

Information for New Investigators

HOW TO GET ACCESS TO THE INTERNAL MESA P&P WEBSITE:

Non-MESA researchers or new MESA authors must obtain the password to the internal site from a MESA sponsor prior to submitting a manuscript.

IMPORTANT ISSUES/PREPARATION FOR NEW MESA PROPOSALS:

Proposals **must** be submitted using the internal MESA website. Select the “Proposal Submissions and New Authors” subheading followed by the “MESA Manuscript Proposal Submission Form” option.

New proposals should be no more than 4 pages in length, excluding the references. Proposals exceeding 4 pages will not be accepted.

All coauthors must have seen and approved the manuscript proposal prior to submission.

Paper proposals will not be considered by the committee unless it is feasible to begin data analysis within 12 months of proposal approval, based on the availability of sufficient endpoint data. This does not include unavailability of data due to technical problems (e.g., re-readings of scans or correction of quality control problems), delays in data cleaning, or delays in data release.

For each paper proposal, MESA P&P requires a Senior MESA author who will act as the responsible, sponsoring author (ideally from the same site).

OVERVIEW OF STEPS IN THE SUBMISSION PROCESS FOR NEW MESA PROPOSALS:

STEP 1

Review previously approved proposals and MESA published manuscripts for potential overlap with your proposal.

STEP 2

Enter administrative summary information directly on the online form.

STEP 3

Summarize the scientific "Proposal Details" in a separate Word document and attach it to your online proposal using the button at the bottom of the form. (Please attach only a Word document - not a PDF.)

An example proposal is listed at the end of this document to show the level of detail this Word attachment should include.

Example MESA Proposal

Alcohol and Coronary Artery Calcium Prevalence, Incidence and Progression: Results from the Multi-ethnic Study of Atherosclerosis (MESA)

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Introduction

Alcohol use has been consistently found to have a J-shaped association with cardiovascular disease, with moderate drinkers (1-2 drinks per day) exhibiting a decreased risk compared to both heavy drinkers and non-drinkers. Studies of the association between alcohol use and subclinical coronary artery disease have been far more conflicted. Vliegenthart et al [2004; Rotterdam Coronary Calcification Study; n=1795 population-based, no CHD] found a U-shaped relationship between alcohol use and the prevalence of extensive CAC (>400 Agatston units). The consumption of 2 or less drinks per day was associated with a lower odds of extensive CAC compared to non-drinkers. Non-drinkers and heavy drinkers were very similar. In contrast Pletcher et al [2005; CARDIA (year 15); n=3037] report a dose-response relationship, where both moderate and heavy consumption had increased CAC prevalence (CAC>0). This association was consistent across numerous methods of quantifying consumption, and after adjustment for many other risk factors. Of interest, they also found that the dose-response relationship was strongest in black men, with only heavy consumption significantly associated with CAC in whites and women.

Tofferi et al [2004] reported no association between alcohol consumption and CAC in a study of 731 US army personnel aged 39-45. The prevalence of CAC in this study was quite low (18% in non-drinkers) and hence power was limited. Point estimates supported a dose response association more so than a J-shape however. Additionally, they could not distinguish former drinkers who had quit from lifelong abstainers. Former drinkers tend to be more similar to current drinkers than to never drinkers, and including them in the reference category may have attenuated the differences between current drinkers and “non-drinkers”.

Ellison et al [2005] also found no association between CAC and alcohol consumption using data on 3166 participants from the Family Heart Study. By subsetting their data they also tried to replicate the findings of Vliegenthart et al (J-shape), and of Pletcher et al (dose-response), but they still found no association and no difference by race. They did not have the ability however to separate out former drinkers, or look at drinking history. Okamura et al [2006] studied 245 Japanese men age 40-49 and found a J-shaped relationship, though the moderate drinkers were not statistically significantly different from the non-drinkers. Heavy drinkers were at significantly increased risk. Former drinkers were excluded from this analysis.

MESA can contribute to the literature on this topic in several important ways. We have unique data to address racial differences, and also to assess CAC incidence and progression. Additionally, we have detailed data on aspects of consumption (such as binge drinking, beverage preference, and former drinking) that were not available (at least simultaneously) in many previous studies. As such, we may be able to resolve some of the discrepant findings reported from prior studies.

Research Questions

- How does self-reported alcohol consumption relate to baseline CAC in MESA? For former drinkers, does this depend on the type of alcohol consumed or on the recency of use? For current drinkers, does “binge” drinking contribute additional risk? Overall, is duration of use important in addition to quantity? If so, can this be captured by a “drink-years” variable similar to pack-years for smoking? Same questions for incident CAC, and CAC progression.
- Do these alcohol relationships vary by gender or race/ethnicity?
- Is there evidence that these associations are mediated through lipid levels? blood pressure? inflammation? glucose intolerance?

Data

All participants with complete information on alcohol use status (never/former/current), and typical quantity consumed will be included, making the resulting sample size 6749. The breakdown of amount consumed by alcohol use status is shown below.

drinks per day	alcohol status			Total
	never	former	current	
never drinker	1,390	0	0	1,390
<1 drink/day	0	1,152	2,939	4,091
1-2 drinks/day	0	210	599	809
>2 drinks/day	0	239	220	459
Total	1,390	1,601	3,758	6,749

Analysis Plan

The pattern of alcohol consumption in MESA will be extensively described by gender and race/ethnicity categories. This will include alcohol status (lifetime abstainers, former drinkers, and current drinkers), and within each of former and current drinkers: number of drinks usually consumed per week, years of alcohol use, recency of use, and beverage preferences (wine, beer, and/or hard liquor). For current drinkers we can summarize the frequency of binge drinking in the past month (5 or more drinks on one occasion), and drinking within the past 24 hours. Additionally, for current drinkers we will use the diet dataset to examine grams of each type of alcohol consumed per day.

The unadjusted association between each alcohol variable and potential confounders (e.g. income, education, body mass index, physical activity, family history of heart attack, and smoking) and potential mediators (lipid levels, blood pressure, CRP, fibrinogen, glucose) of the association between alcohol and CAC will be presented. These will be tested via analysis of variance or chi-squared tests as appropriate.

Relative risk regression will be used to model prevalent and incident CAC>0 as function of alcohol consumption. Robust regression will be used to model baseline log-transformed CAC amount as a function of covariates, and change in CAC (consistent with the Kronmal et al paper on CAC progression). For each alcohol variable of interest we will consider unadjusted models, models adjusted for age, gender and race, models further adjusting for other potential confounders (e.g. income, education, body mass index, physical activity, family history of heart attack, and smoking), and finally for potential mediators (lipid levels, blood pressure, CRP, fibrinogen,

glucose). Interactions of each alcohol variable with gender, race and smoking will be tested. Among current drinkers we can use the diet data to examine if there is a threshold in terms of grams of alcohol consumed per day on average that seems to be associated with increased or decreased risk of incident CAC (overall and for each beverage type). This will be examined graphically using smoothers.

References

Vliegenthart R, Oei HS, van den Elzen APM, van Rooij FJA, Hofman A, Oudkerk M, Witteman JCM. Alcohol Consumption and Coronary Calcification in a General Population. *Archives of Internal Medicine*. 2004; 164: 2355-2360.

Pletcher MJ, Varosy P, Kiefe CI, Lewis CE, Sidney S, Hulley SB. Alcohol Consumption, Binge Drinking, and Early Coronary Calcification: Findings from the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *American Journal of Epidemiology*. 2005; 161: 423-433.

Tofferi JK, Taylor AJ, Feuerstein IM, O'Malley PG. Alcohol intake is not associated with subclinical coronary atherosclerosis. *American Heart Journal*. 2004; 148: 803-809.

Ellison RC, Zhang Y, Hopkins PN, Knox S, Djousse L, Carr JJ. Is alcohol consumption associated with calcified atherosclerotic plaque in the coronary arteries and aorta? *American Heart Journal*. 2005; 152: 177-182.

Okamura T, Kadowaki T, Sekikawa A, et al. Alcohol Consumption and Coronary Artery Calcium in Middle-Aged Japanese Men. *American Journal of Cardiology*. 2006; 98: 141-144.