6. EVALUATION OF RISK MARKERS FOR ACUTE MYOCARDIAL INFARCTION AND HEART FAILURE: PRESENT AND THE FUTURE

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6.1 Aim

- To understand what are the clinical benefits and interpretation of new cardiac markers and markers for heart failure.

- To introduce the evidence-based medicine in this context. EBM also help in the discussion with the clinicians and in the reading of published papers.

- What are the quality and turn-around-time requirements for these tests?

6.2 History

Before the era of tests for the troponins, the diagnosis was based on three components; clinical signs and symptoms, ECG-changes and level of cardiac enzymes. As the evidence accumulated that a small release of troponins (and CK-MB) is important as a prognostic marker for the individual patients, this created the need for new diagnostic criteria.

6.3 Present

Many tests, eg. for the measurement of cardiac troponin I, are available. The standardisation and choice of antibodies of these tests are essential; there are several-fold differences in measured levels and also the time range for positivity is variable. The work of the IFCC committee (C-SMCD) (Chairman Dr. Panteghini) is set to decide the standardisation.

6.4 New markers

Both faster (fatty-acid binding protein) and more sensitive tests (next-generation troponin tests) will be available. Also tests which will detect plaque-rupture may be developed. Last year the first paper to show the possibilities of pregrancy-associated plasma protein A (PAPP-A) measurement was published. New markers for platelet adhesion or markers to identify subgroups with increased risk (natriuretic peptides; ANP and BNP for heart failure)

will be available. They should be analysed together with established markers. If put in practice, they should show extra benefit in the identification of new patients with increased risk, in addition to the current markers. This would also create new problems with the interpretation of these markers.

Some current examples and problems in evaluation of new cardiac markers are introduced and discussed. The use of ROC curves in the evaluation of new diagnostic tests is shown.

6.5 CRP

C-reactive protein is a non-specific marker for inflammation. As a risk marker, slightly increased levels indicate risk for cardiovascular death in the follow-up studies. In the early phases of acute myocardial infarction, levels of 7-20 mg/l (depending on the studies and patient groups) define patients with increased risk, which is additional to the risk indicated by troponin levels. This is, however, not easy to translate for the clinician, who will make decisions. Smoking, other inflammatory diseases and other life-style factors may influence these risk markers. Other inflammatory markers studied include other acute phase proteins and cytokines.

6.6 Organisation of laboratory tests for acute heart diseases

Turn-around time (TAT) is interesting for the clinical unit as they use the test results in order to make clinical decisions. It depends on the individual organisation how they use it and what are the requirements. There is a general requirement of 1 hour for TAT set for cardiac markers if they are used for acute decisions. Discussion between the laboratory and the clinical partners are required to understand and discuss the use and availability of these tests. If the requirements are not met, the clinical unit may want organize their own tests, with point-of-care (POC) analysers. In this setting it is advisable to organise the quality assurance programme and user training schedules with the support of the laboratory. Also the interface into the laboratory information system (LIS) should be discussed.

6.7 Evidence-based Medicicne (EBM)

The clinical use should be based on published, well-controlled studies. This would result in the use of test-specific cut-offs and decision limits. Correlation of one specific method with another one is not enough, but clinical follow-up studies are needed. The clinical end-points include cardiac death, interventions and operations for cardiac disease and number of hospital admissions etc. The clinical chemist/laboratory physician should be aware

of current published papers, as there are new tests continually being produced. The analysis of patients in the paper is very essential, including follow-up studies or other methods to define the clinical outcome (eg. echocardiography for heart failure etc.). The introduction of national or worldwide guidelines are important to deliver a clear message.

6.8 Interpretation in the clinic

The use of cut-offs for clinical decisions should be introduced by the laboratory together with the clinical units (cardiology). The use, TAT and availability should be clear for the clinicians. The lag-time (before the rise in the serum level) after the onset of pain or equivalent, the influence of ECG findings, heart failure, renal failure and rhabdomyolysis should be discussed. The new-generation tests (e.g. more sensitive troponin-tests) should be considered, if they provide extra benefit for the risk-evaluation.

6.9 Point-of-Care (POC) tests

As the diagnostic industry is producing more and more new POC tests and analytes, there is a need for the clinical chemist to understand the evaluation of new tests that are markers for cardiac diseases. The cut-off levels and decision limits of these tests should also be based on clinical studies with relevant end-points and follow-up studies. The available laboratory tests should be considered as a relevant package, together with the clinicians involved.

Recommended literature:

1 Myocardial infarction redefined - a consensus document of the Joint European Society of Cardiology/ American College of Cardiology Committee for the redefition of myocardial infarction. Eur Heart J 2000; 21: 1502-13.

2 Venge P, Lagerqvist B, Diderholm E, Lindahl, Wallentin and the FRISC Group. Clinical performance of three cardiac troponin assays in patients with unstable coronary artery disease. (a FRISC II Substudy). Am J Cardiol 2002; 89:1035-41.

3 Panteghini M, Gerhardt W, Apple FS, Dati F, Ravkilde J, Wu AH Quality specifications for cardiac troponin assays. Clin Chem Lab Med 2001; 39:175-9.

4 Apple FS, Murakami M, Panteghini M, Christenson RH, Dati F, Mair J, Wu AH. International survey on the use of cardiac markers. Clin Chem 2001; 47:587-8.

5 Panteghini M, Pagani F, Bonetti G. The sensitivity of cardiac markers: an evidence-based approach. Clin Chem Lab Med 1999; 37:1097-106.