Conservative, True Selective Invasive, and Routine Invasive Strategies in Non–ST-Segment Elevation Acute Coronary Syndromes

We read with interest the meta-analysis published by Fox et al. (1) of long-term outcome of a routine versus selective invasive strategy in patients with non–ST-segment elevation acute coronary syndromes (1). By pooling individual data from the FRISC (Fast Revascularization During Instability in Coronary Artery Disease) II trial, the RITA (Randomized Intervention Trial of Unstable Angina) 3 study, and the ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes) trial, they analyzed the effects of the management policy in terms of hard events with greater statistical power. The main conclusion was that routine invasive strategy was superior in reducing long-term rates of cardiovascular death or myocardial infarction. This means an important step in the management of non–ST-segment elevation acute coronary syndromes that will further promote the use of invasive approach and, consequently, transferring patients to hospitals with catheterization laboratory facilities (2,3).

Our concern, however, rests on the heterogeneity inherent to the definition of a selective invasive strategy. The differences found in the trials when comparing the 2 strategies could be closely linked to the way the conservative group was treated: the greater the restriction for cardiac catheterization in the conservative arm, the greater the benefit for the invasive arm. For instance, the conservative approach in the FRISC II trial (angiography if spontaneous recurrent angina or severe ischemia on the exercise test defined by ST-segment depression ≥0.3 mV, ST-segment elevation or limited chest pain associated with a low maximum work load or a decrease in blood pressure) and the RITA 3 study (angiography driven exclusively by symptoms), differed substantially from the true selective invasive approach in the ICTUS trial (angiography if spontaneous recurrent angina or clinically significant ischemia on the exercise test) (4–6). As result, the revascularization rates at the index hospitalization in the conservative groups were 9% in the FRISC II study, 10% in the RITA 3 study, and as high as 40% in the ICTUS trial. These differences may explain why the results were favorable to the invasive strategy in the FRISC II and RITA 3 studies, whereas they were neutral in the ICTUS study. Consequently, pooling the 3 studies implies the assumption that all the strategies in the conservative groups were equivalent, which does not seem to be the case. We believe that an individual patient data meta-analysis may have the capacity to account for some degree of heterogeneity in trials design, but not when the exposure variable differed substantially in its definition. Therefore, because of this limitation, the superiority of an invasive versus a true selective invasive strategy is still unresolved.

Our personal view is that patients with non–ST-segment elevation acute coronary syndromes should be invasively managed (7), and that a true selective invasive strategy, as proposed in the ICTUS trial, constitutes a valuable alternative.

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Reply

We thank Dr. Sanchis and colleagues for their interest in our paper and for their comments.

The first point raised was that there was heterogeneity in the definition of the selective invasive strategy, in the 3 studies comprising the meta-analysis. In our paper, we discuss factors that may account for the trial-to-trial differences (page 2,441), and these not only include the differences in the rate of revascularization in the “selective invasive arm” but also differences in inclusion criteria. As we point out, the FRISC (Fast Revascularization During Instability in Coronary Artery Disease) II trial and the