22.1 (21.4)
Mean fluid intake, L/day (SD)	2.0 (0.7)	2.0 (0.8)	2.1 (0.7)	2.3 (0.8)	1.7 (0.6)	2.0 (0.6)	2.1 (0.6)	2.5 (0.6)
Race (%)								
White	94.9	95.2	96.7	96.9	95.0	95.8	97.1	98.0
Black	1.7	1.5	0.6	0.6	1.6	1.1	0.5	0.2
Asian	0.9	0.7	0.4	0.3	1.5	1.3	0.7	0.5
Other/missing	2.5	2.6	2.3	2.2	1.9	1.8	1.7	1.4
Parity (%)								
0	6.3	5.7	6.0	6.3	21.8	21.3	21.8	23.5
1-2	37.5	35.5	34.8	34.9	51.6	51.6	52.1	49.4
≥ 3	56.2	58.9	59.2	58.8	26.7	27.2	26.1	27.1
Cigarette smoking (%)								
Never	51.3	48.2	37.5	30.4	77.5	68.6	56.4	46.6
Past	43.7	44.7	50.3	44.7	18.5	24.7	33.7	31.8
Current, cigarettes/day (%)								
1-14	3.0	4.1	6.5	10.7	2.5	4.2	6.2	10.4
15-24	1.6	2.2	4.6	10.9	1.1	1.9	3.1	8.3
25-34	0.3	0.7	0.7	2.6	0.2	0.4	0.5	2.2
≥ 35	0.1	0.2	0.4	0.8	0.1	0.2	0.2	0.7
Diabetes (%)	7.1	7.4	5.3	4.6	2.1	2.4	1.4	2.1

* Women who became eligible for analysis after baseline are not included in the table (n=2,861).

[†] Percentages may not sum to 100% due to rounding.

Table 2

Multivariable relative risks for incident urinary incontinence, by incontinence frequency, according to caffeine intake

Case definition	Caffeine intake (mg/day)			P	
	0-149	150-299	300-449	≥ 450	trend
Person-years	122,501	49,105	40,086	13,500	
Any UI *					
Cases	8,364	3,117	3,174	1,028	
Adjusted RR (95% CI) [‡]	1.00 (reference)	0.98 (0.94 – 1.02)	1.03 (0.99 – 1.07)	1.00 (0.93 – 1.06)	
Multivariable RR (95% CI) [‡]	1.00 (reference)	0.97 (0.93 – 1.01)	1.02 (0.98 – 1.07)	0.98 (0.91 – 1.05)	0.98
Frequent UI *					
Cases	2,280	795	990	359	
Adjusted RR (95% CI) [‡]	1.00 (reference)	0.99 (0.91 – 1.07)	1.07 (0.98 – 1.15)	1.21 (1.08 – 1.36)	
Multivariable RR (95% CI) [‡]	1.00 (reference)	0.98 (0.90 – 1.06)	1.06 (0.98 – 1.15)	1.19 (1.06 – 1.34)	0.01

* Any UI is defined as incontinence at least once per month; Frequent UI is defined as incontinence at least once per week.

[‡] Adjusted for age (in months) and cohort.

[‡] Adjusted for age (in months), cohort, parity (0, 1-2, 3 or more births), BMI (kg/m², continuous), cigarette smoking (never, past, current: 1-14, 15-24, 25-34, 35 or more cigarettes per day), race (white, black, Asian-American, other/missing), diabetes, total fluid intake (liters/day, continuous), and physical activity (metabolic equivalent-hours per week, continuous).

Table 3

Multivariable relative risks for frequent urinary incontinence, by incontinence type, according to caffeine intake*

Case definition	Caffeine intake (mg/day)				P trend
	0-149	150-299	300-449	≥ 450	
Stress UI					
Cases	910	323	375	148	
Adjusted RR (95% CI) [†]	1.00 (reference)	0.97 (0.85 – 1.10)	0.99 (0.87 – 1.12)	1.17 (0.98 – 1.40)	
Multivariable RR (95% CI) [‡]	1.00 (reference)	0.95 (0.83 – 1.08)	0.97 (0.86 – 1.11)	1.11 (0.92 – 1.33)	0.75
Urgency UI					
Cases	425	139	162	60	
Adjusted RR (95% CI) [†]	1.00 (reference)	0.89 (0.73 – 1.08)	1.20 (0.99 – 1.45)	1.39 (1.05 – 1.84)	
Multivariable RR (95% CI) [‡]	1.00 (reference)	0.88 (0.72 – 1.07)	1.18 (0.97 – 1.44)	1.34 (1.00 – 1.80)	0.05
Mixed UI					
Cases	435	139	187	65	
Adjusted RR (95% CI) [†]	1.00 (reference)	0.94 (0.77 – 1.14)	1.08 (0.90 – 1.29)	1.16 (0.89 – 1.52)	
Multivariable RR (95% CI) [‡]	1.00 (reference)	0.94 (0.78 – 1.15)	1.09 (0.91 – 1.31)	1.21 (0.91 – 1.60)	0.19

* Cases of incident stress, urgency, and mixed urinary incontinence were defined only among women with frequent incontinence, defined as urine leakage at least once per week.

[†] Adjusted for age (in months) and cohort.

[‡] Adjusted for age (in months), cohort, parity (0, 1-2, 3 or more births), BMI (kg/m², continuous), cigarette smoking (never, past, current: 1-14, 15-24, 25-34, 35 or more cigarettes per day), race (white, black, Asian-American, other/missing), diabetes, total fluid intake (liters/day, continuous), and physical activity (metabolic equivalent-hours per week, continuous).