Acute Alcohol Consumption and Discrete Atrial Fibrillation Events

The HOLIDAY (HOw ALcohol InDuces Atrial TachYarrhythmias) Monitors Study

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Disclosures

- Research
  - NIH (NIBIB, NCI, NHLBI)
  - PCORI
  - TRDRP
  - Medtronic
  - Eight Sleep
  - Baylis
- Consulting
  - InCarda Therapeutics
  - Johnson and Johnson
- Equity
  - InCarda Therapeutics (as co-founder)

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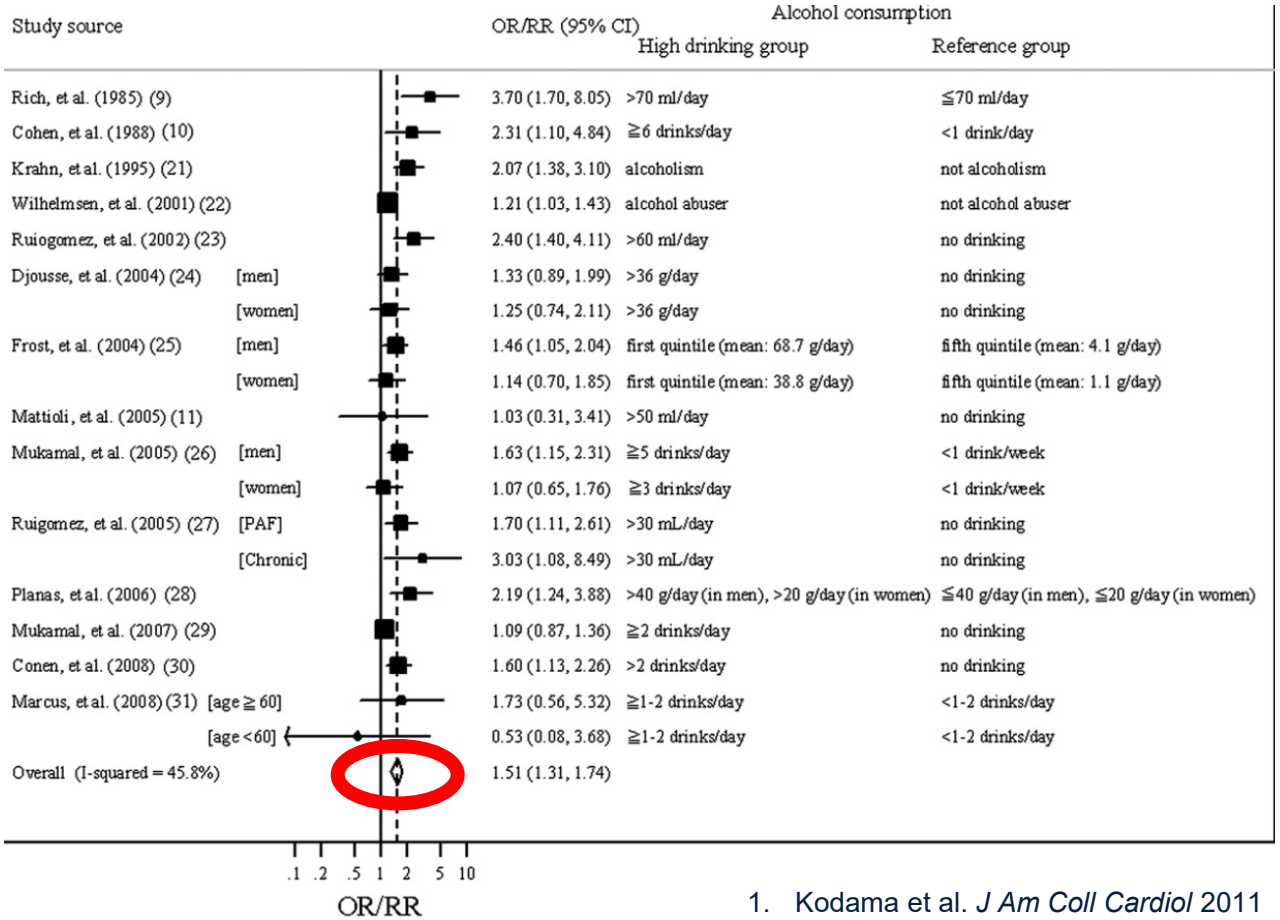


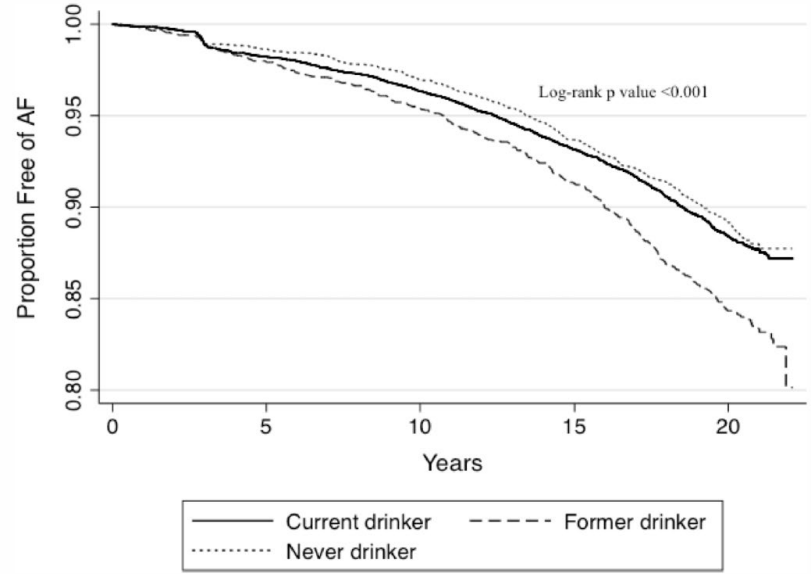
1. Kodama et al. *J Am Coll Cardiol* 2011

PLOS ONE

RESEARCH ARTICLE

Past alcohol consumption and incident atrial fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study

Shalini Dixit[1], Alvaro Alonso[2], Eric Vittinghoff[3], Elsayed Soliman[4], Lin Y. Chen[5], Gregory M. Marcus[1]*



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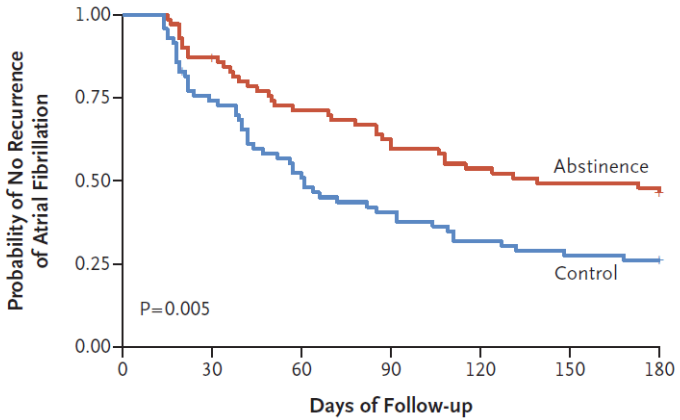
ORIGINAL ARTICLE

N Engl J Med 2020

Alcohol Abstinence in Drinkers with Atrial Fibrillation

Aleksandr Voskoboinik, M.B., B.S., Ph.D., Jonathan M. Kalman, M.B., B.S., Ph.D., Andrew J. Taylor, M.B., B.S., Ph.D., and Peter M. Kistler, M.B., B.S., Ph.D.



No. at Risk							
Abstinence	70	61	49	43	37	34	33
Control	70	51	36	28	22	19	18

Original Descriptors Focused on Acute Effects: The "Holiday Heart Syndrome"

- Small case series relying on self-reported alcohol consumption

The Role of Alcohol in New-Onset Atrial Fibrillation

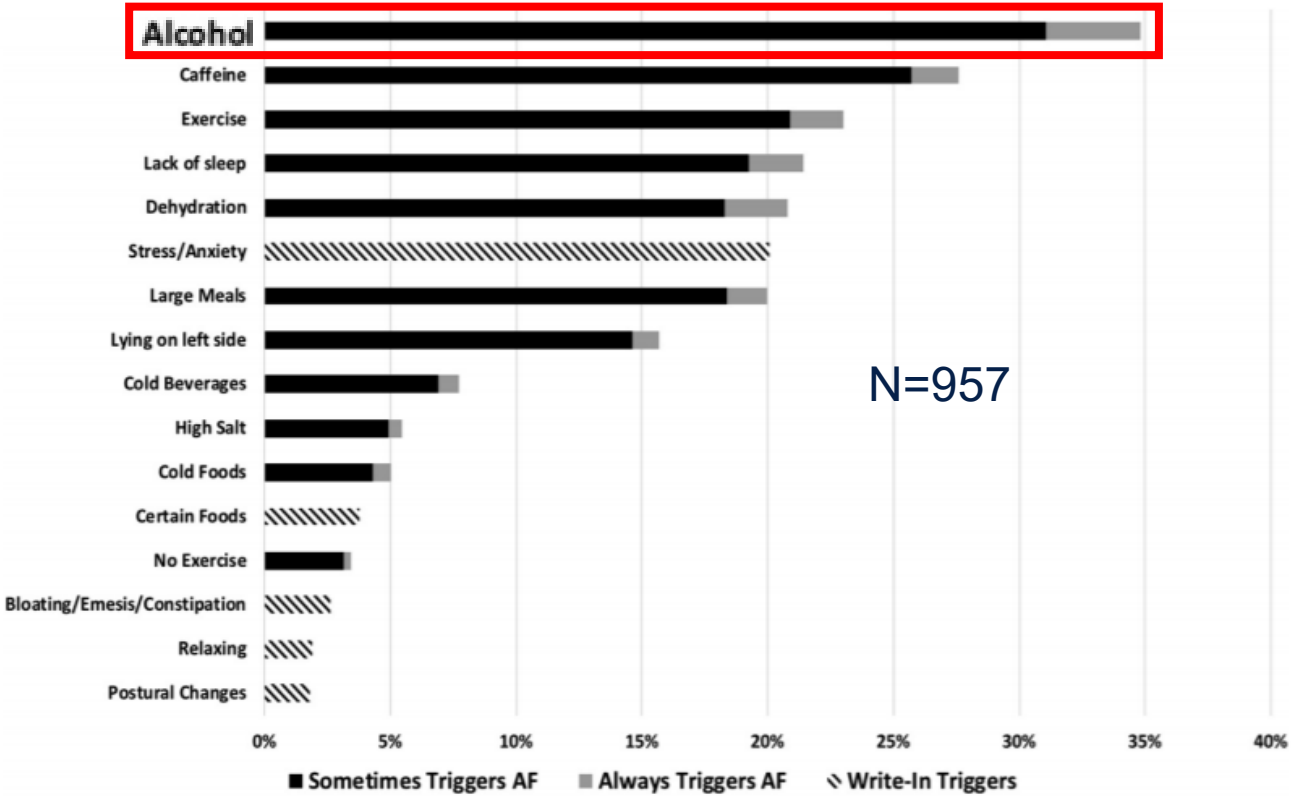
Steven R. Lowenstein, MD; Patricia A. Gabow, MD; John Cramer, MD; Philip B. Oliva, MD; Karen Ratner, MD

Arch Intern Med—Vol 143, Oct 1983

Alcohol and new onset atrial fibrillation: a case-control study of a current series

PEKKA KOSKINEN, MARKKU KUPARI, HANNU LEINONEN, KIMMO LUOMANMÄKI

Br Heart J 1987;57:468–73



Groh CA….Marcus GM. *Heart Rhythm* 2019

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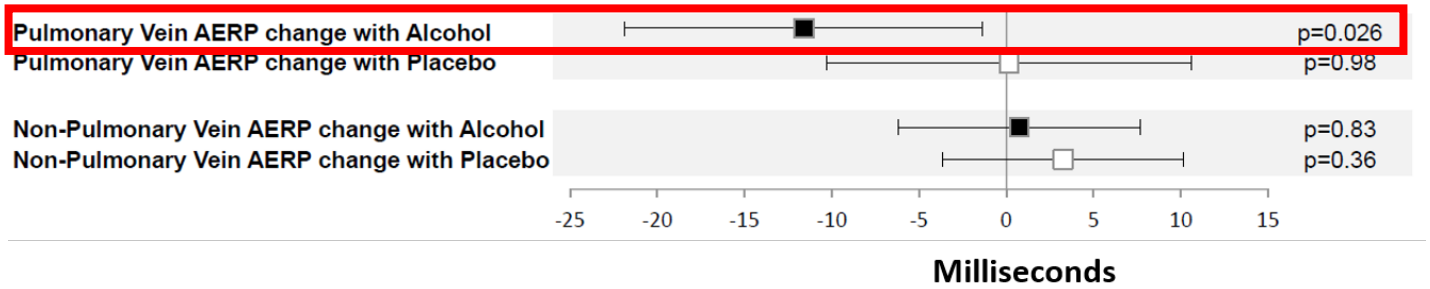
Could patients be mistaken?

- Because alcohol is so commonly consumed, such observations are prone to an “availability heuristic,”[1] where recent exposures might naturally, and yet potentially erroneously, be inferred as causal.

1. Tversky A, Kahneman D. *Science* 1974

Biological Plausibility

- Atrial fibrillation patients randomly assigned to an alcohol infusion titrated to 0.08% breath alcohol concentration versus double-blinded, volume, and osmolality-matched placebo infusion.



- No differences in AF inducibility were observed in this study of near-immediate alcohol-related effects.

Marcus GM et al. *JACC Clin Electrophysiol* 2021

Hypotheses

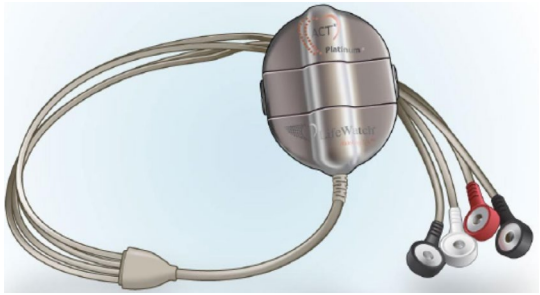
- The timing and occurrence of an atrial fibrillation episode is not due to random chance alone
- Acute alcohol consumption heightens the risk for a discrete atrial fibrillation episode

Methods

- We enrolled 100 consenting paroxysmal atrial fibrillation patients at least 21 years of age who consumed at least one alcoholic drink per month.
  - With no plans to change management in the next 4 weeks
  - No evidence of substance or alcohol use disorders (using chart review and the AUDIT-C questionnaire)

Methods

- 1 month of Wearable continuous ECG monitoring was obtained using:
  - Lifewatch (Lifewatch, Rosemount, Ill) ACT monitor in the first 27 participants
  - Two successive Zio patches (iRhythm, San Francisco, CA) in the remining 73 participants



Methods

- Using these continuously worn ECG monitors:
  - The timing of every AF episode lasting at least 30 seconds was determined
- Participants were instructed to press a patient activator button on the ECG monitor only and every time they had a standard alcoholic drink.
  - Providing a time stamp for each drink
  - A standard drink was defined as a glass of wine, 12 ounce can/ bottle of beer, or a shot of hard liquor/ spirits

Methods

- For passive continuous alcohol monitoring, participants were fit with a transdermal alcohol sensor placed around the ankle, the Secure Continuous Remote Alcohol Monitor (SCRAM, Highlands Ranch, CO).

  - These devices achieve optimal sensitivity when ≥2 drinks are consumed on one occasion
  - A “UCSF Cardiology” sticker was applied to mitigate concern regarding stigma

Methods

- Participants returned for in-person visits at two and four weeks to assure compliance with devices and place new devices (such as the second Zio patch) if needed.
- During those visits, a finger-stick blood spot was collected for phosphatidylethanol testing (PEth, United States Drug Testing Laboratories, Des Plaines, Illinois).
  - PEth is a byproduct of ethanol metabolism indicative of alcohol consumption within the previous 21 days.
  - Optimal sensitivity is achieved with binge drinking.

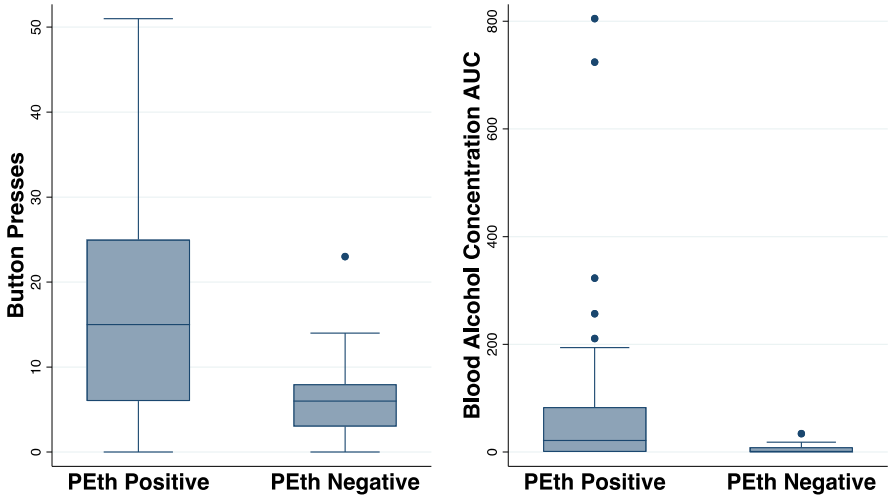
Statistical Analyses

- We employed a case-crossover analysis among all participants that exhibited at least one atrial fibrillation episode during the monitoring period.
- The associations of having an AF episode with alcoholic consumption was estimated using conditional logistic models adjusting for day of week and time of day.
  - The exact time of the first AF episode was compared to the same time on non-AF days
  - The initial “look-back” period for self-reported drinking events was set to 4 hours based on the median time estimated by participants
  - As the transdermal sensor ascertains alcohol levels only every 30 minutes and may exhibit delayed effects, the look-back time for those events was set to 12 hours

Results

- Participants wore the ECG monitor a median of 27 days (IQR 15-28), with 90% wearing it more than 21 days.
- Real-time recordings of alcohol consumption revealed a median of 19 drinks (IQR 10-38) on a median 12 (IQR 7-21) different days.
- 56 participants exhibited at least one atrial fibrillation episode.
- Atrial fibrillation occurred on a median of 5 (IQR 2.5-12.5) different days.

	No AF episode(s) (N=44)	AF episode(s) (N=56)	P-value
Mean Age (years)	64.8 ± 11.6	63.8 ± 16.9	0.72
Male sex	32 (72.7%)	46 (83.6%)	0.19
Race/ethnicity			0.84
White	37 (84.1%)	48 (85.7%)	
Asian	4 (9.1%)	5 (8.9%)	
Black	2 (4.5%)	1 (1.8%)	
LatinX	0 (0%)	1 (1.8%)	
Other	1 (2.3%)	2 (3.6%)	
Hypertension	25 (56.8%)	23 (41.8%)	0.14
Diabetes	5 (11.4%)	6 (10.9%)	0.94
Coronary artery disease	10 (23.3%)	6 (10.9%)	0.10
Congestive heart failure	3 (6.8%)	3 (5.6%)	0.80
Smoking			0.67
Never	20 (45.5%)	30 (54.5%)	
Former	23 (52.3%)	24 (43.6%)	
Current	1 (2.3%)	1 (1.8%)	
Antiarrhythmic Medications			
Amiodarone	1 (2.3%)	0 (0.0%)	0.26
Dronedarone	1 (2.3%)	0 (0.0%)	0.26
Propafenone	2 (4.9%)	5 (9.4%)	0.40
Flecainide	12 (28.6%)	5 (9.3%)	0.014
Sotalol	0 (0.0%)	1 (2.0%)	0.37



- Adjusting for study week and taking repeated measures within individuals into account, every additional participant activation-based drinking event was associated with a 23% greater odds of a positive PEth (OR 1.23, 95% CI 1.09-1.39, p<0.001).
- The Spearman correlation between real-time recordings of alcohol consumption and daily areas under the curve for SCRAM-detected events was 0.52 (p<0.001).

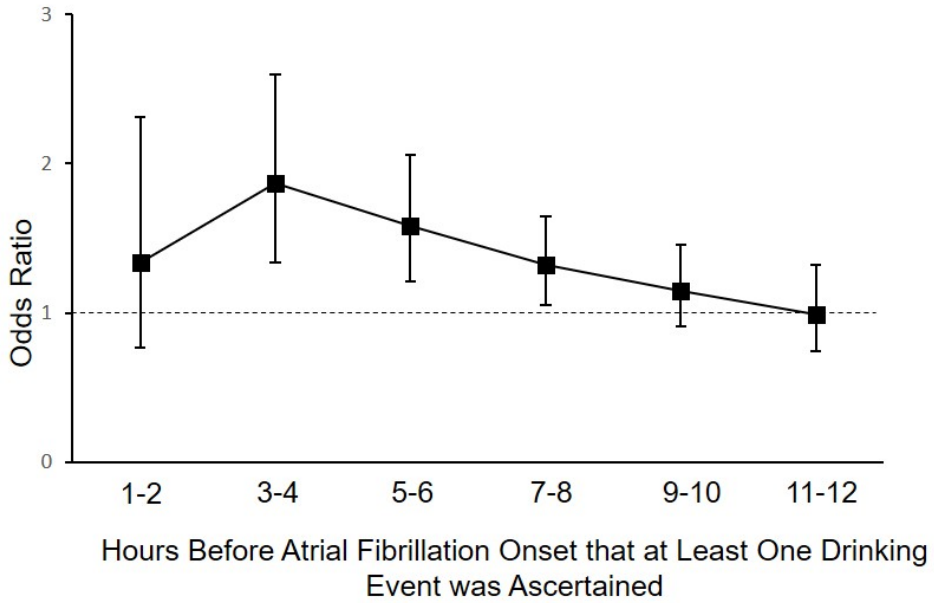
Results: real time self-reported events

Real Time Self-Recorded Drinking Events	Odds of an atrial fibrillation episode within 4 hours after drinking	95% Confidence Interval	P value
Any	2.26	1.50-3.40	<0.001
1	2.02	1.28-3.17	0.002
≥ 2	3.58	1.63-7.89	0.002

Alcohol consumption as a predictor of subsequent discrete atrial fibrillation episodes

Odds ratios are adjusted for day of the week

Results: timing of events



Results: transdermal alcohol sensor

- Every 0.1% increase in the inferred peak blood alcohol concentration in the last 12 hours was associated with a 38% greater odds of an atrial fibrillation episode (OR 1.38, 95% CI 1.04-1.83, p=0.024).
- The total area under the curve of alcohol exposure in the past 12 hours was also associated with a heightened risk for an atrial fibrillation episode:
  - Odds ratio of 1.14 (95% CI 1.06-1.22) per 4.7% increase in alcohol exposure, p<0.001).
- No threshold effects were observed.

Strengths and Limitations

- The case-crossover mitigates against confounding as the same individuals served as cases and controls.
- We cannot exclude the possibility that some concomitant behavior or exposure that occurred with alcohol consumption was a causal factor.
  - Only 1 participant in the analysis smoked
  - Caffeine unlikely to be consumed at the same time
- Poor sleep may occur due to alcohol consumption and lead to atrial fibrillation.
  - Poor sleep in this circumstance would then serve as a mediator (along the causal pathway) rather than a confounder

Conclusions

- Alcohol consumption appears to heighten the risk that a discrete atrial fibrillation event will occur.
- This relationship exhibits a delayed effect of several hours.
- No clear or consistent threshold of alcohol required was observed.
  - With evidence that even one drink may heighten the risk

Conclusions

- These data suggest that the probability a particular atrial fibrillation event will occur is not simply due to random chance.
- A common behavior, alcohol consumption, is a modifiable exposure that may empower patients to influence the risk of an atrial fibrillation event.
- These findings suggest understanding other acute triggers of atrial fibrillation may be a fruitful field of investigation.

Thank You