Overview of Cardiac Markers in Heart Disease

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KEYWORDS

• Laboratory medicine • Cardiac markers • Biomarkers • Cardiovascular disease
• Acute myocardial infarction • Heart failure • Adverse event • Risk factor

KEY POINTS

- The main challenge of the rapidly growing field of cardiovascular biomarkers is to select the most informative combination of biomarkers that would capture various aspects of disease pathophysiology and provide an insight into diagnosis and prognosis, and, ideally, guidance for optimum therapy.
- Troponin I and T assays unquestionably generate critical diagnostic information on acute myocyte injury and are becoming valuable prognostic tools for the prediction of long-term outcomes.
- Assays measuring natriuretic peptides are the undisputed leaders in the heart failure field.
- Multiple ongoing clinical trials and studies will eventually identify several additional complementary, nonredundant biomarkers that will allow diagnosis of acute events, provide long-term prognosis, and inform therapeutic decisions.

INTRODUCTION

The recent growth in the rate of discovery, number of clinical trials, and new clinical applications of disease biomarkers has been truly amazing (**Box 1**). This is particularly true for biomarkers of cardiovascular diseases, be they acute coronary syndrome (ACS), heart failure (HF), or various cardiomyopathies. Applications or cardiovascular biomarkers are no longer limited to diagnosis. Biomarker assays are increasingly used to predict short- and long-term disease-free survival or risk of adverse events and readmissions. Very importantly, baseline biomarker levels are beginning to serve as a tool for selecting the right therapy and sequential monitoring of certain biomarkers, which are used as guidance for adjusting medication dosages.

The list of potentially useful cardiovascular biomarkers is seemingly endless. However, on closer inspection, most of these markers still only qualify as "potentially useful or promising," whereas some have already fallen or are beginning to descend into the

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Box 1
Cardiovascular biomarkers, arranged by the pathophysiological process evaluated. Additional novel uncategorized biomarkers are listed at the end of the table

Myocyte injury

Cardiac troponins I and T

Heart-type fatty-acid protein (h-FABP)

Myocyte stress

B-type natriuretic peptide (BNP, measured either as BNP or N-terminal proBNP, NT-proBNP)

Atrial natriuretic peptide (measured as midregional pro-atrial natriuretic peptide, MR-proANP)

Soluble ST2

Growth differentiation factor-15 (GDF-15)

Neurohormones

Adrenomedullin (measured as the midregional fragment of proadrenomedullin, MR-proADM)

Arginine vasopressin (AVP, measured as the C-terminal pro-arginine vasopressin, CT-proAVP, copeptin)

Endothelin-1 (ET-1, measured as C-terminal pro-endothelin-1, CT-proET-1)

Inflammation

C-reactive protein (high-sensitivity assay, hsCRP)

Tumor necrosis factor-α (TNFα)

Interleukins 1, 6, 18 (IL-1, IL-6, IL-18)

Plaque instability

Matrix metalloproteinase-9 (MMP-9)

Pentraxin 3 (PTX-3)

Oxidative stress

Myeloperoxidase (MPO)

Extracellular-matrix remodeling

Galectin-3

Matrix metalloproteinase 1 (MMP-1)

Matrix metalloproteinase 3 (MMP-3)

Tissue inhibitor of metalloproteinases-1 (TIMP-1)

C-terminal propeptide of procollagen type I (PICP)

C-terminal telopeptide of collagen type I (CITP)

Novel protein biomarkers

Klotho

Fibroblast growth factor-23 (FGF-23)

"outdated" category. At the end of the day, in addition to the handful of firmly established markers such as cardiac troponins (cTn) and natriuretic peptides, there are just a few additional biomarkers that are clearly becoming clinically useful, either by providing solid diagnostic and prognostic information or by enabling monitoring of therapeutic interventions.