Severity of Myocardial Infarction
New Insights on an Elusive Construct

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Cardiovascular disease constitutes a burden of epidemic proportion, and understanding its determinants is essential to designing effective interventions. Doing so requires the ability to track disease burden at the population level. In the United States, without national registries, community surveillance is the method of choice. Community surveillance studies are mostly retrospective by design, rely on diagnostic codes for case finding, and require a defined population in which events can be consistently and reliably captured and validated with standardized approaches. Applied to cardiovascular disease, community surveillance measures its burden in communities by tracking the incidence of events, their severity, and their mortality, thereby enabling the appraisal of the components of cardiovascular diseases in a given population. Because of the aforementioned methodological requirements, few surveillance studies exist in the United States. They include the Atherosclerosis Risk in Communities (ARIC) Study, the Minnesota Heart Survey, the Olmsted County Study, and the Worcester Heart Attack Study. The data from these studies indicate that, although deaths from coronary disease have declined, the incidence of myocardial infarction in the United States has remained mostly stable. Thus, the decline in mortality can be envisioned as reflecting an improvement in survival, which may be mediated by a declining severity of myocardial infarction.

The article by Myerson et al in this issue of Circulation specifically addresses this important and understudied issue in ARIC between 1987 and 2002. They examined severity indicators in ARIC, Worcester, and Olmsted County. The ARIC data reported in this issue of Circulation are the most contemporary and pertain to a large cohort, thereby providing robust evidence that the trends observed in earlier time periods and with smaller sample sizes are confirmed and sustained. Importantly, the ARIC findings are independent of changes in biomarkers because the recent shift to troponin is adjusted for analytically.

Second, these data provide the important opportunity of an in-depth reflection on the meaning and implications of measuring the severity of myocardial infarction, a complex construct reflecting the composite result of disease severity indicators, care-seeking behaviors, and processes of care. For ease of discussion, the indicators of severity of myocardial infarction can be schematically envisioned as reflecting the initial presentation of infarction or its in-hospital course. Cardiogenic shock and ECG ST-segment elevation reflect the initial presentation of myocardial infarction and its characteristics during the initial 24 hours and are unlikely to be affected by in-hospital treatment. The changes in the frequency of cardiogenic shock should be interpreted in light of the trends in out-of-hospital coronary disease deaths. Indeed, declining out-of-hospital coronary disease deaths may result in greater numbers of persons hospitalized who would in the past have died out of hospital. This, in turn, may change the case mix of hospitalized infarction, thereby confounding temporal trends in cardiogenic shock. These considerations notwithstanding, a favorable temporal decline in cardiogenic shock was noted in ARIC and other communities.

In acute myocardial infarction, ECG changes are time dependent so that the time between symptom onset and ECG recording (hence presentation to care) affects the ability to capture ST-segment elevation on the ECG. Thus, changes over time in the time between symptom onset and presentation to care can confound temporal trends in the proportion of patients with ST-segment elevation and should be considered for their interpretation. In ARIC, the time from onset of symptoms to arrival at the hospital did not change over time, with only one third of patients presenting <2 hours after symptom onset. This sobering finding underscores the challenge of reducing total ischemic time by influencing care.
seeking behavior\textsuperscript{12} and the need for renewed efforts in this domain. Conversely, because the time from symptom onset and presentation to care did not change, it is unlikely to confound trends in the proportion of ST-segment–elevation infarctions. A striking finding in the present report is the decreasing proportion of ST-segment–elevation infarctions in the community, which has been consistent across studies\textsuperscript{7–9} and independent of time to presentation. Although the reasons for this observation can be only speculative, one possible explanation is the increasing use of medications for the primary prevention of coronary disease. Indeed, over time, patients presenting with myocardial infarction are more likely to be receiving cardioprotective medications such as aspirin and β-blockers before admission for the acute event.\textsuperscript{13} These agents may reduce the size and severity of the infarction.\textsuperscript{14}

Regardless of these hypothetical considerations, recognizing the temporal decline in cases with ST-segment elevation is essential to optimize care. Indeed, because non–ST-elevation infarctions now constitute the vast majority of infarctions in communities, interventions must be designed that recognize this epidemiological reality. This is particularly important because non–ST-elevation infarctions may be receiving less optimal care compared with ST-segment–elevation infarctions.\textsuperscript{15}

Other severity indicators, including biomarkers (creatine kinase and troponin) and the development of ECG Q waves, reflect the in-hospital course of infarctions and may be influenced by treatment, particularly reperfusion. Evaluating the severity of infarction from biomarker values is subject to measurement error and variations in the timing and frequency of the measurements. The variability of the assays and the frequency of confounding by comorbid conditions may result in recorded values not accurately reflecting the true levels, and longitudinal trends may be affected by assay changes. Furthermore, the recent change in biomarkers with preferential reliance on troponin generates considerable challenges for the longitudinal use of biomarkers to assess the severity of infarction over time. The interpretation of ECG Q waves is equally challenging in that their appearance, like ST-segment elevation, is time dependent\textsuperscript{11} and may be influenced by reperfusion. Nonetheless, the prognostic implications of the development of Q waves have been reaffirmed in an ancillary analysis of the Danish Trial in Acute Myocardial Infarction-2\textsuperscript{10}; thus, Q waves constitute a legitimate severity indicator given their outcome implications.

These considerations underscore the complexity of evaluating the severity of myocardial infarction. The concomitant use of several different indicators is an important strength of the present study; the consistency across indicators provides reassurance of the robustness of the trends. Given the aforementioned influences of treatment, either primary prevention or acute care, on all severity indicators, it is likely impossible to untangle the natural history of myocardial infarction from its management. Furthermore, one may also question the mere existence and relevance of the concept of natural history applied to one of the manifestations of coronary disease, which has been the subject of intense therapeutic efforts over the past decades.

Pragmatically, the most important construct in this context is the improvement in the health of the population and patients. Hence, these results underscore the progress made over time in terms of decreasing severity and case fatality rates during a period characterized by major therapeutic advances, in turn identifying the vital importance of striving for optimal quality of care as measured by access, affordability, and alignment with the strongest evidence in primary prevention, treatment, and secondary prevention of acute coronary syndromes.

Finally, the findings presented by Myerson et al help interpret population trends in coronary heart disease and heart failure. Indeed, to appropriately contextualize this report and its relevance to our understanding of the evolving burden of cardiovascular disease, it is important to remember that the heart failure epidemic is often attributed to the growing number of infarction survivors.\textsuperscript{11} Certainly, the absolute number of individuals living with myocardial infarction, which reflects the combined effect of the increase in the population, its aging, and the decreasing case fatality rate of myocardial infarction, can be expected to increase the number of persons at risk for heart failure. Yet, these factors do not entirely explain the so-called heart failure epidemic because the decline in the severity of infarction documented in this and other studies would lead one to hypothesize that less severe infarctions should result in less subsequent heart failure. Indeed, in several community studies, the incidence of heart failure after myocardial infarction most often remained stable or decreased.\textsuperscript{17–19} Thus, the data on the declining severity of infarction and the trends in subsequent heart failure underscore the importance of evaluating other contributors to the heart failure epidemic.

In summary, the paper by Myerson and colleagues reminds us of the importance of community surveillance in understanding cardiovascular disease trends and of the fundamental implications of community surveillance for patient care. To this end, indicators of myocardial infarction severity may to a large extent be a proxy for the quality of care and thus make contemporary trends in infarction severity challenging to dissect from a causality standpoint. Conversely, the pragmatic interpretation of these trends suggests that progress has occurred because infarctions are becoming less severe. The present report also underscores that we must recognize the increasing predominance of non–ST-elevation infarctions to move forward with interventions to improve the care of those patients who now constitute the majority of those who present with infarctions.

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Disclosures

None.

References

Roger Severity of Myocardial Infarction 491


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