Incidence, Predictors, and Significance of Abnormal Cardiac Enzyme Rise in Patients Treated With Bypass Surgery in the Arterial Revascularization Therapies Study (ARTS)

To the Editor:

The recent report from the Arterial Revascularization Therapies Study (ARTS) trial describing the long-term implication of creatine kinase (CK-MB) release after coronary artery bypass grafting (CABG)\textsuperscript{1} is an important contribution to the literature because the adverse long-term prognostic significance of CK-MB release after percutaneous coronary interventions is now well-recognized.\textsuperscript{2} Briefly, in the ARTS trial, 1-year outcome was stratified in almost 300 CABG patients according to the magnitude of CK-MB release early after surgery (normal in 38%; \( > \times 1 \) to 3 in 43%; \( > \times 3 \) to 5 in 8%; \( > \times 5 \) in 12%). At 1-year, in patients with normal CK-MB levels early after surgery compared with those with greater than 5-fold elevations, the respective rates of death were 1\% versus 10\% and the risk of myocardial infarction 1\% versus 12\%.

The relevance of this finding is, however, thrown into doubt by the relative lack of specificity of CK-MB in exclusively indicating cardiac, rather than skeletal muscle, injury after CABG. In contrast to the situation after percutaneous cardiac intervention, where CK-MB is solely released from cardiac muscle, after CABG it is also released, albeit in smaller quantities, from skeletal muscle.\textsuperscript{3}

This is of particular importance when considering the number of internal mammary arteries (IMA) used. There is limited evidence of survival benefits of bilateral IMA grafts\textsuperscript{4} and in the ARTS trial 93\% of CABG patients received at least one arterial graft.\textsuperscript{1} However, CK-MB is elevated to a greater extent in patients with bilateral rather than single IMA grafts because of additional chest wall (intercostal muscle) dissection even when cardiac troponins, which have specific protein isoforms distinct from the skeletal muscle variety, are identical in the 2 groups.\textsuperscript{3}

The number of IMA grafts used should, therefore, have been included in the multivariate analysis of CK-MB release after surgery with CABG in the ARTS trial. This omission emphasizes again that cardiac-specific biochemical markers are essential in quantifying myocardial injury or assessing the efficacy of postulated cardioprotective strategies in adults and children\textsuperscript{5} after cardiac surgery.

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Response

Drs Taggart and Neubauer raised some interesting concerns about the relative clinical impact of creatine kinase MB isoenzyme (CK-MB) release after bilateral internal mammary (IMA) bypass. They base their beliefs on speculative information, namely that (1) bilateral IMA bypass grafts improve survival as compared to single IMA; (2) the levels of CK-MB are higher after bilateral IMA as compared with single IMA grafts. These two hypotheses, while interesting, have yet to be documented clearly in the literature.

Dr Taggart et al concluded in a recent original publication that “bilateral and single internal thoracic artery grafting results in similar levels of myocardial injury.”\textsuperscript{3} Moreover, they make an apparent contradictory statement that levels of CK-MB may be higher after bilateral IMA grafts due to additional chest wall dissection. As we have previously discussed,\textsuperscript{1} 2\% to 4\% of the total CK-MB level can result from skeletal muscle injury during coronary artery bypass graft (CABG). However, it remains unproven that major variations in the total level of CK-MB may occur between patients with minimal and those with more extensive skeletal muscle injury.

Concerning their statement—survival benefit of bilateral mammary use—there is no prospective randomized trial comparing bilateral and single IMA revascularization procedures.\textsuperscript{2}

The baseline clinical status may vary considerably among patients undergoing CABG (presence of diabetes, degree of left ventricular dysfunction, number of vessels involved, location of lesions, etc). Accordingly, a variety of possible combinations of surgical techniques can be used, which may also affect the outcome, such as different modalities of myocardial protection, use of additional artery conduits (ie, radial), number of saphenous vein grafts used, etc. Thus, it seems difficult to draw any conclusion regarding the potential benefit of bilateral IMA over single IMA based on observational or retrospective studies.

In the ARTS trial, detailed procedural data were prospectively collected and independently analyzed. The number of mammary conduits were, in fact, entered into the multivariate regression model but had no correlation with the levels of CK-MB after CABG (\( P=0.2 \)). However, these findings should be interpreted with caution since the ARTS study was not designed to test this hypothesis.

We agree with Drs Taggart and Neubauer that cardiac biochemical markers provide information essential to patient care after cardiac surgery. Unfortunately, these biochemical markers, including CK-MB and troponins, are often neglected in routine clinical practice. The issues raised by the group at Oxford are controversial, extremely interesting, and certainly warrant further investigations.

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