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converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs). The investigators present a number of highly plausible hypotheses to explain the potential mechanisms by which the renin-angiotensin-aldosterone system (RAAS) blockade with these agents might reduce the burden of AF, such as antiarrhythmic effects and reversed cardiac remodeling by left ventricular hypertrophy regression and reduced left atrial stretch.

We would like to offer additional pathophysiological insights into the benefits of these drugs on AF and its complications. First, there is mounting evidence to support an association between inflammation and AF. For example, atrial biopsies taken from patients in AF have demonstrated evidence of inflammatory infiltrates within the atrial tissue (2,3). Furthermore, consistent links exist between inflammatory markers, such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, white cell count, and the presence/development of AF. It is also clear that angiotensin (ang) II has several proinflammatory properties (4). For example, ang II can act locally as a chemokine and inflammatory molecule, increasing the production of several proinflammatory cytokines (e.g., IL-6 and TNF-α), adhesion molecules (such as vascular cell adhesion molecule-1 [VCAM-1] on endothelial cells, intracellular adhesion molecule [ICAM]-1 and osteopontin, a known macrophage chemotactic and adhesion molecule), chemoattractant protein (MCP)-1 (further increasing monocyte recruitment), and various selectins (such as P-selectin and s-selectin, leading to leukocyte tethering and rolling) (5–8).

There is also histological evidence to confirm that AF (both persistent and paroxysmal) can lead to increased ang II receptor expression (9). In a key study, Cardin et al. were able to link increased atrial expression of ang II receptors with increased atrial cell death and leukocyte infiltration, again supporting a potential link among the RAAS, inflammation, and AF (10). It would also appear that the relationship between ang II and inflammation is reciprocal, as not only does ang II cause inflammation, but the converse is also true with inflammation itself acting as a stimulus for increased ang II production.

Moreover, RAAS blockade influences the complications associated with AF; also, AF confers a hypercoagulable state, even in the absence of underlying heart disease; abnormalities of hemostasis, fibrinolysis, endothelium, and platelets have all been described in this arrhythmia, which may increase the risk of stroke and thromboembolism (11). Furthermore, there is an established link among inflammation, AF, and thrombosis (12). Indeed, ang II has known prothrombotic properties, and in the AF substudy of the Losartan Intervention For End Point Reduction in Hypertension (LIFE) trial, a significant reduction occurred in stroke among losartan- versus atenolol-treated AF patients, despite equivalent blood pressure reduction (13).

Finally, there appears to be prevailing links between AF and inflammation, thrombosis, and angiotensin II activation. Consequently, RAAS blockade (by ACEIs and ARBs), with subsequent reduction in AF burden and its complications, is consistent with the reduction in the inflammatory and prothrombotic substrate related to AF.

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REPLY

Based on a growing body of evidence implicating inflammation in the development of atrial fibrillation (AF) (1–3), Drs. Mascitelli, Pezzetta, Boos, and Lip have postulated that angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) may prevent AF by reducing inflammation. We agree that this is a plausible mechanism for AF prevention, particularly because a recent randomized-controlled trial has found that systemic corticosteroids reduce both C-reactive protein and the rate of recurrent AF in patients following cardioversion (2). However, none of the trials included in our meta-analysis (4) contained data on inflammatory markers; thus, we did not make this potential mechanism a focus of our discussion. Instead, we examined available trial data, such as the class of medication evaluated and the patient group studied, in an attempt to explain the significant heterogeneity in the results of individual trials (4).

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Quantification of Coronary Lesions by 64-Slice Computed Tomography Compared With Quantitative Coronary Angiography and Intravascular Ultrasound

With great interest we have read the recent study by Leber et al. (1). They report an excellent accuracy of the new 64-slice computed tomography to diagnose proximal coronary lesions and its correlation with intravascular ultrasound. This important study reflects the rapid progression of multidetector computed tomography (MDCT) and underscores the potential of MDCT in clinical practice. In the editorial by Achenbach and Daniel (2) it is stated that, with these rapidly evolving techniques, MDCT will be able to rule out hemodynamically important stenoses in the near future, thereby replacing invasive diagnostic techniques. Although we acknowledge the great improvements in MDCT to diagnose coronary stenoses, we believe there are fundamental limitations to this technique. In this perspective we agree with Achenbach and Daniel that there is "more than meets the (angiographic) eye" when it comes to coronary lesions.

Visual estimation of the degree of coronary stenoses on coronary angiograms remains a difficult problem in clinical practice of interventional cardiologists. This assessment usually results in an overestimation of the stenosis, even when this estimation is performed by an experienced cardiologist (3). Although quantitative coronary angiography will define the degree of stenosis more accurately, it still provides no information on the functional severity of the stenosis. Fractional flow reserve was introduced to eliminate this visual bias and measure the functional significance of a lesion (4). This diagnostic procedure has since been the gold standard for evaluating coronary artery stenoses and has a great value in predicting which lesions will benefit from percutaneous coronary interventions and which lesions will not. Therefore, especially in case of intermediate coronary lesions, other diagnostic tools such as myocardial perfusion imaging with methoxyisobutylisonitrile (MIBI), single-photon emission computed tomography, and fractional flow reserve are needed in addition to coronary angiography to decide on the optimal treatment strategy in individual patients.

Naturally, MDCT has some important advantages over coronary angiography, as MDCT is not only able to show the luminal narrowing, but also provides insight in surrounding tissues and plaque morphology. However, considerable doubt can be raised as to whether stenosis visualization by MDCT will be able to correctly identify and differentiate between functionally significant and nonsignificant stenoses, in particular as quantification of stenoses by MDCT still remains difficult (1,5). So, although MDCT may be very accurate in the detection of coronary artery disease, when treatment strategies have to be made for individual patients more emphasis should be given to functional instead of anatomical tests. Therefore, in our opinion, MDCT will not replace invasive or noninvasive procedures to evaluate the hemodynamic severity of coronary lesions; rather, it will complement the currently available assortment of anatomy-oriented visualization techniques.

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REPLY

We thank Dr. Wijpkema and colleagues for their interest in our editorial (1). They clearly outline the limitations of purely morphologic imaging of coronary artery lesions. Undoubtedly, assessment of the hemodynamic relevance of coronary artery stenoses—for example, by measuring the functional flow reserve—is very valuable for clinical decision making. This is the case, especially as they correctly state, "in case of intermediate coronary lesions . . . in addition to coronary angiography." By no means does our editorial suggest that we would consider computed tomography (CT)