Audio summaries from
Dr. Valentin Fuster,
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2. Such gradients in adipocyte size around coronary arteries are detectable by CT imaging. We have recently presented a new imaging biomarker, the CT-Fat Attenuation Index (FAI), for the noninvasive phenotyping of coronary PVAT (**Figure 1**). CT-FAI has been validated in histology, gene expression studies of adipose tissue explants, and against ^{18F}FDG PET/CT imaging (3). CT-FAI mapping of PVAT allows for the detection of vascular inflammation, discriminates between stable and unstable coronary plaques, and dynamically responds to variations in the levels of vascular inflammation (3).

To date, imaging has been focused on the assessment of luminal or structural characteristics of the vascular wall. The only modality that allows quantification of inflammation is ^{18F}FDG PET/CT, but its use is limited by its low availability, high cost, and radiation. CT-FAI mapping of coronary PVAT overcomes these limitations and offers new opportunities for the detection of the vulnerable patient. CT-FAI could potentially be used for the risk stratification of patients with (or at risk for) coronary heart disease, an issue that is currently investigated in large-scale clinical cohorts.

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REPLY: New Aspects of Vasospastic Angina

Coronary Adventitial and Perivascular Adipose Tissue Inflammation

We greatly appreciate Dr. Ciliberti and colleagues and Drs. Antonopoulos and Antoniades for their interests and comments on our recent study "Coronary adventitial and perivascular adipose tissue inflammation in patients with vasospastic angina" (1). First, in response to the comments by Dr. Ciliberti and colleagues, we fully agree that focal coronary spasm at the significant organic stenosis could play a pathogenetic role in poor prognosis of patients with vasospastic angina (VSA). However, in the current study, we excluded patients with focal spasm and/or significant organic stenosis due to its potentially different pathophysiology from diffuse spasm without organic stenosis (2). It remains to be elucidated in future studies whether inflammation in the spastic site with significant organic stenosis contributes to development and/or destabilization of the atheroma. Second, although we previously demonstrated that combination therapy with calcium channel blockers (CCBs) and statins reduces inflammation and Rho-kinase activity in an atherosclerotic mouse model (3), it remains to be elucidated whether this combination therapy is also effective for VSA patients. However, in the current study, we were able to demonstrate that even CCBs alone could decrease coronary adventitial and adipose tissue inflammation in VSA patients (1). Third, regarding the possible racial differences, we are currently conducting an international prospective multicenter registry study for VSA patients (UMIN000003304), which will provide evidence on the racial differences in the disorder.

In response to the comments from Antonopoulos and Antoniades, first, we congratulate that they have elegantly showed that "inside-out" signaling occurs where signals released from the vascular wall affect adjacent fat biology in atherosclerosis (4). In the current study, we were unable to clarify the causal relationship between coronary perivascular inflammation and VSA. However, we previously demonstrated that coronary spasm could be induced in a porcine model with coronary adventitial application of interleukin-1β, which suggested that "outside-in" signaling has important roles in the pathogenesis of VSA (5). Second, we also agree that the computed tomography−Fat Attenuation Index could be a novel imaging biomarker for the noninvasive phenotyping of coronary perivascular adipose tissue (4).

Development of noninvasive and clear imaging techniques to evaluate coronary adventitial and perivascular adipose tissue inflammation is warranted.

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Cost of Therapies in Acute Coronary Syndromes

A Relevant Factor Not Reflected in the Trials

We have read the paper written by Motovska et al. (1) and the editorial by Chatzizisis and Stefanadis (2) regarding the 1-year follow-up of the PRAGUE-18 (Prasugrel Versus Ticagrelor in Patients With acute Myocardial infarction treated With Primary Percutaneous coronary intervention) study, and the investigators should be congratulated for exposing a situation of indubitable relevance. The fact that one-half of the patients changed to clopidogrel mainly due to economic reasons forces us to recognize the weight of this variable in the choice of the most appropriate therapy. This figure undoubtedly reflects the different realities between countries and groups of patients. As another example, in Spain, the

pharmaceutical copayment depends on the income of each patient, and although pensioners pay a maximum between 8.61€ and 61.75€ per month, active workers contribute between 40% and 60% of the price of medicines, with the exception of certain drugs with total funding. The group with the lowest income (<18,000€ annual gross income) contributes 40% and represent a remarkable 49% of the population, well ahead of the 23.4% of pensioners, 5.19% of those who are exempt, and the 22.3% with higher income (3). This concern is not foreign to the United States, where initiatives such as the Affordability Index have been proposed. The impact of cost as a key driver towards de-escalating $P2Y_{12}$ inhibiting therapy is also emphasized in a recently reported international expert document (4). Usually doctors warn patients about the potential side effects of medications, but they are less likely to address the price of drugs. In a survey in 2016 of >2,000 adults taking a prescription medication, only 6% knew its cost during the doctor's visit, and 63% did not know until they went to the pharmacy (5). An interesting point would be to find out the knowledge of the physicians regarding the amount of money that the patient needs to pay for the prescribed medication. It would also be convenient if the computer system showed the cost of the medication and the degree of coverage of the insurance policy of the patient in real time, which should be easy to implement.

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