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RITA (Randomized Intervention Trial of Unstable Angina) 3 trial had a wide separation in the frequency of revascularization rates between the 2 arms of the respective trials compared with a modest difference in the ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes) trial.

However, despite these differences, there is clear evidence of superior outcome at 5 years with the routine invasive strategy. The heterogeneity would tend to minimize the statistically significant differences. In short, we agree that the substantial difference in revascularization rates between strategies in the FRISC II study and the RITA 3 study are likely to have contributed to the observed superior outcomes of those respective studies. We would also like to point out, as shown in Figure 2 of our paper, that the confidence intervals for the respective trials overlap, and that is true for cardiovascular death or myocardial infarction, cardiovascular death alone, and for myocardial infarction alone. Hence, the overall result is consistent with the findings from the individual trials in view of the overlap of the confidence intervals.

We agree that more work needs to be done in the selection of patients with most benefit from revascularization, and that is the rationale for the presentation of the simple "integer score." Although patients in the highest risk group were demonstrated to have most absolute gain, this group was the smallest numerically. Nevertheless, there was evidence of benefit in the remaining groups and even in the lowest risk group the absolute benefit was about 2%, and this is greater than that seen in many pharmacological studies.

The second point made by Dr. Sanchis and colleagues is that "pooling the 3 studies implies the assumption that all the strategies in the conservative groups were equivalent. . . ." In contrast, one assumes that the trials have sufficient common ground to be meta-analyzed. It is inevitable in any meta-analysis that there will be differences in specific rates of treatment. As pointed out, this heterogeneity will contribute to "noise" and tend to minimize the chance of revealing a statistically robust effect.

We disagree with the conclusion of Dr. Sanchis and colleagues that the "superiority of the invasive strategy versus the true selective invasive strategy is still unresolved." As demonstrated in this long-term outcome study, and despite the differences in strategy from trial to trial, there is nevertheless a net treatment effect observable at 5 years, and it is of a magnitude greater than seen in many trials of pharmacological therapy.

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Electrocardiographic Differential Diagnosis Between Takotsubo Syndrome and Distal Occlusion of LAD Is Not Easy

Kosuge et al. (1) present an interesting analysis on differentiating Takotsubo cardiomyopathy from anterior acute myocardial infarction using electrocardiographic criteria. However, we would like to draw attention to certain aspects of this paper. The authors do not report how the Takotsubo diagnosis was established; coronariography was not performed in 24% of the patients. In this regard, the presence of a normal coronary tree (2) does not confirm the diagnosis, because there are other causes of left ventricular apical ballooning (3).

A group of patients with anterior acute myocardial infarction was used for comparison without taking into account the site of occlusion of the left anterior descending (LAD) artery, which is of paramount importance for the interpretation of electrocardiographic results. The relationship of ST-segment elevation in V_1-V_2 to V_4-V_6 with the morphology of the ST segment in II, III, and aVF allows determining whether the occlusion is proximal or distal to the first diagonal branch (D1) (4,5). If it is proximal, the anterior muscle mass affected is large, and the lesion dipole is directed forward and upward; that explains the mirror image of ST-segment decrease in II, III, and aVF. Conversely, if the occlusion is distal to D1, the lesion dipole is directed anteriorly and slightly downward, generally resulting in an isoelectric or ascending ST-segment in II, III, and aVF. The example of a Takotsubo electrocardiogram pattern in Figure 1B by Kosuge et al. (1) is also typical of ST-segment elevation myocardial infarction due to occlusion that is distal to D1 (6).

We believe that the ST-segment shift in leads aVR and V_1 can help to differentiate Takotsubo syndrome from anterior acute myocardial infarction due to LAD occlusion that is proximal to D1, but not distal, in patients admitted within 6 h of the onset of symptoms.

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Reply

We thank Dr. Carrillo and colleagues for their interest in our paper (1). They have raised concerns regarding the diagnosis of Takotsubo cardiomyopathy (TC) in our study and questioned whether our electrocardiographic (ECG) criteria accurately differentiated TC from anterior acute myocardial infarction (AMI) with left anterior descending (LAD) coronary artery occlusion distal to the first diagonal branch (D1).

Dr. Carrillo and colleagues assert incorrectly the number of patients who underwent coronary angiography (CAG). In our study (1), all patients with TC underwent CAG during hospitalization, and "emergency" CAG was performed in 25 patients (76%). Formal diagnostic criteria for TC have yet to be established, and TC was diagnosed according to the Mayo Clinic diagnostic criteria (2) in our study.

As Dr. Carrillo and colleagues stated, deviation of the ST-segment in anterior AMI is influenced by the site of the culprit lesion of the LAD coronary artery. They assert that the ECG of TC in Figure 1B, which fulfills our ECG criteria—namely, the presence of ST-segment depression in lead aVR (ST-segment elevation in lead −aVR) and the absence of ST-segment elevation in lead V_1—is typical of anterior AMI with LAD coronary artery occlusion distal to D1. However, we assume that the presence of LAD coronary artery occlusion distal to D1 alone does not result in this ECG pattern. Because lead −aVR faces the apical and inferolateral regions, ST-segment elevation in this lead would require that the LAD coronary artery has a large perfusion territory, including these regions. In addition, the absence of ST-segment elevation in lead V_1, which faces the right paraseptal region, would require occlusion of the LAD coronary artery distal not only to D1, but also to the first septal branch (S1). One can speculate that among patients with anterior AMI, those who have all of these coronary anatomical findings are relatively rare. Therefore, we believe that our ECG criteria can help to accurately differentiate TC from anterior AMI in patients who are admitted within 6 h after symptom onset. However, we agree that it might be difficult to distinguish patients with TC from some patients who have anterior AMI with distal occlusion of the LAD coronary artery, which extends to the apical and inferolateral regions, with the use of our ECG criteria alone. Further studies in larger numbers of patients are thus needed to verify our results.

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