MSNA burst frequency) − (1.303 × exercise MSNA burst frequency) ($r = -0.59$; $p = 0.02$) (Fig. 1). VO_{2peak} percent predicted also correlated with the absolute change in MSNA burst frequency elicited by exercise ($r = -0.59$; $p = 0.02$) (not shown).

The novel finding presented in this correspondence is that in middle-aged subjects, peak exercise capacity relates inversely (and independently of resting MSNA) with the magnitude of MSNA elicited by moderate-intensity leg cycling exercise: approximately one-third of the predicted VO_{2peak} could be attributed to exercise-induced MSNA. This also represents the first report of fibular MSNA recorded during contralateral dynamic leg exercise in patients with HF. An augmented neurogenic vasoconstrictor response to dynamic exercise in patients with HF, as has been demonstrated for handgrip (1), could impair exercise capacity by limiting muscle blood flow or altering its distribution. Whether exercise training attenuates exercise MSNA of patients with HF merits investigation.

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Letters to the Editor

Effects of Habitual Coffee Consumption on Vascular Function

We read with interest the article by O'Keefe et al. (1). The authors reviewed existing data regarding the effects of chronic coffee consumption, with a focus on cardiovascular (CV) health. They concluded that coffee can be included as part of a healthy diet for the general public and for those with elevated CV risk or CV disease. However, the authors did not present the vascular effects of chronic coffee consumption. In this setting, we examined the association between habitual coffee intake and endothelial function in elderly inhabitants of Ikaria Island. We found that habitual coffee consumption was associated with improved endothelial function in elderly individuals (2). Moreover, there was no association among coffee consumption, endothelium-independent vasodilation, and baseline brachial artery diameter, highlighting the association of coffee consumption with endothelial-dependent dilation (3). Interestingly, this correlation of daily coffee consumption with endothelial function was also constant in hypertensive patients and was not affected by other parameters related to general health (e.g., smoking, diabetes mellitus, hypercholesterolemia) (3). Our findings present a further explanation how chronic coffee consumption can favorably affect CV risk, providing a new connection between nutritional habits and CV health.

It should be noted that the favorable effects of coffee on vascular function appear to be attributed to a synergy among multiple, intricate mechanisms involving its phenolic antioxidant properties, the prevention of low-density lipoprotein cholesterol oxidation and the inhibition of platelet aggregation (4). Moreover, caffeine has a direct effect on endothelial function, stimulating the production of nitric oxide (NO) and the release of calcium from the reticulum, favoring the activation of endothelial NO synthase (4). Furthermore, caffeine enhances endothelial cell migration and re-endothelialization, partly through an AMP protein kinase–dependent mechanism, suggesting a beneficial role of caffeine on endothelial repair (5). Importantly, other substances of coffee beverages, beyond caffeine, can affect endothelium. Caffeic and ferulic acids appear to improve vascular function by reducing reactive oxygen species production and enhancing the bioavailability of NO. Last, coffee consumption not only exhibits inherent antioxidant properties but also activates the endogenous antioxidant defense system by increasing plasma levels of glutathione.

Thus, daily coffee consumption seems to be beneficial for vascular function, and this may affect cardiovascular prognosis.

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Reply

Effects of Habitual Coffee Consumption on Vascular Function

We thank Dr. Siasos and colleagues for pointing out that habitual coffee consumption has been associated with improved endothelial function in elderly inhabitants of Ikaria Island (1). The improvement in endothelial function may in part account for the associations of moderate coffee intake (about 2 to 4 cups daily) with lower risks for coronary heart disease and stroke (2). Indeed, even in the setting of endothelium damage, coffee has the ability to prevent arterial thrombus formation, a benefit that is independent of its caffeine content (3). Recent studies also indicate that moderate daily coffee intake may confer protection against nonalcoholic fatty liver disease (NAFLD), which is present in approximately 30% of American adults (4,5). NAFLD is an independent risk factor for coronary atherosclerosis (6), and thus coffee's ability to mobilize fat from the liver may also contribute to its apparent protective effects against coronary heart disease. The strong tendency for regular coffee use to promote dependence, although problematic in some aspects (e.g., headache and malaise are common caffeine withdrawal symptoms), might also paradoxically contribute to coffee's health benefits by reinforcing daily consumption. Even so, chronic coffee intake may be best limited to no more than 4 cups daily to avoid potential adverse effects (7).

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Diagnosis and Treatment of Obstructive Sleep Apnea Is Key to Achieving Optimal Results After Catheter Ablation of Atrial Fibrillation

Fein et al. (1) report that obstructive sleep apnea (OSA) adversely affects the results of ablation for paroxysmal or persistent atrial fibrillation (AF) except in those who reported using continuous positive airway pressure. Clearly, the study advances our understanding of the role that OSA may play in AF and its management.

The indications for testing for OSA in the study cohort were not reported, but what is likely, given that patients were predominantly middle-aged men, is that OSA was underdiagnosed, as the authors indicated. A key conclusion from this study is that testing patients with AF for OSA should be undertaken more systematically.

The current definition of obstructive sleep apnea *syndrome* requires not only ≥5 apneas/hypopneas per hour but also daytime sleepiness. This is despite data showing that <25% of patients with repetitive obstructive apneas are sleepy (2) and that there is no relationship between daytime sleepiness and the cardiovascular consequences of OSA (3) in most studies.

In addition, definitions of OSA severity based on the average number of apneas per hour of sleep may be also overly simplistic. In sleeping humans with obstructive apneas and in pig models of obstructed breathing, a single apnea can trigger AF. Factors that lead to the persistence of AF are not entirely understood (4), but clearly electroanatomic atrial remodeling plays a role in those with a high burden of AF (5).

We have previously advocated the concept that although OSA presents with respiratory symptoms, the most important adverse health effects are cardiovascular (6). In the case of AF, OSA is such a potent trigger that a case can be made for regarding it as a symptom of sleep apnea whether or not the patient happens to have daytime sleepiness. Therefore, if we are to test patients with heart disease for sleep apnea, we should not restrict our testing to sleepy patients, as is currently recommended.

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