angiographic no-reflow and infarct size. We have shown both in patients receiving thrombolytic therapy (2) and in patients undergoing primary percutaneous intervention (3) that grade 3 ischemia is the strongest independent predictor available on admission for the no-reflow phenomenon. Because electrocardiography is the most widely available and least expensive tool at our disposal, and because this simple parameter is a robust predictor of no-reflow, we believe that it should be widely used to predict the risk of no-reflow and possibly to select patients for protective therapies.

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Value of a High Exercise Workload to Rule Out Myocardial Ischemia

We thank Drs. Zahger and Wolak for their interest in our paper (1) and for the observation about the role of grade of ischemia on surface electrocardiography (ECG) in the prediction of no-reflow. Many ECG-derived indexes including the QRS score (number of Q waves) (2) and the QRS duration (3) along with terminal distortion of the QRS, known as grade of ischemia (4), have been used in the assessment of no-reflow risk. In our review (1), we mentioned the QRS score because it is the most widely used ECG index in the triage of ST-segment elevation myocardial infarction patients. We acknowledge that other indexes including grade of ischemia may be useful in risk stratification before primary percutaneous coronary intervention. Interestingly, in a previous study performed by Wolak et al. (4), grade of ischemia was associated with infarct size, thrombus burden, and admission glyceremia, which may all contribute to the multifactorial pathogenesis of no-reflow. We agree with Drs. Zahger and Wolak that, in an era of superspecialist and expensive tools that are not widely available, such as cardiac magnetic resonance imaging, inexpensive and readily available ECG still has a central role in the management of ST-segment elevation myocardial infarction patients with regard to microvascular obstruction after primary percutaneous coronary intervention. Indeed, ECG is useful for risk prediction and diagnosis of no-reflow, for monitoring the efficacy of mechanical or pharmacological therapies against no-reflow, and finally, for prognostic information.

We read with great interest the paper by Bourque et al. (1) regarding the value of a high exercise workload to rule out significant myocardial ischemia. In that study, only 2 (0.4%) of 473 patients reaching ≥10 metabolic equivalents (METs) and ≥85% of maximum age-predicted heart rate (MAPHR) had ≥10% left ventricular ischemia on myocardial perfusion imaging. Furthermore, of the 430 patients reaching ≥10 METs and ≥85% MAPHR without exercise-induced ST-segment depression, none had significant myocardial ischemia. These results suggest that the information provided by cardiac imaging in these patients is questionable.

Our group previously assessed the prevalence and prognostic value of myocardial ischemia on exercise echocardiography in a population of 1,433 patients with known or suspected coronary artery disease achieving a high exercise workload (defined as ≥10 METs in men and ≥8 METs in women) (2). Of them, in 437 (30%) patients, new or worsening wall motion abnormalities developed during exercise. Over a follow-up of 2.3 ± 1.5 years, 201 (14%) patients underwent coronary revascularization and 57 (4%) patients had a hard cardiac event. Furthermore, exercise echocardiography was shown to provide incremental value for predicting hard cardiac events in these patients.

It might be argued that, in this study, 19% of the patients failed to achieve >85% of MAPHR, and ST-segment changes during the tests developed in 14% of the patients. Thus, we further explored whether the findings obtained by Bourque et al. (1) would...
replicate in a population of patients fulfilling the criteria used in their study. We recently evaluated 4,004 patients with interpretable electrocardiograms undergoing treadmill exercise echocardiography in whom chest pain or ischemic electrocardiographic changes during exercise did not develop (3). Applying the criteria used in the study by Bourque et al. (1) to this population would yield 2,005 patients who achieved both $\geq 10$ METs and $>85\%$ of MAPHR. Of them, new or worsening wall motion abnormalities developed in 301 (15%) patients, 187 (9.3%) patients had ischemia involving at least 3 myocardial segments, and 138 (6.9%) patients underwent coronary revascularization. Thus, these results do not suggest that a high exercise workload may confidently rule out myocardial ischemia or significant coronary artery disease in our patients. It is important to point out that images were acquired at peak exercise, which enhanced the sensitivity of the tests (4).

Although patients achieving a high exercise workload undoubtedly have a better prognosis, a correct diagnosis is still desirable, even when coronary revascularization is not deemed necessary. It would be interesting to validate the results obtained by Bourque et al. (1) at other institutions, with different noninvasive imaging modalities, and using cardiac events or coronary angiography results as end points.

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Reply

We thank Dr. Bouzas-Mosquera and colleagues for their comments regarding our paper (1). They report the prevalence of ischemic wall-motion abnormalities by stress echocardiography in 2 studies that seem to have fundamental differences compared with ours (2,3). One important distinction is the variation in study cohort clinical characteristics. They analyzed 1 group of 1,433 patients with high exercise capacity and a 30% rate of stress-induced wall-motion abnormalities (3). Compared with our population, this cohort had a higher prevalence of previous myocardial infarction (29.0% vs. 11.8%) and included individuals with exercise ST-segment depression (14%) and achievement of $<85\%$ of their maximum age-predicted heart rate (19%). We excluded these types of patients from our low-risk cohort (1). Their inclusion in the analysis by Bouzas-Mosquera and colleagues likely contributed to the increased ischemia observed in their cohort. Moreover, they included women who reached only 8 metabolic equivalents (METs) of exercise workload compared with our cutoff of $\geq 10$ METs for both men and women. This is an important difference because those patients in our study who achieved 7 to 9 METs of workload had a 10-fold increase in the prevalence of $\geq 10\%$ left ventricular ischemia (4.3% vs. 0.4%).

The analysis of ischemia in our study was quantitative in nature. The qualitative (i.e., visual) approach used by Bouzas-Mosquera et al. (2) is associated with a higher rate of false positives for ischemia, especially in the setting of resting dysfunction, as seen in previous myocardial infarction.

To match our population more closely, Bouzas-Mosquera et al. (2) examined a second population reaching $\geq 10$ METs and $\geq 85\%$ of maximum age-predicted heart rate that expectedly had a lower prevalence of stress wall-motion abnormalities (15%) than in their other cohort (30%). It is unclear how many of these positive echocardiographic studies represent true ischemia versus false positivity because the echocardiographic results were not correlated with coronary angiography and no cardiac outcomes were provided. Thus, the 15\% ischemia prevalence in this population was not validated against a gold standard and seems high for patients achieving a high workload. In our study, the rate of any ischemia in such patients was 4.0%, which is more in line with what is expected in individuals reaching high exercise workloads and target heart rate and with what has been described in previous reports. This suggests that a significant proportion of the stress wall-motion abnormalities in the study of Bouzas-Mosquera et al. (2) may have been falsely positive for ischemia. If there were in fact such a high rate of ischemia in their $\geq 10$ METs cohort (15%), an increased event rate could be expected. Unfortunately, the survival data for this subgroup were not provided. Previous prognostic studies show low mortality rates in patients with high exercise capacity.

We agree with Dr. Bouzas-Mosquera and colleagues that additional research is necessary to confirm that the very low risk of significant ischemia in our population is associated with a comparably low rate of cardiac events. In fact, we performed a preliminary outcomes analysis of our cohort that showed no cardiac deaths over 1 year for subjects achieving $\geq 10$ METs and $\geq 85\%$ maximum age–predicted heart rate during exercise stress myocardial perfusion testing (4).

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