Three-year duration of benefit from abciximab in patient receiving stents for acute myocardial infarction in the randomized double-blind ADMIRAL study

We would like to raise the following issues in response to the article reporting results of the ADMIRAL study by Montalescot et al.1

Although the initial ADMIRAL trial2 demonstrated superiority of combined glycoprotein IIb/IIIa receptor inhibitor and coronary stenting therapy, the outcomes of the 3-year follow-up data are subject to limitations. First, the effect of confounders such as status of coronary risk factors, life-style modifications and treatment compliance in both study groups on outcomes at 3 years of unblinded follow-up is unclear.

Secondly, ascertainment of outcomes is subject to recall bias when self-reported data from a patient questionnaire is utilized for surveying endpoints.3 If recall bias exists, this can lead to misclassification of outcomes that may invalidate study findings.

Further, the results of primary and secondary endpoints were either marginal or not statistically significant at an alpha level of 0.05 with wide confidence intervals that include the null hypothesis. Therefore, caution needs to be exercised when concluding that the ‘treatment elicits favourable clinical outcomes through the third year’, given the marginal differences between treatment groups, especially when the role of bias and confounding factors on outcomes are not fully clarified.5

Blinded, controlled term-long randomized interventional studies are further needed to clarify the interesting observations raised by this informative study.

References


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Three-year duration of benefit from abciximab in patient receiving stents for acute myocardial infarction in the randomized double-blind ADMIRAL study: reply

We have read carefully Dr Kanna’s comments trying to perform a critical appraisal of our manuscript, but it appears that most of these critics are inaccurate. Potential confounders such as coronary risk factors are important to consider, but by definition randomization is used to balance the different groups and the ADMIRAL study was randomized and the two study groups were well balanced for all baseline characteristics.1 Treatment compliance, another concern in Dr Kanna’s letter, is unlikely to be an issue because abciximab is administered intravenously for 12 h during and immediately after PCI and of course there was no further treatment compliance, another concern trying to perform a critical appraisal of our study: reply

The following concern in the letter is about the validity of self-reporting data in patient questionnaires but as we indicated this was not the only mode of data collection, and physicians were surveyed, medical records consulted… and for hard endpoints, especially mortality which was the main objective, self-reporting is clearly not an issue.

Finally, the author does not concur with the conclusions of a favourable effect of abciximab in primary stenting of STEMI. However, ADMIRAL is a positive study for its primary hypothesis showing the superiority of the study drug over placebo to reduce death, re-infarction, and urgent revascularization at 30 days, confirmed also at 6 months. Because we believe that it is important to provide information on the long-term, a three-year follow-up was conducted to determine whether the benefit observed initially was preserved; we acknowledged that the study was not powered to detect a difference in hard clinical endpoints at 3 years. However, the expression of the results with Kaplan-Meier curves demonstrated the preservation of the initial absolute benefit, with two parallel curves for death or MI, over 3 years.

Our data along with other studies confirm the benefit of GPIIbIIIa inhibition with abciximab in primary PCI. Meta-analyses have also shown a significant impact on mortality2 and a greater benefit when the drug is administered early.3-4 All guidelines recommend its use in primary PCI.

References


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Tako-tsubo syndrome: a form of spontaneous aborted myocardial infarction?

We read with great interest the article by Verheugt et al.1 on aborted myocardial infarction. We agree with the fact that after the onset of acute coronary syndrome (ACS), the best scenario would be the spontaneous or mechanical abolition of the myocardial infarct. This myocardial infarct abortion could also induce wall motion abnormalities that may recover within hours or days. We want to highlight those cases of spontaneous myocardial infarction because of auto-thrombolysis and raise the question whether we could diagnose an aborted myocardial infarction when the thrombus responsible for the event has been completely lysed.

Tako-tsubo syndrome (also named transient left ventricular apical ballooning) presents with all the signs and symptoms of myocardial infarction, slight or no enzymatic release, and apical left ventricular akinesia that recovers within the first 2 weeks.2 These patients present on angiography and under the state-of-the-art antithrombotic–anticoagulant therapy with no significant coronary artery stenosis. Because of the latter, ACS as the cause of the syndrome has usually been ruled out.3 Could tako-tsubo also represent spontaneous aborted myocardial infarction? Could it be in this population the balance between coronary thrombosis and endogenous fibrinolysis (eventually modulated by vasoconstriction) falls on the fibrinolysis side and, therefore, no thrombus is seen on angiography? This hypothesis becomes more plausible when it has been reported in tako-tsubo patients that disrupted eccentric atherosclerotic plaques of the left anterior descending have been visualized by IVUS, but were not visible by contrast angiography.4 Could the transient akinesias seen in these patients be the result of stunned plaques or interesting abnormalities due to dysfunctional platelets?5-6 We agree with the fact that the tako-tsubo syndrome has usually been ruled out.3 Could tako-tsubo also represent spontaneous aborted myocardial infarction? Could it be in this population the balance between coronary thrombosis and endogenous fibrinolysis (eventually modulated by vasoconstriction) falls on the fibrinolysis side and, therefore, no thrombus is seen on angiography? This hypothesis becomes more plausible when it has been reported in tako-tsubo patients that disrupted eccentric atherosclerotic plaques of the left anterior descending have been visualized by IVUS, but were not visible by contrast angiography.4 Could the transient akinesias seen in these patients be the result of stunned plaques or interesting abnormalities due to dysfunctional platelets?5-6