Towards a more precise definition of heart failure aetiology

See page 228 for the article to which this Editorial refers

Heart failure is a multifaceted syndrome with a multiple aetiology. In some cases the aetiology remains hypothetical or undefined. Obviously this is not without consequences since, even if advanced heart failure therapy is independent of the disease that brought on the decompensation, it is also true that, especially during the initial or intermediate phases of heart failure, knowledge of the cause can be crucial to plan the therapy.

The epidemiological context

The available epidemiological data confirm the variability, and thus the indeterminateness, of the aetiology of heart failure in various settings. According to the available data, coronary artery disease and hypertension (either singly or together) seem to account for the great majority of cases of heart failure within the developed world, whereas rheumatic heart disease, infections, and nutritional diseases are more common causes in the developing world. Thus heart failure is more common in young–middle-age groups in under-developed countries, and in the elderly population in developed countries. Among the elderly, the senescent modifications of the myocardium together with degenerative alterations of the cardiac valves, in particular of the aortic valve, are cofactors of increasing importance.

Trends of heart failure causes have changed in recent decades[1]. In the Framingham study, coronary artery disease was the primary attributable cause of heart failure in 22% of patients in the 1950s, 36% in the 1960s, 53% in the 1970s, and 67% in the 1980s. In contrast, valvular heart disease has markedly declined as a causal factor in the last few decades in the western world. The data on the prevalence rate of hypertension in heart failure are rather discordant. In the Framingham population it was noted that 91% of patients with heart failure had a history of hypertension[2]. In contrast, an overview of 31 studies indicated that hypertension was the primary aetiological factor in only 4% of heart failure patients[3]. In hospitalized populations, hypertension was found as the primary factor in 15–17% of patients[4,5]. More recently, hypertension also appeared to play a diminished causal role in the Framingham population; prevalence decreased by about 10% in men and 30% in women[1]. The decreasing prevalence of left ventricular hypertrophy associated with the effective treatment of hypertension paralleled the declining incidence of heart failure in treatment trials and probably underlies the declining causal role of hypertension in heart failure[6]. In contrast, the prevalence of diabetes is rising in heart failure patients. In the Framingham population, the rate of increase was 20% per decade[1]. A reduced glucose tolerance, a marker of insulin resistance, can also be considered as an indicator of a metabolic pattern favouring heart failure. Atherosclerosis accounts for up to 60% of all diabetes-related deaths. Impaired glucose tolerance and diabetes mellitus type 2 are often linked to a metabolic syndrome (insulin resistance, hypertension, central upper body obesity, dyslipidaemia with or without hyperglycaemia) at high risk of macrovascular disease, whereas in type 1 diabetes microvascular complications are a predominant feature linked to hyperglycaemia. Overall these findings suggest that coronary artery disease, hypertension and diabetes are the leading causes of heart failure.

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Of particular interest, and at the same time a cause for concern, is the inter-relationship of the epidemiological trends of ischaemic heart disease and heart failure. Over the past 30 years, the mortality rate from ischaemic heart disease has declined by more than 50%, and in the 1990s it declined by 2-6% per year[7]. In spite of that, in 1990 ischaemic heart disease accounted for 6-26 million deaths out of 50 647 000 deaths worldwide (29%), and this percentage is expected to rise to 36% in 2020[8]. As for heart failure, all sources of information are concordant in showing that both incidence and prevalence increased exponentially over the last few decades, probably, in part, as a consequence of the reduced mortality rate of ischaemic heart disease, and in part due to the ageing of the population[9,10]. Because the incidence of ischaemic heart disease and heart failure are public health issues of great importance, most patients with ischaemic heart disease and secondary prevention targeted to heart failure are under-estimated in daily clinical practice.

Accordingly, primary prevention of ischaemic heart disease and secondary prevention targeted to heart failure are public health issues of great importance. Most patients with ischaemic heart disease and heart failure have had a myocardial infarction. GISSI-2 short-term prognostic data[11] and GISSI-3 long-term prognostic data[12] clearly show that by far the dominating factor for the outcome of the post-infarction patient is left ventricular function, and that this is much more important than residual ischaemia. In the GISSI-2 trial, the predictive value of the evidence of myocardial ischaemia during exercise was low, and around half of recurrent infarctions occurred without any harbinger. On the other hand, clinical and instrumental evidence of left ventricular dysfunction had strong predictive value. This was particularly significant in the GISSI-2 context, where the rate of revascularization during the observation period was low, thus leading to a limitation in the influence of the work-up bias, consisting of the apparent reduction of the predictive power of residual ischaemia as a result of the therapeutic strategies, in particular myocardial revascularization, that this induces. It is interesting to note that the evidence of the low predictive power of residual ischaemia and the high predictive power of left ventricular dysfunction does not appear to influence medical behaviour at all regarding the prognostic stratification in the post-infarction phase and consequent decision making. In an observational study undertaken in Italy, the GISSI Prognosis trial, dealing with the diagnostic-therapeutic processes of some 1500 post-infarction patients in 60 cardiological centres[13], it was noted that those who had objective evidence of residual ischaemia, whether accompanied or not by symptoms, were seven times more likely to experience subsequent coronary angiography and revascularization compared with those having no residual ischaemia (OR 7·0%, 95% CI 5·6–8·7), while the presence of left ventricular dysfunction represented by an ejection fraction <40% had no effect on the doctor’s decisions regarding coronary angiography (OR 1·1, 95% CI 0·8–1·3) and thus the revascularization procedures. In practice, even though it is by now clear that in two-thirds of acute myocardial infarctions the thrombotic occlusion of the coronary vessel that causes the event occurs at a haemodynamically non-critical vascular alteration before the thrombotic event, the post-myocardial infarction risk stratification continues to have as its primary aim the search for haemodynamically critical stenoses. Left ventricular dysfunction and myocardial viability seem to be considered as less important. It is thus likely that the pathogenetic role of left ventricular dysfunction linked to coronary artery disease with regard to heart failure is under-estimated in daily clinical practice.

Ischaemic heart disease as a cause of heart failure

This issue presents a paper by Fox et al[14] aimed at evaluating the role of ischaemic heart disease as a cause of heart failure in an unusual setting for cardiological research: that of the community. The work by Fox and his associates is important for various reasons.

First, it is one of the few studies that reliably measures the incidence of heart failure in the community by means of a collaborative network with 151 general practitioners working in 59 practices (292 000 individuals) around London and a close monitoring of Emergency Rooms and non-cardiac wards in the hospitals concerned. Increasing the awareness of the general practitioners with regard to the diagnosis of heart failure is of prime importance; this must take into account the difficulties of the diagnosis of heart failure, on the one hand, and the need to spread the diagnostic criteria beyond the cardiological area, on the other. We know that in most Western countries heart failure patients admitted to cardiological centres represent less than 20% of the total of heart failure patients. Heart failure is thus a prototypical area in which to experiment with operational and collaborative links among areas of specialized medicine, general medicine, and doctors working in the...
community. The European Society of Cardiology is attempting, by means of Study Groups, to experiment with models for heightening the awareness of heart failure (Study Group SHAPE) and to establish links among cardiologists working in hospitals, outside hospitals, and general practitioners (Study Group IMPROVEMENT). What the authors of this study have achieved may represent a useful reference model.

Second, the study sets out the role of the various aetiological factors in heart failure, in particular ischaemic heart disease. To do this at least four criteria should be met: (1) the certainty that the doctor of first recourse—that is, the general practitioner—can identify all the incident cases of heart failure; (2) the diagnostic certainty of heart failure; (3) the diagnostic certainty of ischaemic heart disease; (4) the determination of the aetiological role of myocardial ischaemia with regard to heart failure. None of these conditions is easy to achieve, and all four have been reasonably obtained in this study. An aspect that the authors of the study pass over is what is meant by abnormality in myocardial function. For a diagnosis of heart failure the presence of symptoms was required, along with signs of fluid retention, evidence of abnormalities of myocardial function, and, in cases of doubt, the response to therapy. The entry criterion used in all the trials on heart failure is a reduction in the left ventricular systolic function expressed by an ejection fraction <35–40%. This has led to the systematic exclusion from the trials of patients with a preserved left-ventricular systolic function. The question arises as to whether or not the same process was followed in this study. The median age of 76 years. This is not an easy task. Anatomically significant (>50% coronary narrowing) coronary artery disease was detected from angiograms in 67% of patients under 75 years of age who underwent angiography. To assign coronary artery disease as heart failure aetiology the case definition panel required further evidence that the anatomical disease was related to the ventricular dysfunction in the form of regional wall motion abnormalities, myocardial perfusion abnormalities or ischaemic valvular dysfunction. Taking into consideration all the non-invasive and invasive available data, coronary artery disease was considered aetiological in 52% of cases. Performing coronary angiography altered the allocated aetiology in 26% of 70 cases who underwent angiography for the first time subsequent to study entry (then to ascertain the aetiology of heart failure). These data confirm both the importance of the coronary angiogram as well as the need for a comprehensive, and not solely anatomical, approach regarding the diagnosis of heart failure with ischaemic aetiology.

Should we then definitely conclude that heart failure has an ischaemic aetiology in around half the cases? From an overview taken from the various trials, ischaemic heart disease was considered the determining aetiological factor in 68% of cases of heart failure. Obviously crucial in this prevalence are the inclusion and exclusion criteria used in the
trials, in particular age (which nevertheless is not that different from the subgroup <75 years of age who were studied by means of coronary angiography in the present study), and a low ejection fraction, which was constantly used as an enrollment criterion in the trials. The ejection fraction value in the population studied by Fox and co-workers is not given in the paper. It has always been thought that non-thorough diagnostic evaluation would lead to an under-estimation of ischaemic heart disease as an aetiological factor. In fact, performance of instrumental tests resulted in an increase in aetiological diagnoses of ischaemic heart disease, from 29% to 52% of the population that had undergone coronary angiography in this study. However, there is a remarkable difference between 52% and 68%. It is also possible for non-thorough evaluation of the causal responsibility of ischaemic heart disease, with regard to heart failure, to lead to an over-estimation of myocardial ischaemia as an aetiological factor if coronary angiography is systematically performed. In fact, coronary artery disease was present in 67% of the patients <75 years of age in this study, but in 15% of them it was not considered to play an aetiological role for heart failure. Among the over 12 000 subjects with heart failure included in the Italian IN-CHF database, ischaemic heart disease was considered as the causal factor for heart failure in 40% of the cases. The role of arterial hypertension as a causal factor of heart failure was clearly seen to be less important: 4% in the population <75 years of age and 9% in the heart failure was clearly seen to be less important: 4% in the population that experienced heart failure for the first time: 76 years. By considering this we should not be surprised about the exponential increase of heart failure over the last few decades. The increase in the average lifespan by around 10 years has meant that many people now live into their eighth decade of life, a period never experienced before by a large population of human beings, which turns out to be critical for the heart, particularly for the occurrence of heart failure.

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References