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Reference: Zuchinali P, et al. Short-term Effects of High-Dose Caffeine on Cardiac Arrhythmias in Patients With Heart Failure: A Randomized Clinical Trial. *JAMA Intern Med.* 2016, 176(12):1752-1759.

Question: Is high-dose caffeine associated with increased number of ventricular or supraventricular arrhythmias, either at rest or with exercise, in patients with heart failure?

Introduction: Arrhythmias are a common cause of sudden death in patients with heart failure. Many physicians routinely recommend that these patients avoid caffeine, based on the intuitive idea that caffeine may increase the risk of arrhythmia. However existing human data is limited – particularly in the subset of patients with known heart failure.

Methods: This was a randomized, double-blind clinical trial with a crossover design which took place at a single tertiary care hospital in Porto Alegre, Brazil. A total of 51 patients with heart failure (EF <45% and NYHA functional class I-III) were included, and randomized to either receive decaf coffee with caffeine powder (100 mg x 5 with one-hour intervals), or decaf coffee with placebo powder. Patients were monitored via continuous EKG for all 5 one-hour intervals, then for a period of exercise on a treadmill and a short rest period (~6 minutes) following exercise. This was followed by a 7 day washout period, after which the placebo and caffeine groups were switched. Primary outcomes were number & percentage of ventricular and supraventricular premature beats. Secondary outcomes included episodes of non-sustained ventricular or supraventricular tachycardia, ICD firing, plasma caffeine concentration and BNP levels, and number of premature beats during the treadmill test.

Results: Two patients dropped out early due to nausea and headaches. There were no significant differences in number or percentage of ventricular or supraventricular premature beats, either at rest or during exercise. There were no significant differences in BNP levels between groups. There was no effect of sequence order of crossover. No significant differences were found between subgroups (higher vs. lower serum caffeine levels, habitual vs. non-habitual coffee drinkers, use of amiodarone and digoxin). The only significant difference between groups was higher peak systolic and diastolic blood pressure in the caffeine group during exercise.

Discussion & Limitations: In this double-blind RCT, the authors found no significant association between caffeine ingestion (500 mg over 5 hours) and episodes of arrhythmia, either at rest or with exercise, in patients with heart failure. This calls into question the common practice of warning patients with heart failure to avoid or limit caffeine intake. There is a lack of consistent literature showing a direct relationship between caffeine ingestion and arrhythmias in humans, although there are numerous case reports of fatal caffeine ingestions – usually at extremely high doses. **Limitations**: to this study include the relatively small sample size (n=51), the exclusion of patients with diastolic heart failure, the short-term period of monitoring, and the exclusion of patients with a recent history of heart failure related hospitalization or recent documented episodes of unstable arrhythmias (the very patients one might speculate could be at highest risk for caffeine-induced arrhythmias). Furthermore, the "high dose" caffeine used in this study was 500 mg, corresponding to two tall cups of Starbucks coffee over 5 hours, which may not be applicable to very heavy coffee drinkers.