Rapid estimation of myocardial infarct size

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Received 30 July 1999; accepted 2 August 1999

See article by de Groot et al. [9] (pages 315–324) in this issue.

Although the use of biochemical markers of acute myocardial infarction started in 1954 [1], their value in estimating myocardial infarct size was demonstrated roughly 20 years later. The groups of Hermens and colleagues [2] and Sobel and colleagues [3] independently reported methods to calculate infarct size on the basis of serial serum enzyme activities, such as creatine kinase (CK) and α-hydroxybutyrate dehydrogenase (αHBDH). The methods employed were based on the same principle: an input of marker (e.g. an enzyme) from the infarcted myocardium into the circulation is calculated by correction of the enzyme’s activity-vs-time curve for the output (clearance) of that marker from the circulation. To that purpose Sobel and colleagues used the late linear decline of CK’s logarithmic activity-vs-time curve [3]. Hermens and colleagues stressed the fact that the use of slowly cleared enzymes, such as αHBDH, greatly diminished the influence of error in estimated clearance rates [4]. However, for slowly cleared enzymes it appeared that their longer presence in the circulation causes extravasation of the enzyme (and back), so that incorporation of efflux to and from the extracellular space had to be taken into account in the biophysical model.

These classical methods to estimate enzymatic infarct size have proven their value when used to assess novel therapies of acute myocardial infarction, such as thrombolytic therapy. Early thrombolytic therapy in patients with acute myocardial infarction was associated with limitation of enzymatic infarct size by 30%, leading to less impairment of regional and global left ventricular function and less mortality [5]. The slogan “time is myocardium” was substantiated by showing that the earlier thrombolysis was applied, the greater the limitation of infarct size [6]. Likewise, recent improvements in therapy of acute myocardial infarction by inducing rapid reperfusion using primary PTCA were observed to be associated with further limitation of enzymatic infarct size [7]. Earlier, we demonstrated that thrombolytic therapy had no influence on the relation between infarct size estimated with αHBDH and left ventricular performance, indicating that coronary reperfusion has no influence on the recovery of myocardial αHBDH in plasma [8].

Although the benefits of enzymatic infarct size estimation have been demonstrated in several randomized trials, the method has the drawback that the data of infarct size of the individual patient becomes available relatively late, i.e. too late to have influence on acute care. The article of de Groot and colleagues describes modifications of the method to estimate infarct size [9]. The first modification is the use of concentration-vs-time curves of relatively small proteins (15-20 kD) that are rapidly cleared from the circulation, such as fatty acid-binding protein (FABP) and myoglobin. These proteins are cleared by the kidneys, whereas proteins like CK and αHBDH (or LDH) are cleared by the reticuloendothelial system, particularly the liver. The second modification is the use of individual clearance rates for FABP and myoglobin, instead of the use of mean clearance rates for large proteins like CK and αHBDH (or LDH). Individual clearance rates for FABP and myoglobin are calculated using glomerular filtration rates (estimated from plasma creatinine concentrations and corrected for age and gender) and plasma volume (corrected for age and gender).

By employing these modifications, de Groot et al. have demonstrated that infarct size as estimated from FABP and myoglobin in the first 24 hours after onset of symptoms equalled the enzymatic infarct size as estimated by CK and αHBDH in the first 72 hours after onset of symptoms. Therefore, the obvious benefit of using serum FABP or myoglobin concentrations to estimate infarct size is the marked shortening of the sampling procedure: 24 hours with FABP and myoglobin as opposed to 72 hours with CK and αHBDH. That implies that, if FABP and myoglobin are assayed rapidly, a reliable estimate of infarct size will become available while the patient is still in the acute
care department. The only extra determinations to be performed are those of plasma creatinine in blood samples obtained at admission, and 12 and 24 hours thereafter.

Although it will not be easy to acquire infarct size estimations on the basis of FABP or myoglobin on a daily routine basis, recent advances in marker protein research for (minimal) myocardial damage and myocardial infarction are shifting the optimal marker panel from the classical enzyme activities (LDH, CK, CK-MB) to “new” markers, such as troponin I, troponin T, FABP, myoglobin and C-reactive protein [10]. As the assays of these novel markers are being implemented in modern clinical chemistry departments, estimation of myocardial infarct size using FABP and/or myoglobin after the first day in the acute care department will become feasible in the near future.

References


