

Cardiovascular Effects of Chronic + Binge Drinking in Adult and Aged Mice

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Background

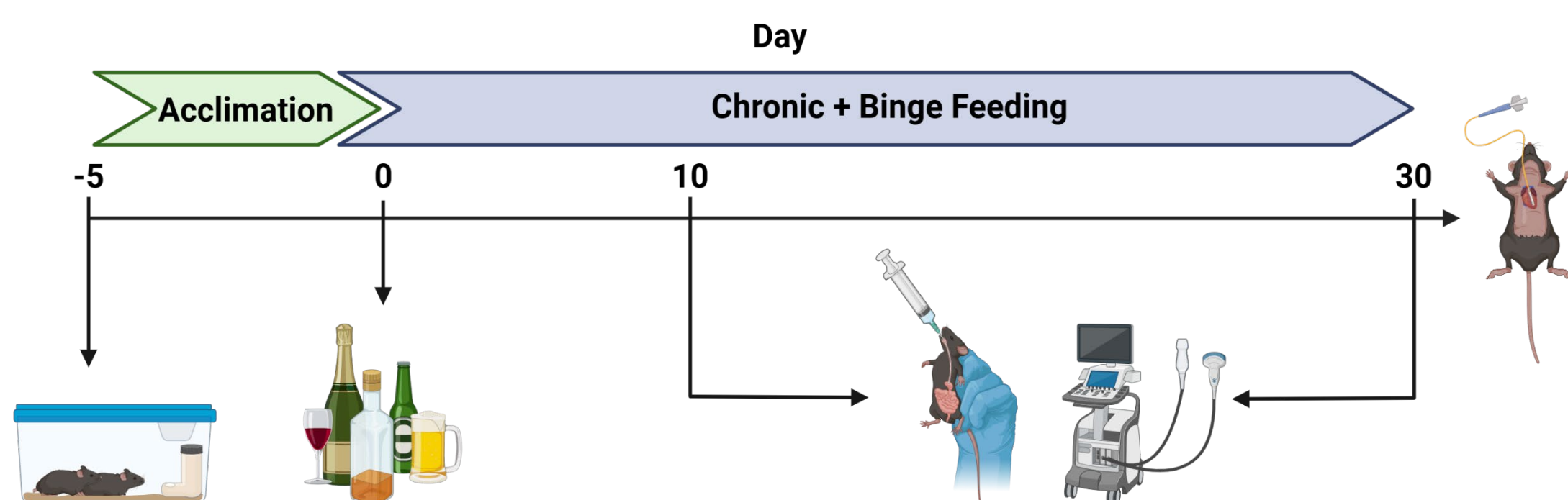
- Alcohol misuse is a growing public health concern, especially among adults aged 50 and older.^{1,3,4}
- Excessive alcohol use is a risk factor for cardiovascular disease (CVD) which can contribute to the development of non-ischemic alcohol-associated cardiomyopathy (ACM), marked by ventricular weakening and dilation. Age-related susceptibility to alcohol-associated cardiac dysfunction remains unclear, despite being well-characterized clinically.^{5,6}
- This study examines the impact of chronic plus binge alcohol exposure on cardiac function in adult and aging male C57BL6/J mice.

Hypothesis

We hypothesize that chronic plus binge alcohol exposure will promote premature cardiovascular aging and functional deterioration in mice.

Methods

- In this study, two experimental groups were used based on a previously published feeding paradigm: pair-fed (PF) and ethanol-fed (EF) mice, given an isocaloric Lieber-DeCarli liquid base diet.
 - PF = control diet fed based on intake of EF group
 - EF = ethanol diet fed *ad libitum*
- Both PF and EF groups subdivided by age
 - Adult = 13 weeks at onset
 - Aging = 72 weeks at onset



- The mice were acclimatized to the liquid diet for a 5-day period before starting experimental diets.
- Maltose dextrin (9 g/kg) and ethanol (5 g/kg) gavages were given on days 10 and 30.
- Follow-up echocardiographic data was collected 24 hours after the day 10 and 30 binges.
- The endpoint pressure-volume catheterization procedure was performed 24 hours after the day 30 binge and aortas were collected for wire myography.
- Wire myography was performed on aorta rings via mounting onto a thin wired force transducer measuring contractile tension generation while being suspended in a physiological solution. The solution was exposed to ACh, Phenylephrine, and SNP.

Results

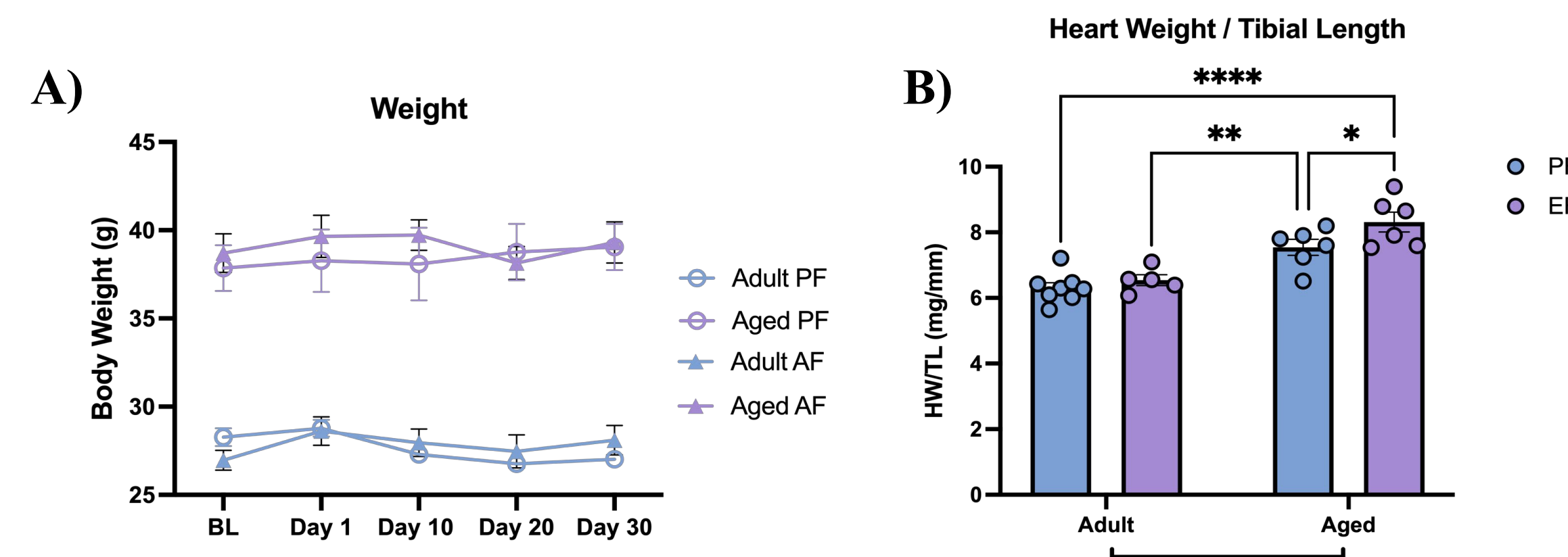


Figure 1: Body weight and heart weight following the feeding paradigm. A) Body weight (g) over the course of feeding. B) Heart weight normalized to tibial length (mg/mm). n=5-8 per group, HW/TL analyzed by 2way ANOVA, main effect of Age and Alcohol, Post-hoc analysis using Fisher's LSD. * $p < 0.05$, *** $p < 0.0001$.

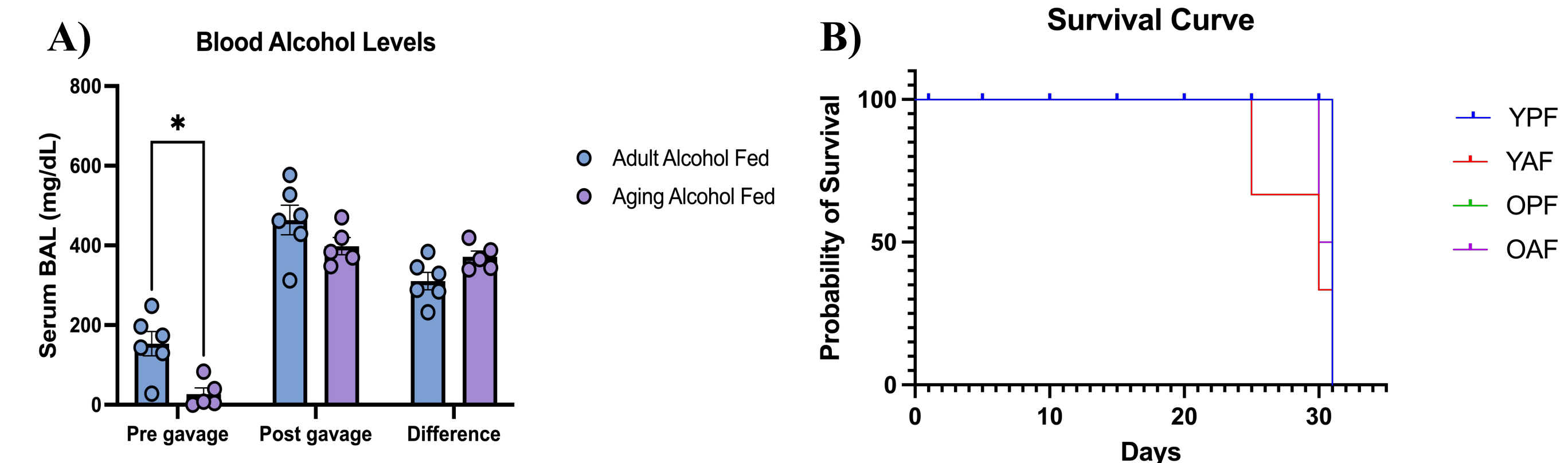


Figure 2: Blood alcohol levels and survival curve following the feeding paradigm. A) Serum BAL (mg/dL) pre and post gavage. B) Probability of survival (%) by feeding group. n=5-6 per group, BAL analyzed by 2way ANOVA, main effect of Age, Post-hoc analysis using Fisher's LSD. * $p < 0.05$.

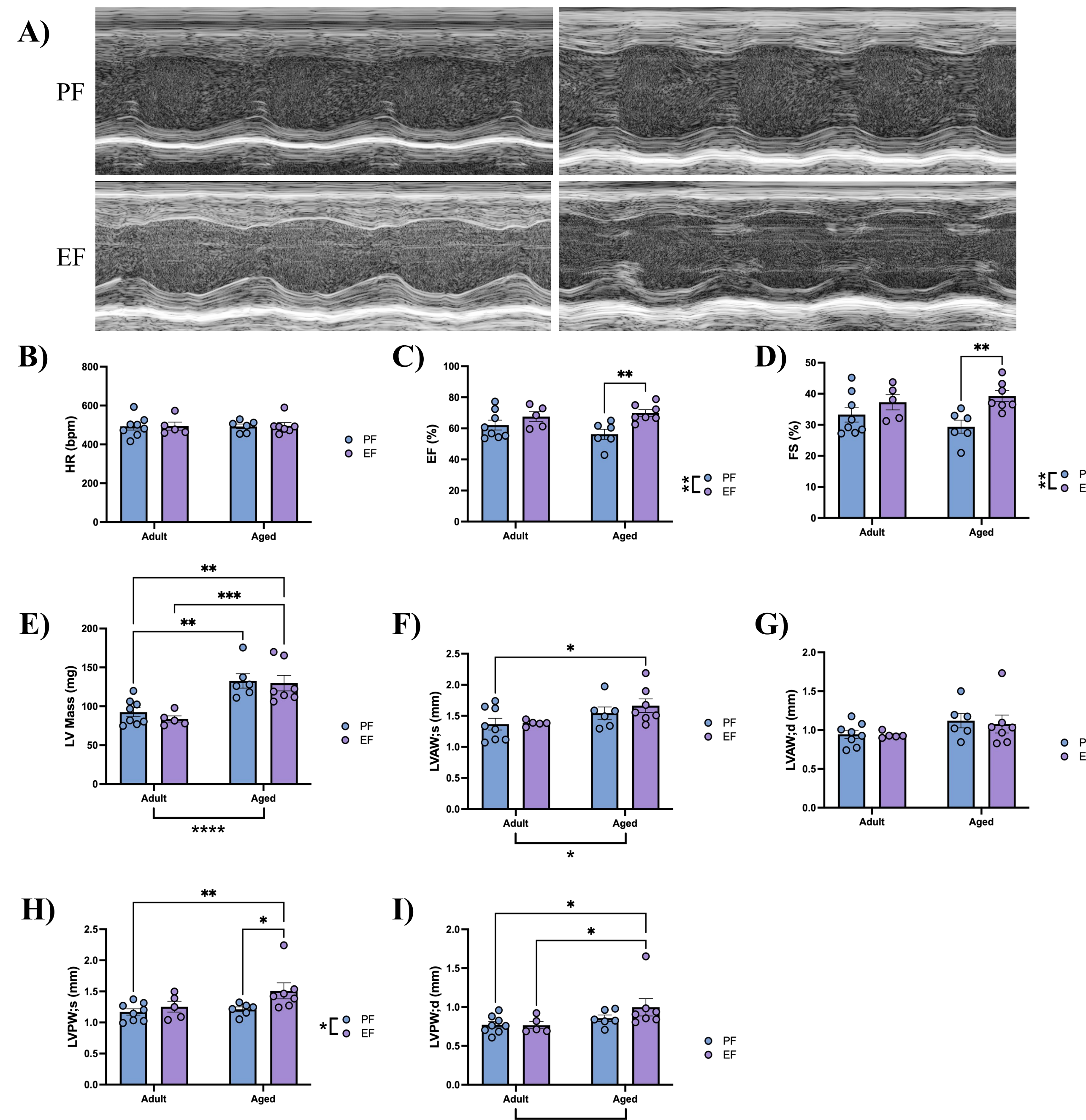


Figure 3: Echocardiography measured 24 hours post the final binge. A) Representative images, B) Heart rate, C) Ejection fraction, D) Fractional shortening, E) Left ventricle mass, F) Left ventricle anterior wall thickness during systole, G) Left ventricle anterior wall thickness during diastole, H) Left ventricle posterior wall thickness during systole, and I) Left ventricle posterior wall thickness during diastole. n=5-8 per group, 2way ANOVA. Post-hoc analysis using Fischer's LSD.

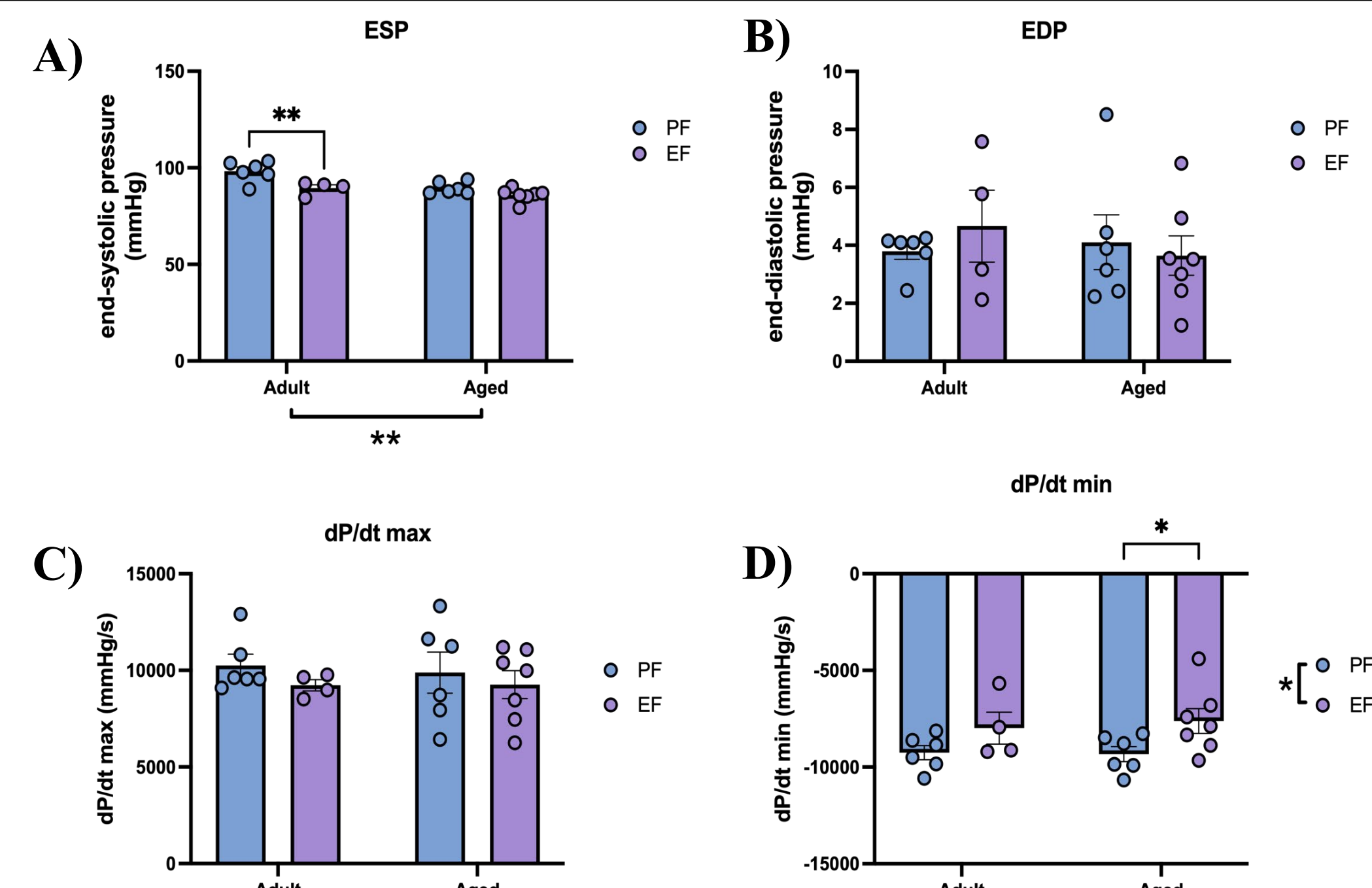


Figure 4: Preliminary pressure data from left ventricle pressure volume catheterization. A) End systolic pressure, B) End diastolic pressure, C) Maximum change in pressure during systole, D) Minimum change in pressure during diastole. n= 4-7 per group. analyzed by 2way ANOVA, main effect of Age and Alcohol, Post-hoc analysis using Fisher's LSD. * $p < 0.05$, ** $p < 0.01$.

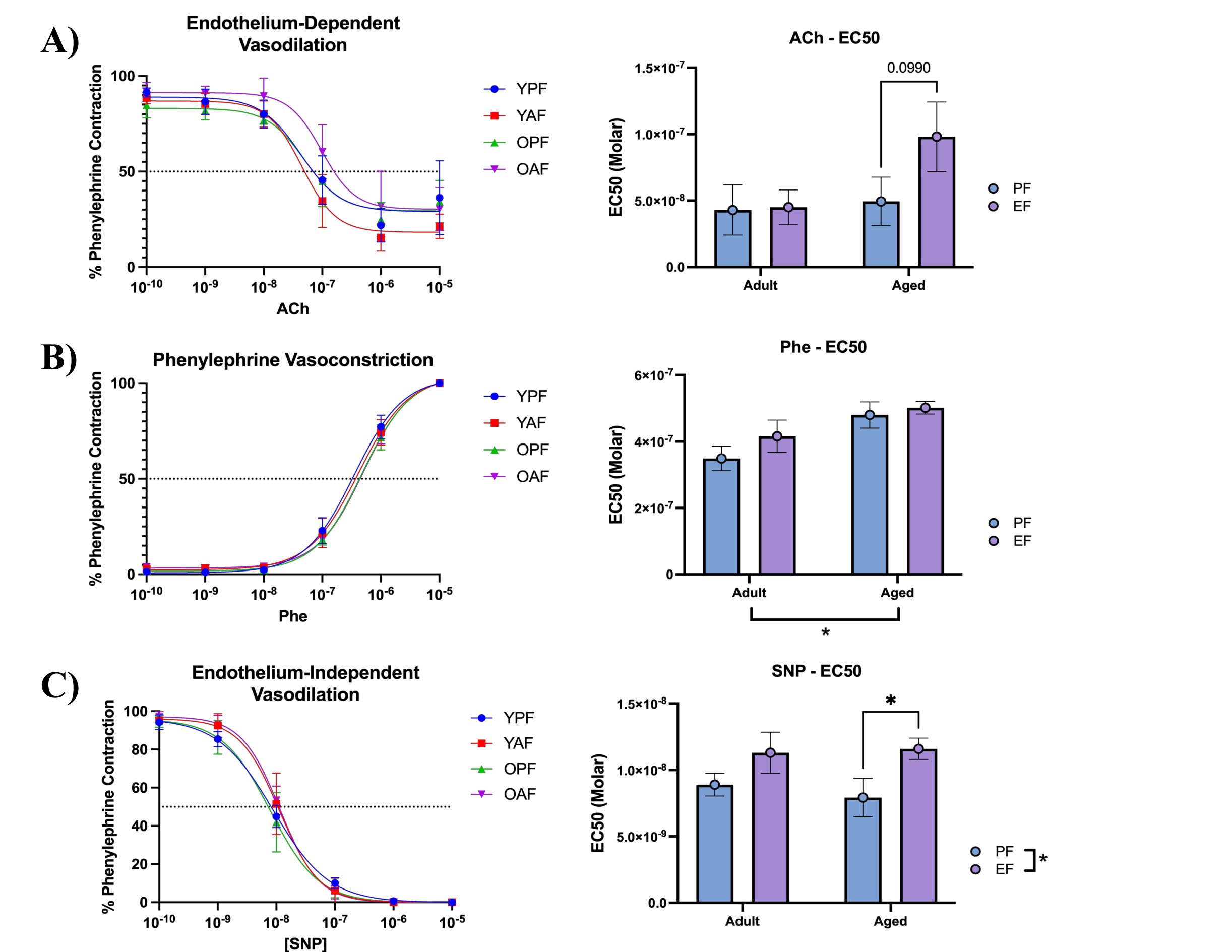


Figure 5: Pin myography of aortic rings from adult and aged mice. (A) Endothelium-dependent vasodilation measured by acetylcholine response curve. (B) Constriction following treatment of the vessels with phenylephrine (alpha adrenergic receptor agonist). (C) Endothelium-independent vasodilation measured by sodium nitroprusside (NO donor). n=4 per group, 2way ANOVA of EC50. Post-hoc analysis using Fischer's LSD.

Conclusion & Future Directions

- Chronic plus binge alcohol exposure in aging mice tends to increase vascular tone by potentially impairing nitric oxide-dependent vasodilation.
- Chronic plus binge alcohol exposure-induced increased vascular tone promotes morphological changes in the myocardium of aging mice, resulting in the deterioration of diastolic function.
- Future research will validate the morphological changes and add more diastolic functional parameters.

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