Association of Alcohol Intake With Incidence of Uterine Fibroids

AA D'Aloisio[1,2], DD Baird[2], DB Dunson[2]

[1]University of North Carolina at Chapel Hill; [2]National Institute of Environmental Health Sciences, NIH, DHHS

NIEHS
National Institute of Environmental Health Sciences

Abstract

Objective: We examined the effect of alcohol consumption on incidence and progression of uterine fibroids.

Methods: The study population consisted of 1,324 black or white women from the NIEHS Uterine Fibroid Study. Participants were randomly selected 35-49 year-old members of an urban health plan. Assessment of uterine fibroids was primarily through transvaginal ultrasounds while accounting for prior diagnosis. The Bayesian method involves use of a stochastic model to represent tumor incidence, followed by growth. Each woman's contribution to the likelihood function depends on age at any prior diagnosis, size of largest fibroid, and age at study enrollment, with postmenopausal women censored at age of menopause. Self-report of alcohol intake at age 30 and at time of study interview provided exposure data. Specification of the prior assumed no alcohol association. A Markov chain Monte Carlo algorithm was used for posterior computation separately by race. Estimated effects of alcohol are reported separately for tumor incidence and tumor growth, adjusting for vigorous exercise, age at menarche, parity, and BMI.

Results: Among white women, decisive evidence supported a relationship of increasing number of drinks weekly with increasing incidence of uterine fibroids (Bayes factor=95.1) while minimal evidence existed for an increase in tumor growth (Bayes factor=1.4). An increase in incidence occurred for those reporting even 0.5-2 drinks/wk. For black women, there was also strong evidence of increasing number of drinks weekly with increasing incidence of uterine fibroids (Bayes factor=74.8) and little evidence for an increase in tumor growth (Bayes factor=2.9). However, unlike for white women, incidence increased primarily among those reporting 7 or more drinks/wk, rather than for low intake.

Conclusions: This study suggests the involvement of alcohol intake in the onset rather than progression of uterine fibroids.

Background

Uterine fibroids

- Benign tumors which are the leading indicator for hysterectomies.
- Hormonal dependence for growth suggests the role of estrogen-promoting factors.
- Limited epidemiologic studies have investigated their etiology.
- Racial disparity with African Americans having greater prevalence and severity compared to Caucasians.

Alcohol intake

- Associated with higher concentrations of estradiol, estrone, and estrogen precursors among premenopausal women.
- Implicated in the etiology of another hormonally-dependent condition, breast cancer.

Aim

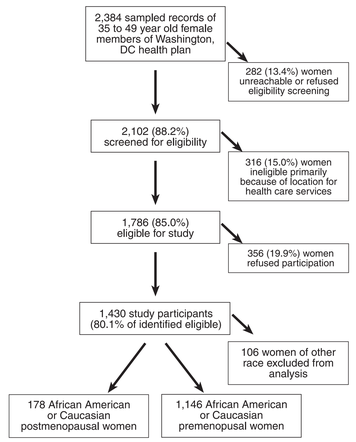
- To test hypothesis that alcohol intake increases risk of fibroid development:
  - ❍ Evaluate effects on incidence of tumors.
  - ❍ Evaluate effects on tumor growth.

Acknowledgement

This research was supported by a grant from NIEHS (P30ES10126).

Methods

Figure 1. Eligibility and response rate for study population



Uterine fibroids assessment

Premenopausal women

- Assessed primarily through transvaginal ultrasounds performed by study screening exam (66.9%), by recent clinical ultrasounds (19.6%), and 3.8% based on self-report of prior diagnosis. Accurate fibroid assessment could not be made for 9.6% of premenopausal African American or Caucasian women.

Postmenopausal women

- Assessed through either medical record verification (55.6%) or self-report (30.3%). Fibroid status could not be established for 14% of postmenopausal African American or Caucasian women.

Fibroid cases categorized by size of largest tumor

- Categories: none (reference), <2 cm, 2-3.99 cm, and 4+ cm.

Alcohol intake assessment

- Self-administered questionnaires for intake within the past 12 months and at 30 years of age.
- Drinks per week calculated based on 1) how often women reported drinking and 2) the number of drinks typically consumed.
- Nondrinkers defined as women who consumed less than 0.5 drinks per week.
- Drinkers further categorized in dose response analyses into the following groups (based on distribution): 0.5-2 drinks, >2-<7 drinks, and 7+ drinks per week.

Analysis

Logistic regression (premenopausal women)

- Prevalence odds ratios and 95% confidence intervals calculated using:
  - ❍ Race-stratified unconditional logistic regression for the relationship of alcohol consumption with the prevalence of uterine fibroids
  - ❍ Race-stratified polytomous logistic regression examined the alcohol intake associations with the tumor size categories in reference to women without tumors
- Separate analyses assessed relationships of alcohol intake at study entry and alcohol intake at 30 years of age with uterine fibroid outcomes.
- All odds ratio estimates adjusted for age, current vigorous exercise, age at menarche, parity (25+ years of age), and BMI.
  - ❍ BMI defined at study entry for analyses involving current alcohol consumption
  - ❍ BMI at 30 years of age for analyses involving alcohol intake at 30 years

Bayesian methods (premenopausal and postmenopausal women)

- Multistate model allowed for tumors to progress stochastically in order to simultaneously measure separate effects of alcohol intake (4 categories) on incidence and progression of uterine fibroids.
- Each woman's contribution to the likelihood function depends on current status of uterine fibroids and age at possible past diagnoses.
- Unlike logistic regression analysis, this method includes information from post-menopausal women.
- Tumor size is informative for not only rate of progression but also onset since smaller tumors assumed to have developed more recently.
- Used prior probability of 0.5 and a Markov chain Monte Carlo (MCMC algorithm) for posterior computation.
- Accounted for separate effects on incidence and progression for current vigorous exercise, age at menarche, parity (25+ years of age), and BMI.
- Empirical Bayes factors calculated as measure of evidence for separate effects of alcohol intake.
- Estimated posterior summaries of average risk ratios for category specific effects of alcohol compared to nondrinkers.

Results

Frequency distribution by race of study characteristics

	All (1,324)		Premenopausal (1,146)	
	African American (820)	Caucasian (504)	African American (691)	Caucasian (455)
	N (%)	N (%)	N (%)	N (%)
Outcome				
Uterine fibroids				
None	166 (20.2)	207 (41.1)	161 (23.3)	201 (44.2)
<2 cm	112 (13.7)	77 (15.3)	103 (14.9)	72 (15.8)
2-<4 cm	233 (28.4)	99 (19.6)	205 (29.7)	93 (20.4)
4+ cm	223 (27.2)	72 (14.3)	151 (21.9)	50 (11.0)
Missing	86 (10.5)	49 (9.7)	71 (10.3)	39 (8.6)
Exposures				
Current alcohol drinks per week				
0-<0.5	387 (47.2)	78 (15.5)	327 (47.3)	68 (15.0)
0.5-2	157 (19.2)	131 (26.0)	135 (19.5)	117 (25.7)
>2-<7	79 (9.6)	118 (23.4)	70 (10.1)	110 (24.2)
7+	82 (10.0)	113 (22.4)	66 (9.6)	104 (22.9)
Missing	115 (14.0)	64 (12.7)	93 (13.5)	56 (12.3)
Alcohol drinks per week at age 30				
0-<0.5	383 (46.7)	92 (18.3)	318 (46.0)	83 (18.2)
0.5-2	170 (20.7)	143 (28.4)	156 (22.6)	132 (29.0)
>2-<7	77 (9.4)	112 (22.2)	63 (9.1)	103 (22.6)
7+	74 (9.0)	93 (18.5)	60 (8.7)	81 (17.8)
Missing	116 (14.2)	64 (12.7)	94 (13.6)	56 (12.3)
Covariates				
Age at study entry				
Mean (SD)	42.4 (4.2)	42.8 (4.4)	41.9 (4.1)	42.4 (4.3)
Menarche Age (years)				
≤10	98 (12.0)	28 (5.6)	77 (11.1)	20 (4.4)
11	141 (17.2)	75 (14.9)	111 (16.1)	68 (15.0)
12	221 (27.0)	143 (28.4)	187 (27.1)	128 (28.1)
13	184 (22.4)	159 (31.6)	164 (23.7)	146 (32.1)
14	83 (10.1)	56 (11.1)	71 (10.3)	51 (11.2)
15+	90 (11.0)	41 (8.1)	78 (11.3)	40 (8.8)
Missing	3 (0.4)	2 (0.4)	3 (0.4)	2 (0.4)
Current body mass index				
Under to Normal Weight (<25)	206 (25.1)	294 (58.3)	185 (26.8)	268 (58.9)
Overweight (25-<30)	237 (28.9)	122 (24.2)	204 (29.5)	109 (24.0)
Obese (30-<35)	172 (21.0)	45 (8.9)	137 (19.8)	39 (8.6)
Severely obese (35+)	200 (24.4)	43 (8.5)	163 (23.6)	39 (8.6)
Missing	5 (0.6)	0	2 (0.3)	0
Body mass index at 30 years				
Under to Normal Weight (<25)	494 (60.2)	422 (83.7)	427 (61.8)	383 (84.2)
Overweight (25-<30)	203 (24.8)	57 (11.3)	166 (24.0)	50 (11.0)
Obese (30+)	122 (14.9)	25 (5.0)	97 (14.0)	22 (4.8)
Missing	1 (0.1)	0	1 (0.1)	0
Parity (25+ years of age)				
0	420 (51.2)	326 (64.7)	348 (50.4)	288 (63.3)
1	255 (31.1)	74 (14.7)	213 (30.8)	70 (15.4)
2+	145 (17.7)	104 (20.6)	130 (18.8)	97 (21.3)
Vigorous exercise (hours per week)				
0-<3	727 (88.7)	388 (77.0)	607 (87.8)	349 (76.7)
3+	92 (11.2)	116 (23.0)	83 (12.0)	106 (23.3)
Missing	1 (0.1)	0	1 (0.1)	0

Alcohol intake with uterine fibroids among premenopausal Caucasians

	Current drinkers			Drinkers at 30 years of age		
	No. (%)	OR	95% CI	No. (%)	OR	95% CI
Uterine fibroids						
None	151 (80.8)	REF		145 (77.5)	REF	
Any	164 (86.8)	1.9	1.0, 3.5	155 (82.0)	1.3	0.8, 2.2
<2 cm	61 (93.9)	4.3	1.4, 12.9	53 (81.5)	1.3	0.6, 2.7
2-<4 cm	69 (86.3)	1.7	0.8, 3.7	65 (81.3)	1.2	0.6, 2.4
4+ cm	34 (77.3)	1.1	0.5, 2.6	37 (84.1)	1.5	0.6, 3.7

Alcohol intake with uterine fibroids among premenopausal African Americans

	Current drinkers			Drinkers at 30 years of age		
	No. (%)	OR	95% CI	No. (%)	OR	95% CI
Uterine fibroids						
None	67 (45.6)	REF		66 (44.9)	REF	
Any	181 (44.0)	1.0	0.7, 1.6	195 (47.5)	1.1	0.8, 1.7
<2 cm	46 (48.9)	1.2	0.7, 2.1	40 (42.6)	0.9	0.5, 1.6
2-<4 cm	78 (42.9)	1.0	0.6, 1.6	89 (48.9)	1.3	0.8, 2.0
4+ cm	57 (42.2)	1.0	0.6, 1.6	66 (48.9)	1.2	0.7, 1.9

Figure 2. Assessment of dose response relationship of current alcohol intake with uterine fibroids among Caucasians

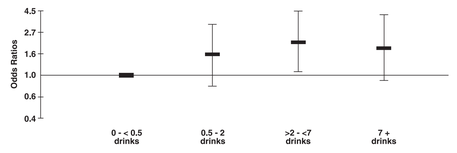
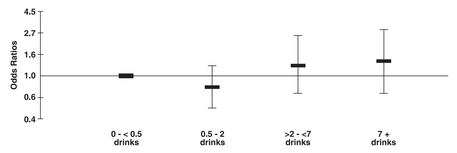


Figure 3. Assessment of dose response relationship of current alcohol intake with uterine fibroids among African Americans



Bayesian analysis: Average risk ratios for tumor onset with alcohol intake categories

	Caucasians		African Americans	
	RR	95% CI*	RR	95% CI*
Alcohol drinks per week				
0-<0.5	REF		REF	
0.5-2	1.4	1.0, 2.0	1.0	1.0, 1.1
>2-<7	1.5	1.1, 2.2	1.1	1.0, 1.2
7+	1.6	1.1, 2.3	1.2	1.1, 1.4

* Order-restricted assumption results in lower confidence limit ≥ 1.0

Summary

Caucasians

Logistic regression (premenopausal women)

- Odds of having uterine fibroids was 1.9 (95% CI: 1.0, 3.5) times greater among current drinkers compared to current nondrinkers.
- Weak positive association of having uterine fibroids with alcohol intake at 30 years of age.
- Strongest association with current drinking status estimated for tumor size of < 2 cm (OR=4.3; 95% CI: 1.4, 12.9).
- Alcohol intake at age 30 was more strongly related to having large tumors (4+ cm) (OR=1.5; 95% CI: 0.6, 3.7) than current alcohol consumption.
- Threshold effect of alcohol intake indicated in which increased odds of having uterine fibroids is related to consumption of at least 0.5 drinks per week rather than a dose response relationship (Figure 2).

Bayesian methods (premenopausal and postmenopausal women)

- Strong evidence of increase in incidence with increasing numbers of drinks weekly even for those women reporting as few as 0.5 to 2 drinks per week. No further increase occurred among those women with intake of at least 7 drinks per week (Bayes factor=95.14).
- No evidence of positive relationship between drinks per week and progression of uterine fibroids (Bayes factor=1.36).

African Americans

Logistic regression (premenopausal women)

- Only very weak associations of having uterine fibroids with drinkers compared to nondrinkers at either time point.
- Strongest association with current alcohol intake estimated for tumor size of < 2 cm (OR=1.2; 95% CI: 0.7, 2.1).
- Alcohol intake at age 30 was more strongly related to having larger tumors of at least 2 cm than current alcohol consumption.
- Weak positive association with current intake of greater than 2 drinks per week with prevalence of uterine fibroids (Figure 3).

Bayesian methods (premenopausal and postmenopausal women)

- Strong evidence of increase in incidence with increasing numbers of drinks weekly but effect was primarily observed among those consuming 7 or more drinks per week (Bayes factor=74.84).
- No evidence of positive relationship between drinks per week and progression of uterine fibroids (Bayes factor=2.89).

Strengths/Limitations

Strengths

- First epidemiologic study to examine relationship of alcohol intake with uterine fibroids among both racial groups.
- Screening through transvaginal ultrasounds for assessment of uterine fibroids rather than merely using clinical diagnoses and/or hysterectomies.

Limitations

- No estimate of uterine fibroids incidence for women less than 35 years of age.
- Alcohol consumption based on self-report.
- No information on alcohol intake prior to 30 years of age.
- Missing fibroid or alcohol information for approximately 15% of women.
- Differences in recall according to age at study entry for alcohol intake at 30 years.

Conclusions

- **Alcohol intake associated with development of uterine fibroids in both Caucasians and African Americans, but different dose response**
  - ❍ **Caucasians: even lowest dose (0.5-2 drinks/wk) showed significant effect**
  - ❍ **African Americans: little effect below 7+ drinks/wk**
- **Alcohol intake associated with tumor onset, not tumor progression**
  - ❍ **Suggested by association of current alcohol intake with small tumors and alcohol at age 30 with large tumors**
  - ❍ **Confirmed by Bayesian analysis**
- **Relationships with tumor size may reflect reduced drinking with larger tumors because of greater severity of symptoms, but preliminary analyses did not suggest relationship of alcohol consumption with symptoms.**
- **Further investigation needed with study designed to identify incident cases and follow early growth of tumors.**
- **Future examination of biological mechanisms for the association of alcohol intake with the onset of uterine fibroids is necessary.**

UNC SCHOOL OF PUBLIC HEALTH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Environmental Health Sciences