Optimizing classification of acute myocardial infarction: from diagnosis to prognosis

See page 1459 for the article to which this editorial refers

Accurate diagnosis and prognostic assessment are key facets in the evaluation of any illness. Diagnosis of acute myocardial infarction has traditionally been based on the (World Health Organisation) WHO criteria which for a definite diagnosis requires either definite ECG changes or ischaemic symptoms with abnormal enzymes.[1]

The WHO ECG criteria for the diagnosis of acute myocardial infarction are based on the Minnesota code. This code was published by Blackburn et al. in 1960 and subsequently became one of the most widely used ECG classification systems, thus providing important consistency in diagnosis across different epidemiological studies.[2] However, the usefulness of the Minnesota code as a prognostic indicator is less clear. Among infarct survivors, the Coronary Drug Project found it to provide prognostic information independent of other clinical variables.[3] ST segment depression after discharge with a recent myocardial infarct was found to be the most powerful predictor of subsequent mortality, whereas a normal Minnesota code in an ambulant male survivor indicated a favourable prognosis. In contrast, the Multicenter Post Infarction Risk Stratification Trial (MPIP) found the Minnesota code to correlate poorly with clinical events and mortality data.[4] Subsequent to this, many other ECG scoring systems have been proposed which correlate with infarct size and ventricular function with varying results.

The WHO definition of ‘abnormal enzymes’ for the diagnosis of acute myocardial infarction is a rise to at least twice the upper normal limit of either total creatine kinase activity and creatine kinase MB activity or total creatine kinase activity and one of aspartate aminotransferase or lactic dehydrogenase within 72 h of admission or onset of acute event (whichever is later).[1] The more rapid increase of creatine kinase in the serum after acute myocardial infarction and the specificity provided by the isoenzyme creatine kinase MB, quickly established this as the marker of choice. Creatine kinase MB activity assays are now increasingly being replaced by creatine kinase MB mass assays which measure the protein concentration of creatine kinase MB rather than its catalytic activity. Creatine kinase MB-mass assays have been shown to have less analytical interference leading to improved specificity for acute myocardial infarction, and an improved signal-to-noise ratio leading to improved sensitivity for acute myocardial infarction and probably minor myocardial necrosis.[5] Furthermore, increases in creatine kinase MB mass may be detected 1 h earlier than creatine kinase MB activity.[5] However, the search for even more...
sensitive and/or specific parameters has continued with several biochemical markers including myoglobin, myosin light chains, cardiac specific troponins T and I, heart fatty acid binding protein, and glycogen phosphorylase isoenzyme BB having been proposed. Of these, only cardiac troponins have gained widespread acceptance affording both increased myocardial specificity and high sensitivity for both acute myocardial infarction and minor myocardial necrosis.

In addition to improving diagnosis, biochemical markers have been shown to have important prognostic value. In the pre-thrombolytic era, peak enzyme levels of creatine kinase and creatine kinase MB have been shown to have good correlation with infarct size — one of the best predictors of outcome. Unfortunately, the washout phenomenon with thrombolytic therapy has somewhat limited their value, unless frequent serial samples are measured to estimate the area under the release curve. In contrast, probably because of their increased sensitivity and specificity for myocardial necrosis, and their extended window of release, cardiac specific troponins T and I have provided valuable prognostic information independent of other clinical and laboratory parameters.

In this issue of the journal, Porela et al.\(^6\) compare the diagnostic and prognostic value of the WHO classification (as used in the MONICA study) with an enzyme-based criteria. Patients with suspected acute myocardial infarction were retrospectively diagnosed based on three different classifications (a) WHO criteria, (b) a combination code based on symptoms and creatine kinase MB mass, (c) enzymatic criteria based on the highest level of creatine kinase MB mass during hospitalization. Three key observations were noted. First, with respect to diagnosis, the WHO and combination criteria resulted in many patients unsatisfactorily being assigned to a ‘possible’ acute myocardial infarction group, whereas the creatine kinase MB mass-based classification resulted in most patients being assigned to definite acute myocardial infarction or no acute myocardial infarction groups. Second, while a finding of definite acute myocardial infarction by all three classifications carried prognostic value, the creatine kinase MB mass-based classification resulted in most patients being assigned to a ‘possible’ acute myocardial infarction group, highlighting the limitations of use of an intermediate group when using classification systems incorporating subjective criteria.

This carefully performed study is of considerable interest. However, several factors should be borne in mind when interpreting the results. The authors compared a classification based on creatine kinase MB mass with WHO classification which incorporates creatine kinase MB activity. As creatine kinase MB mass has higher sensitivity and specificity for diagnosis of acute myocardial infarction, it is thus not surprising that it was found to be of greater prognostic value. Furthermore, the creatine kinase MB mass classification was based on the highest creatine kinase MB mass value during hospitalization, whereas other markers were assessed only for 3 days. Thus patients who re-infarcted during hospital stay may have recorded higher enzyme values, which is of relevance as recurrent ischaemia/infarction is clearly associated with adverse prognosis. Finally, it should be noted that mortality was the only reported endpoint. Non-fatal myocardial infarction is also an important outcome measure which may correlate more strongly with Minnesota ECG criteria.

In summary, where do we currently stand regarding the optimal classification of acute myocardial infarction and is the ECG now obsolete? Clearly this is not the case. The ECG remains the cornerstone for the early diagnosis of acute ischaemia, showing ST segment change within seconds of the ischaemic insult. Recent studies have shown that the performance of the 12-lead ECG may be enhanced even further by additional spatial sampling such as provided by body surface mapping\(^7\). In contrast, despite the availability of rapid bedside assays, biochemical markers remain suboptimal for early diagnosis. Cardiac troponin T or I take 4–6 h to rise, and do not reliably exclude acute myocardial infarction until \(\geq 12\) h after symptom onset. Myoglobin rises rapidly 2–4 h after onset of acute myocardial infarction, but has poor specificity for acute myocardial infarction. Indeed it is possible that cytosolic markers such as myoglobin or glycogen phosphorylase isoenzyme BB may be released in the absence of necrosis following reversible ischaemia\(^5\).

Nevertheless, for a definitive retrospective diagnosis of acute myocardial infarction, it would now appear to be time to move to a biochemical classification. Which marker should be employed? Creatine kinase MB mass is one possibility. However, we would argue that the improved detection of minor myocardial necrosis provided by the troponins would
make them the preferred choice. The importance of biochemical classification for prognosis is now clearly established, with the weight of current evidence again supporting the use particularly of troponins, although the admission ECG remains of independent predictive value as demonstrated both in this study and others.

It is indeed time for a change in the epidemiological classification of acute myocardial infarction. Optimum initial ECG assessment with optimum biochemical quantification are the key elements required.

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Comprehensive cardiac rehabilitation: an issue to be readdressed

See pages 1465 and 1473 for the article to which this Editorial refers

A multifactorial and multidisciplinary approach is imperative nowadays in order to meet the challenges of reducing the progression of coronary disease, the rate of cardiovascular events and of improving the quality of life in patients with proven coronary artery disease. According to meta-analytical data from more than 4000 patients, cardiac rehabilitation attained a reduction in cardiac and overall mortality of about 25% during a 3-year follow-up period[1].

A crucial point is not to consider cardiac rehabilitation as exercise training, but as a programme based on the individual’s requirements, aiming at the improvement of the quantity and quality of life by means of: reduction (or abolition, when possible) of the classical risk factors, such as smoking and cholesterol levels, modification of dietary habits, increase and maintenance of endurance training, psychological support, and guidance on returning to work.

A problem that health care systems are facing in all developed countries is the exponential increase of the ageing population. At the beginning of cardiac rehabilitation, the referral of elderly patients to cardiac rehabilitation programmes was considered as contraindicated. In contrast, in the current issue of the journal Stahele et al[2] provide very appropriate data on the value of cardiac rehabilitation in patients above the age of 65 years, demonstrating a positive influence of cardiac rehabilitation on exercise capacity and quality of life (better feelings of well-being and performance of daily activities).

According to previous data[3], the initial gain is partially lost at mid–long term if the scheduled programme is limited to the initial period (12 weeks in this study) after the index coronary event. This is particularly relevant in the elderly, whose physical activity is ‘naturally’ less than patients below the age of 65 years; therefore, continued organized training seems even more relevant for the preservation of the initial success. To further underscore this concept, we should remember that Oldridge et al.[4] have...