Is heart failure the critical warning sign for death following myocardial infarction?

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This editorial refers to ‘The timing of development and subsequent clinical course of heart failure after a myocardial infarction’† by A. Torabi et al., on page 859.

The prognostic dilemma

We try to predict the future of our patients with myocardial infarction (MI) in order to intervene and improve the prognosis, and this ambition is highlighted by concepts such as a ‘widow-maker stenosis’ or ‘tombstone ST-segment elevation’. However, in reality, our predictions are highly uncertain. With marked—and fortunately—rare exceptions such as cardiogenic shock, the predictive value of our observations are only valuable for groups of patients and highly uncertain for the individual patient. An important sign such as reduced left ventricular systolic function clearly separates groups, but in all groups the majority of patients live for years and the predictive value remains highly uncertain. New risk markers including natriuretic peptides continue to appear—and each has predictive value but each fails to provide certainty for the individual. The consequence of this situation is that many lifesaving procedures including the implantable defibrillator need to be provided for many patients, while the real benefit is for few. The current status of risk stratification is mainly to include baseline variables in statistical models. To do so, large registers are necessary when attempting to create precise estimates of the contribution of different risk factors. What nearly all of these registers have in common is that they provide one assessment of each risk factor and use this in the modelling. There are several reasons why only one estimate is used. First, it is simple, and makes it very easy to carry out subgroup analyses. Secondly, it is difficult to perform serial testing in large unselected populations. Thirdly, one time point estimate makes the problem with the role of confounders less critical, i.e. is renal function decreasing as a function of decreasing blood pressure or addition of an aldosterone antagonist? The complexity can be enormous.

Is heart failure the warning sign to track?

One possible step forward in this situation is demonstrated by the study of Torabi et al., to seek warning signs during the course of time that are markers of events to happen after the appearance of these markers.¹ The study adds important information to our understanding of the timing/development of heart failure following MI. A total of 896 consecutive patients hospitalized for an MI in a region of the UK were studied. Following discharge, 441 patients (63% of those discharged alive) were discharged without heart failure and not treated for heart failure during the index MI. Of these, 272 did not develop heart failure during a 4–6 year period, and their mortality was 16%. In contrast, 145 did develop heart failure during follow-up, and their mortality was 54% and, strikingly, of all deaths 84% were preceded by heart failure at some time point.

This fits well into the concept that the progression of cardiovascular disease can be regarded as a continuum of events. According to this concept, the presence of risk factors such as hypertension, diabetes, and hyperlipidaemia predisposes to the development of atherosclerosis and left ventricular hypertrophy. This will lead to overt coronary artery disease, cardiac failure, and eventually death.

Were other warning signs important?

To understand the potential importance of heart failure development, it is necessary to focus on the mechanisms leading to heart failure. Even though the development of breathlessness (i.e. heart failure) in the setting of coronary artery disease requires left ventricular filling pressures to be elevated, the cause of this may be a complex interplay of multiple factors including myocardial ischaemia, neurohormonal activation, loss of atrial contraction, renal failure, left ventricular remodelling, hypertrophy, effective chamber compliance, etc. Thus, it is also important to examine
to what degree heart failure is a reflection of other equally important prognostic confounders.

The study of Torabi et al. provides some insight into the mechanisms/confounders of the development of heart failure after discharge. There was a striking interaction between heart failure and new ischaemic events. For example, if the development of heart failure after discharge was associated with a new ischaemic event, mortality was 65%, without an ischaemic event 46%; and if the patient had experienced breathlessness during the index admission a new ischaemic event was associated with 89% mortality. Unfortunately these data were not available for other important events such as atrial fibrillation and renal failure. Thus, the prognostic importance of heart failure after discharge may reflect other equally important events. Data from studies of selected populations have suggested that serial changes in left ventricular size, brain natriuretic peptides, left ventricular filling pattern, QRS duration, etc. provide prognostic information incrementally to a single baseline assessment alone.\(^2\)\(^-\)\(^3\) Foremost the pattern, QRS duration, etc. provide prognostic information incrementally to a single baseline assessment alone.\(^2\)\(^-\)\(^3\) The present data clearly highlight the detrimental effect of heart failure, where the time course of development was carefully accounted for.

**The implication**

The present data clearly highlight the detrimental effect of heart failure on the outcome of patients with MI. How should this information be used? In terms of understanding the course of the disease, this study should inspire further exploration into events that take place in the years after an MI. While the current study used available hospital records, it could be hoped that future studies follow the course of the disease in more detail—optimally serial measurements of many risk factors should be included to clarify to what extent heart failure development is preceded by ischaemic events or other more subtle changes.

A practical implication of the study by Torabi et al. is that it may be possible to identify warning signs during follow-up after an MI, warning signs that identify truly high risk groups that may benefit particularly from selected interventions such as an implantable defibrillator.

It would therefore be highly valuable if trials of implantable defibrillators and similar interventions were interrogated in a similar manner as the infarct population studied by Torabi et al. If changes in risk factors preceding serious events could be identified, this could inspire trials which could identify patients with the greatest benefit much more accurately.

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**References**