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## The Impact of Caffeine on Brachial Endothelial Function in Healthy Subjects and in Patients with Ischemic Heart Disease

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Background: Coffee is one of the most widely used pharmacologically active beverages, however, its impact on the cardiovascular system is controversial.

Methods: To explore the impact of acute caffeine ingestion on vascular endothelial function, 80 consecutive subjects [40 healthy volunteers and 40 patients with documented coronary artery disease (CAD)] were assessed on 2 separate mornings, 1-2 weeks apart. Following overnight fasting and discontinuation of all medications for  $\geq$  12 hours, and absence of > 48 hour caffeine, participants received 200 mg of caffeine tablets or placebo in a prospective, randomized, double-blind, placebo control and cross-over study. An hour after the study drug ingestion, participants underwent brachial artery endothelium-dependent flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NTG), using high resolution ultrasound.

Results: CAD patients were older, had more diabetes, hypertension and dyslipidemia compared to healthy subjects (all p<0.01). Additionally, the use of aspirin, plavix, angiotensine-enzyme inhibitors, beta blockers, and statins was significantly more common in CAD patients compared to healthy controls (all p<0.01). At baseline, FMD, but not NTG, was significantly lower in CAD patients compared to controls ( $5.6\pm5.1\%$  vs  $8.4\pm2.9\%$ , p<0.01 and  $13.1\pm5.2\%$  vs  $12.9\pm3.9\%$ , p=0.27, respectively). However, caffeine ingestion significantly increased FMD (CAD:  $5.6\pm5.1\%$  vs.  $14.6\pm5.1\%$ ; Healthy:  $8.4\pm2.9\%$  vs.  $18.6\pm6.9\%$ ; all p<0.001), NTG (CAD:  $13.1\pm5.2\%$  vs.  $17.9\pm6.1\%$ ; Healthy:  $12.9\pm3.9\%$  vs.  $22.9\pm10.1\%$ ; all p<0.001) and significantly reduced high-sensitivity C-reactive protein (CAD:  $2.6\pm1.4$  mg/L vs.  $1.4\pm1.2$  mg/L; Healthy:  $3.5\pm3.0$  mg/L vs.  $1.3\pm1.0$  mg/L; all p<0.001) in both study groups compared to placebo.

Conclusion: Acute caffeine ingestion significantly improved endothelial function assessed by brachial artery FMD in healthy subjects and CAD patients associated with reduced plasma markers of inflammation.