

IMPROVED CARDIAC PATIENT MANAGEMENT THROUGH CARDIAC MARKERSNAPREDAK U LEČENJU SRČANIH BOLESNIKA ZAHVALJUJUĆI
UPOTREBI SRČANIH MARKERA*Birgit Herzig**Cardiac Area Business Development, Wiesbaden, Germany*

Summary: Cardiac markers enable the diagnosis and characterization of cardiac diseases. While the highly sensitive troponin assay is specific for myocardial infarction, myeloperoxidase is a powerful tool for early determination of plaque formation. Homocysteine is independently associated with numerous neurodegenerative diseases, cardiovascular events and stroke in particular. Elevated plasma concentrations predict outcome and help identify high-risk groups most likely to benefit from prevention and therapy. Homocysteine turned out as a valuable marker for early diagnoses of folate and B-vitamin deficiencies that are involved in anemias and numerous chronic diseases. This article presents the innovative marker MPO, the well established marker troponin and the versatile and useful marker homocysteine, and explains their importance in cardiac patient management.

Keywords: cardiovascular disease, dementia, homocysteine, myeloperoxidase, myocardial infarction, troponin

Troponin, myeloperoxidase (MPO) and homocysteine are markers for the diagnosis and characterization of cardiac diseases. While cardiac troponin assays are established tools for exclusion of coronary disease, MPO is a new powerful marker for the identification of high risk patients with atherosclerotic plaque ruptures. Homocysteine is a versatile marker for cardiovascular events and dementia. Abbott Diagnostic offers automated troponin and homocysteine assays on the Architect and AxSYM platforms. A full automated MPO assay is available on the Architect.

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Kratak sadržaj: Srčani markeri omogućuju dijagnostikovanje i karakterizaciju srčanih oboljenja. Visokoosetljivi test za troponin specifičan je za infarkt miokarda, dok je mieloperoxidaza moćna alatka za rano otkrivanje nastanka plaka. Homocistein je povezan sa brojnim neurodegenerativnim bolestima, kardiovaskularnim događajima a naročito šlogom. Na osnovu povišenih koncentracija u plazmi može se predvideti ishod i mogu se prepoznati grupe sa visokim rizikom kojima bi pomogle prevencija i terapija. Homocistein se pokazao kao dragocen marker za rano dijagnostikovanje deficita folata i vitamina B koji su uključeni u anemije i brojne hronične bolesti. U ovom radu predstavljeni su inovativni marker MPO, dobro poznati marker troponin i višestruko korisni marker homocistein, i objašnjen je njihov značaj u lečenju srčanih bolesnika.

Ključne reči: kardiovaskularna bolest, demencija, homocistein, mieloperoxidaza, infarkt miokarda, troponin

Troponin today is regarded as the myocardial infarction (MI) marker of choice. Cardiac troponin I (cTnI) and cardiac troponin T (cTnT) are myofibrillar proteins of heart muscle cells released when cells are damaged in the course of myocardischemia. Due to their specificity they are the preferred biochemical markers for determining myocardial cell damage. A range of commercial assays is available for measuring cTnI and cTnT. A clear determination of a cardiovascular disease, however, is only possible with troponin assays featuring high clinical sensitivity. According to the ESC/ACC (European Society of Cardiology/American College of Cardiology) Consensus Guidelines the 99th percentile is recommended as cut-off. To evaluate the clinical significance of the different assay systems, James et al. measured cardiac troponin concentrations

Abbreviations: Hcy, homocysteine; MI, myocardial infarction; MPO, myeloperoxidase; TnI, cardiac-specific troponin I; TnT, cardiac-specific troponin T.

of patients using various cTnI and cTnT assays (patient samples from GUSTO IV study) (1). James et al. compared the results produced by the individual assays and evaluated them on the basis of one-year mortality. The assay systems used differed in the selection and number of antibodies used and featured varying sensitivities in reference to these.

This study demonstrated that inclusion of at least two monoclonal antibodies against epitopes at the N-terminal part of the heart specific region of troponin seemed critical for optimum performance. It identified epitopes 41 to 49 to be a decisive region. The Architect TnI assay is based on three different antibodies against the stable NH₂ terminal end (regions 24 to 40 and 41 to 49) and against the mid stable COOH terminal end (region 87 to 91; *Figure 1*). In the study, significantly superior clinical sensitivity was obtained with the Architect TnI assay compared to the Elecsys TnT and Immulite TnI assays. Another advantage of the Architect TnI assay is its quick turn around time of less than 18 minutes. Integration with clinical chemistry is possible, enabling fully integrated cardiac testing.

The lysosomal enzyme myeloperoxidase (MPO) plays a major role in the regulation and termination of inflammatory processes. It is a hemoprotein stored in the leukocytes and will be secreted during phagocyte activation. MPO has emerged as an important potential participant in the atherosclerotic process. It is both a disease marker in atherosclerosis with vulnerable plaques and an event marker for plaque rupture, and thus helps in the early diagnosis of acute myocardial infarction. Clinical studies have shown MPO to be an independent early marker in the prognosis and risk stratification of patients with chest pain and suspected acute coronary syndrome (2). Here MPO offers decisive advantages over troponin and other biomarkers for early diagnosis. It is significantly increased during the first four hours after the onset of chest pain and then slowly decreases again to reach a plateau after 24 hours. Troponin, on the other hand, usually increases after four hours or later (depending on the clinical sensitivity). As a marker of risk for worsening heart failure, increasing tertiles of plasma MPO levels were predictive of mortality. Elevated MPO levels can also predict future risk of coronary artery disease in apparently healthy individuals (3).

Homocysteine (Hcy) is a non-protein amino acid and part of different metabolic pathways like the methionine cycle (*Figure 2*) for the vitamin -B-dependent transfer of methyl groups for biosynthesis (4).

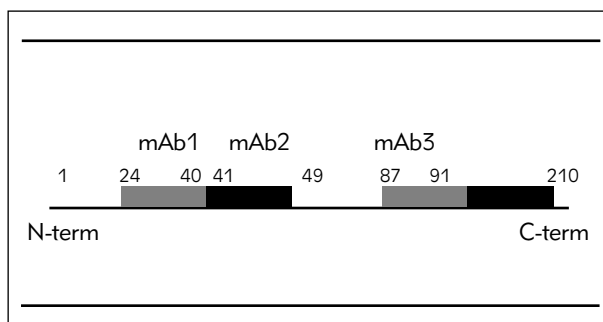


Figure 1 Schematic design of troponin. mAb1, mAb2 and mAb3 are three monoclonal antibodies used in the Architect and AxSYM TnI assays for troponin measurement.

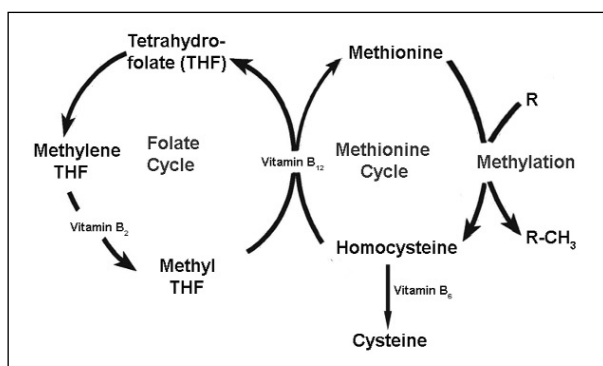


Figure 2 Metabolic pathways of homocysteine. Illustration of the different cycles and essential vitamins, e.g. folic acid, vitamin B12, and vitamin B6.

Elevated Hcy levels have a pro-oxidative effect and directly increase the risk for atherothrombotic disease, dementia, e.g. Alzheimer's disease, depression and osteoporosis. Hcy has a toxic effect on cells and is also an independent risk marker for cardiovascular disease, stroke, diabetes and cognitive impairment. Folic acid, vitamin B12 or vitamin B6 deficiencies cause Hcy levels to increase. Patients with high concentrations of total homocysteine have an increased risk of stroke. In arterial fibrillation the risk is increased more than four-fold (5). As Hcy and diabetes have synergistic detrimental vascular effects, Hcy screening of diabetes patients is recommended (6). In addition, diabetes patients have an incremental risk for developing cardiovascular disease and cognitive impairment, if Hcy is elevated. In studies, both the Architect and the AxSYM homocysteine assays demonstrated high performance and reproducible results. Architect homocysteine showed a good correlation to AxSYM homocysteine.

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