LETTERS TO THE EDITOR

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Correlating infarct size and patient prognosis: are cardiac biomarkers truly insufficient?

I read the recent article by Lonborg et al.,1 on the prognostic value of late gadolinium enhancement-cardiovascular magnetic resonance (LGE-CMR) in ST-segment elevation myocardial infarction (STEMI) patients, with great interest.

Recently, a single troponin measurement at either 72 or 96 h post-infarction provided an accurate estimate of infarct size and the prognostic impact of this has also been demonstrated.2-5 As myocyte necrosis culminates in the formation of scar tissue, it is unsurprising that there is also a relationship between magnitude of troponin release and scar burden assessed by LGE-CMR.6 LGE-CMR allows visualization and measurement of infarct size but, due to logistical and economical barriers, cardiac biomarkers remain the most cost-effective means of estimating the infarct size in contemporary clinical practice. Furthermore, in our times of global austerity, it is imperative that a newer, more expensive test (in this case LGE-CMR) demonstrates not just equivalence but clear superiority over the current test of choice (troponin).

Against this background, the results of the Cox regression analysis are particularly important. The authors highlight that infarct size by LGE-CMR was a predictor of outcome in both univariable and multivariable analyses but neglect to highlight that peak troponin T concentration was similarly an independent predictor of outcome! Thus, both parameters are significant over and above adjustment for the other (and the other variables in the analysis). The second point regards the composite outcome selected: there were just eight hard events and 27/35 (77%) events were hospitalization for heart failure (HF). While this is an important outcome with associated cost implications, prompt attention in the community for patients with worsening breathlessness or peripheral oedema, as can be provided by HF nurse specialists, can allow appropriate tailoring of medical therapy (e.g. increased dose of diuretics) which has been shown to reduce rates of hospitalization.7 Consequently, it is difficult to extrapolate these rates across countries due to variations between health care systems. Additionally, the reasons for HF hospitalization are numerous, ranging from a poor social support network to non-compliance with medication. It is for this reason that hard events, such as death or myocardial infarction, are the preferred outcome measure for outcome (prognosis) studies.

Thirdly, and most importantly, the authors have acknowledged that the key clinical question here is whether making a clinical decision based upon the LGE-CMR result improves patient outcome significantly more than if the decision were made based upon ejection fraction or, for that matter, peak troponin concentration. As pharmacological secondary prevention measures would be similar whether the infarct was small or large, the key issue pertains to selection of patients for defibrillator therapy. The authors are correct that a randomized controlled trial is now warranted to determine whether the significantly greater up-front cost of routine LGE-CMR in STEMI patients (compared with the cost of a troponin assay) is outweighed by the incremental clinical benefit this information provides. Until that trial is performed; however, peak troponin T concentration appears an entirely reasonable—and affordable—method for estimating infarct size.

References

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Correlating infarct size and patient prognosis: are cardiac biomarkers truly insufficient?: reply

We welcome the insightful and constructive comments by Dr Benoy N. Shah with regard to our recent paper on the association between final infarct size measured by cardiovascular magnetic resonance (CMR) and long-term outcome in patients with ST-segment elevation myocardial infarction (STEMI).1 Dr Benoy N. Shah questions the use of admission for heart failure as a clinical endpoint, since it may be more prone to bias than reinfarction and mortality. While we agree that admission for heart failure is not quite as straightforward to define as reinfarction and mortality, admission for heart failure may still be considered as a well-defined endpoint, and is used frequently. Also, the two latter endpoints may also be prone to bias affected by poor social status, comorbidity, and non-compliance to medications including anti-thrombotic. For the same reason, we adjust for...
some potential confounding factors in the multivariable analysis. Reinfarction relates to the disease within the coronary artery lumen, whereas heart failure relates to the function and damage to the myocardial. Thus, when it comes to cardioprotection and reduction in infarct size, mortality and heart failure seem to more relevant endpoints than reinfarction. Moreover, 4.7% develops clinical heart failure 1-year following a STEMI and 35% develops heart failure following discharge over 10 years. In elderly, the prevalence of heart failure following acute myocardial infarction is around 6.2% and 35% of patients who die after an acute myocardial infarction have symptoms and signs of heart failure preceding death, and patients who are continuously admitted for heart failure is at risk of dying of heart failure.6,7 Thus, we believe that this is a highly relevant endpoint.

With regard to troponin T we would like stress that it is not our belief or the purpose of our study to evaluate whether that infarct size by CMR could replace troponin T. Nevertheless, infarct size by CMR may serves as a supplement for Troponin T as a more precise measurement of the infarct size. While troponin T correlates with infarct size by CMR, the correlation is not perfect with r-values around 0.6,8 probably because the slopes of rise and fall in troponin T vary between patients and depend on time of reperfusion and flow. Troponin T at fixed time points following PCI does, therefore, not only depend on the infarct size, and peak values may easily be missed. Whereas the infarct size by CMR measured 1 month after the index STEMI (final infarct size) remains constant over time.10 Also, using biomarkers it is not possible to assess the final infarction size. In clinical research, it is important with precise and reliable methods to detect differences, and infarct size by CMR has long been considered the gold standard for measuring the infarct size in clinical research, and accordingly it is used increasingly as endpoint in clinical trials. The strong independent predictive value of the final infarct size as demonstrated in our study further encourages the use of the infarct size by CMR in clinical trials. However, with regard to the clinical use of CMR, it seems that we agree with Dr Benoy N. Shah that future studies needs to determine the clinical role of CMR in the risk assessment in STEMI patients.

References

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