Redefinition of myocardial infarction: new challenges and opportunities

Véronique L. Roger*

Department of Cardiovascular Diseases, 200 First Street, SW, Rochester, MN 55905, USA

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This editorial refers to ‘The effect of correcting for troponins on trends in coronary heart disease events in Finland during 1993–2002: the FINAMI study’ by V. Salomaa et al., on page 2394

Heart disease is the number one cause of death in the western world and as such constitutes an immense public health problem. The analysis of the trends in the incidence and outcome of myocardial infarction coupled to that of coronary disease mortality provides crucial insights into the determinants of heart disease, which is essential to its treatment and prevention. For example, in the face of stable incidence trends, a decline in coronary mortality most likely reflects the impact of secondary prevention and medical care, whereas increasing incidence of disease conversely would point to primary prevention. Within this framework, it is important to recognize that the trends in the incidence and outcome of coronary disease are complex, likely multifactorial, and evolve over time. Indeed, as the respective role of these two theoretical determinants varies across person, time, and place, continued surveillance is essential to detect change in the trends and their determinants and to evaluate the effectiveness of clinical and public health strategies to combat coronary disease. Effective surveillance in turn mandates standardization of the criteria used to define the events under surveillance. This is a prerequisite for the validity and interpretation of trends measured in different settings and in different time periods.

Myocardial infarction as a chief indicator of the burden of heart disease

Myocardial infarction plays a crucial role in the surveillance of the population burden of coronary disease in part related to the existence of established criteria for its diagnosis, which are amenable to standardization. Thus, the medical and scientific communities have tracked the incidence of myocardial infarction over time as chief indicator of progress in the battle against coronary disease, studied the prognosis of myocardial infarction, and dedicated enormous resources to improve it. Within this context, it is thus intuitive that a common definition of myocardial infarction, which can be used by all stakeholders, clinicians, and scientists alike, is critical. In 2000, the European Society of Cardiology and the American College of Cardiology recommended a new definition for myocardial infarction. The new definition combines rise and fall of biochemical markers of myocardial necrosis with any of the following conditions: ischaemic symptoms, ECG changes, and coronary intervention. The biomarkers recommended were the troponins (T or I), which are more specific than creatine kinase and its MB fraction for the diagnosis of myocardial infarction in the setting of associated skeletal muscle damage or injury including surgery. Thus, the change in the biomarker of choice to identify myocardial infarction was central to the new definition proposed by the European Society of Cardiology and the American College of Cardiology. The recommended troponins have higher sensitivity and allow for the detection of very small amounts of myocardial necrosis, which would have gone undetected by creatine kinase and its MB fraction. The new definition can be expected to result in an increase in the number of infarctions, the magnitude of which will depend on the threshold chosen to define positive troponin, which is still evolving and varies across assays. The European Society of Cardiology and the American College of Cardiology recommendations recognized that the change in myocardial infarction criteria, as they rely highly on more sensitive biochemical markers, ‘will confuse efforts to follow trends in disease rates and outcomes’. Thus, it is important to conduct studies that evaluate the impact of troponin on the trends in myocardial infarction and coronary disease incidence.

Assessing the burden of coronary disease when definitions change

The report of the FINAMI study by Salomaa et al., is of utmost importance to characterize the challenges related to the redefinition of myocardial infarction, as it provides essential information to understand the implications of the introduction of troponin. This study examined the trends in coronary disease events in Finland over a decade (1993–2002). The environment is unique as the FINAMI registry pertains to four geographical areas in Finland and ensures complete capture and ascertainment of all coronary events. The report of the FINAMI study by Salomaa et al., is of utmost importance to characterize the challenges related to the redefinition of myocardial infarction, as it provides essential information to understand the implications of the introduction of troponin. This study examined the trends in coronary disease events in Finland over a decade (1993–2002). The environment is unique as the FINAMI registry pertains to four geographical areas in Finland and ensures complete capture and ascertainment of all coronary events.

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* Corresponding author. Tel: +1 507 284 0519; fax: +1 507 266 0228. E-mail address: roger.veronique@mayo.edu

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mortality declined steeply except in elderly women. Concomitantly, among persons aged 35–74, the incidence of the first coronary event declined by 2% per year in men and 1% per year in women. The magnitude of the decline was statistically significant in men but not in women. Among persons aged 75 or greater, the incidence of first coronary events did not change over time. To account for the effect of troponin, the authors applied correction coefficients derived from a large number of myocardial infarctions in the FINAMI registry with simultaneous determination of troponin and previously used enzymatic markers. Correction for the effect of troponin resulted in unmasking a larger decline in the incidence of first coronary events in both sexes and all age groups. The 28-day case fatality rate declined over time but changed only marginally after correcting for the use of troponin.

It is important to review several methodological points to assist in the interpretation of these important data. The coefficients used to correct for the effect of troponin were determined from a large number of infarctions from several hospitals in which both the new and the previous biomarkers were used. The large size and the diversity of the cases used for the determination of the correction coefficients constitute strengths. However, the variety of centres can also interfere with the determination of the correction coefficients because diverse hospitals are likely to exhibit heterogeneous clinical practices, adopt different assays, and use different thresholds of positivity for these different assays. Indeed, as the use of the biomarkers and its selection was driven by clinical practice, it is conceivable that variations in case mix across sites and types of cases in whom clinicians elected to measure multiple biomarkers result into bias akin to confounding by indication and hence affect the resulting coefficients. The type of assays as well as the cut-points defining abnormal values and the interpretation of coexisting conditions that can affect the interpretation of abnormal troponin values, which are numerous and frequently encountered, may also have varied across centres within the registry. These diverse factors can have variable and diverging effects on the ascertainment of myocardial infarction and their impact, which is challenging to interpret in one centre may become quite complex to account for in studies combining several centres.

These methodological points notwithstanding, the study by Salomaa et al. has several important implications. As reported, the previously documented temporal reduction in coronary mortality has persisted in Finland in the 1990s. Within the framework of this decline, the analyses of secular trends in first coronary event and case fatality provide important insights into the mechanisms of the decline in coronary disease mortality, which, in FINAMI results from both changes in incidence as well as in case fatality. These findings illustrate the value of coronary disease surveillance to understand disease patterns and underscore the importance of monitoring such trends to devise approaches to reduce the burden of coronary disease. Importantly, the declining trends in the incidence of coronary events were partially masked by the effect of troponin. These key findings thus directly validate the concern stemming from the redefinition of myocardial infarction by documenting that the change in the biomarker indeed ‘confuses’ the interpretation of temporal trends in coronary disease. These findings also support the stated recommendation that the previous definition of myocardial infarction be ‘retained by specific epidemiological centres’. Indeed, these data underscore the crucial importance of rigorously analysing the effect of troponin on the incidence and outcome of acute myocardial infarction. Such analyses will have the greatest yield if designed prospectively with simultaneous use of all cardiac biomarkers in the same patient irrespective of clinical practice to avoid potential biases related to confounding by indication. The FINAMI study also has important clinical implications. Indeed, it illustrates that reliance on one biomarker or the other will alter the categorization between types of acute coronary syndromes. Advocates of the widespread use of troponin have argued that acute coronary syndromes represent a continuum of disease, a concept quite familiar to clinicians, and that any increase in cardiac biomarker had prognostic implications.

However, although the implications of the shift across types of acute coronary syndromes may arguably be rather modest from a pathophysiological point of view, the consequences of a diagnosis of myocardial infarction for employment, health insurance, evaluation of health care delivery, epidemiology, and public health are enormous.

For this reason, operational definitions of acute coronary syndromes have been proposed, which include a purposeful effort to categorize such events while also specifically identifying myocardial infarctions that would have met criteria using the previous enzymatic biomarkers. This approach would enable health care providers to relate the newly defined myocardial infarctions to the previous classification. Thus, as the new myocardial infarction criteria generate continued reflexion and discussion, more data on their clinical and epidemiological implications are clearly needed. The article by Salomaa et al. constitutes an important step towards gaining this needed knowledge and underscores the need to broaden the approach to coronary disease surveillance to include acute coronary syndromes rather than focusing primarily on myocardial infarction as traditionally defined. This is critical to understand the trends that will be measured over the next decade marked by the change in biomarkers and to accurately evaluate the burden of heart disease.

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References

Clinical vignette

Giant right atrial aneurysm in a symptomatic adult—a rare congenital malformation
Andreas Kühn1*, Christian Schreiber2, Jörg Hausleiter3, and Manfred Vogt1
1Department of Pediatric Cardiology and Congenital Heart Defects at the Technical University, German Heart Center Munich, Lazarettstr. 36, D-80636 Munich, Germany; 2Department of Cardiovascular Surgery at the Technical University, German Heart Center Munich, Lazarettstr. 36, D-80636 Munich, Germany; 3Institute for Radiology and Nuclear Medicine at the Technical University, German Heart Center Munich, Lazarettstr. 36, D-80636 Munich, Germany
* Corresponding author. Tel: +49 89 1218 1363; fax: +49 89 1218 3013. E-mail address: kuehn@dhm.mhn.de

Aneurysms of the right atrium (RAA) are a rare congenital malformation with about 20 cases reported world-wide and may occur in any age group from foetus to adults. In symptomatic cases, it may be associated with pulmonary embolism and atrial rhythm disturbances. We report on a 56-year-old man who presented with acute chest pain. In his past history an Ebstein’s anomaly of the tricuspid valve had been diagnosed 40 years ago. At that time he was symptomatic with atrial fibrillation and had received repeated external cardioversions. In 1998, pulmonary embolism was diagnosed and he was put on oral anticoagulation. Transoesophageal echocardiography (Panel A) showed a 12 to 7 cm right atrial enlargement in front of a normal sized right atrium and right ventricle. The tricuspid valve was normal in morphology and function. The entrance from the right atrium to the RAA was 2 cm in the vertical and 4.6 cm in the horizontal plane. Spontaneous echo contrast was present within the RAA as a sign of low flow. Multi-slice computed tomography (CT) confirmed the diagnosis of the huge RAA (Panels B and C). The wall of the RAA appeared paper-thin. There was no evidence for thrombus formation within the aneurysm. As the patient had been symptomatic with arrhythmia and pulmonary embolism for many years, the indication for the operative resection was established. After opening the chest in the operation room, the paper-thin wall of the aneurysm (Panel D) could be resected with the help of normothermic cardiopulmonary circulation.

Panel A. Transoesophageal echocardiogram, transversal view.
Panel B. CT-scan: the picture is rotated so that the orientation is comparable with that of the echocardiography.
Panel C. CT-scan: three-dimensional reconstruction of the RAA.
Panel D. Intra-operative finding: marked dilatation of the RAA with a paper-thin wall. Asterisk indicates the entrance of the RAA. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; RAA, right atrial aneurysm.

References