

Caffeine does not significantly reduce the sensitivity of vasodilator stress MPI: Rebuttal

Whether caffeine affects the diagnostic performance of vasodilator stress myocardial perfusion scintigraphy (MPS) remains a matter for debate.^{1,2} Attenuation of stress-induced coronary vasodilation by caffeine was first demonstrated in studies using dipyridamole. In the “cons” position of the debate, Saab et al. argued that this early evidence cannot be generalized to adenosine and other related compounds because of the indirect and therefore variable vasodilator effect of dipyridamole.¹ Experimental and clinical studies have shown that dipyridamole is not inferior to adenosine for inducing maximal or near-maximal coronary hyperemia with dipyridamole and adenosine MPS having similar sensitivity and predictive value for the detection of coronary artery disease.³ An increased susceptibility to caffeine because of a less consistent vasodilator effect is therefore unlikely. With regard to the effect of caffeine on adenosine MPS, two of the three studies addressing this issue showed no effect of caffeine on adenosine-induced perfusion abnormality.^{4,5} In these two studies, average plasma caffeine concentration was half the concentration attained in the only study documenting a positive effect.⁶ Of note, the levels of caffeine detected in this study were close to those reported in the early dipyridamole work. In all three studies, caffeine did not appear to affect the hemodynamic response to adenosine stress. In the positive study, the addition of exercise was a confounder; in the negative studies, no confounder is identified, which would support the argument for a suboptimal caffeine load as the likely explanation. Caffeine metabolism obeys first-order elimination kinetics at small amounts, but zero-order occurs at higher doses.⁷ This might partly explain the lack of a dose-response relation for the extent of inducible perfusion abnormality observed in the only study investigating the effect of caffeine on regadenoson MPS.⁸ In this regard, Saab et al. argued that the observed changes in perfusion defect were small and within the reproducibility of serial imaging. The study however showed that these changes, albeit small, were significantly different from those expected from two consecutive stress MPS studies alone.

Moreover, additional analysis demonstrated that a non-negligible proportion of patients moved to a lower ischemic category after caffeine intake, suggesting that the burden of disease could be underestimated in some individuals. In summary, there is currently no robust evidence to reject the hypothesis that caffeine can have a negative impact on the diagnostic performance of vasodilator MPS, especially at moderate to high concentrations. Until new data become available, caffeine consumption before vasodilator stress would be best avoided.

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