The Management of Heart Failure: A Matter of Definition?

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Summary. The term heart failure has become a label for more than one clinical entity. For many years heart failure has been used to denote patients with various heart diseases who have begun to suffer from fluid retention, pulmonary venous hypertension, or systemic venous hypertension, either alone or in combination. More recently, the term heart failure has been applied to the combination of effort intolerance and reduced left ventricular contractility due to ischemic heart disease or other myocardial disease. Comparison of the results of epidemiological studies and therapeutic trials is complicated by variation in the composition of the patient populations selected for study. Drug treatment of heart failure remains fairly empirical. Distinction should be made between immediate or prognostic benefits related to the etiological diagnosis, and benefits related specifically to prevention and relief of, for example, fluid retention, rhythm disturbances, or ventricular hypertrophy. The response of individual patients to several forms of drug treatment, including digoxin, ACE inhibitors, and beta-blockade, is unpredictable. Prospective identification of patients liable to respond well to these drugs is not yet possible, but would greatly assist the choice of treatment. At present, trial of therapy is required in each patient to establish benefit and to avoid long-term treatment of nonresponders.

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What is Heart Failure?

Recommendations for the clinical management of congestive cardiac failure require some definition of what is to be included in the diagnosis. Failure to do this can lead to the misapplication both of therapy and of the findings of clinical trials of treatment for "heart failure." Previous definitions of cardiac failure tend either to be definitions of heart "disease" or are too nonspecific to be of any practical clinical value. Physiological definitions center on the failure of the ventricle to maintain an adequate cardiac output in all circumstances. Such definitions include forms of symptomatic heart disease that the physician would not normally classify as clinical cardiac failure. Clinicians have traditionally used the term congestive cardiac failure to label the symptoms and physical signs of three separate phenomena resulting from heart disease, without necessarily specifying the heart disease responsible.

These are

1. The effects of pulmonary venous hypertension and pulmonary edema
2. The effects of systemic venous hypertension
3. The effects of salt and water accumulation associated with weight gain and, finally, peripheral edema.

Each of these conditions may be present alone or in combination and may appear and disappear during the course of the heart disease that is responsible for them. The patient in relapse is described as having "gone into cardiac failure" and in remission as having "come out of cardiac failure," even though the underlying heart disease was present all the time. Other physical signs traditionally associated with cardiac failure, such as those due to loss of ventricular contractility and compliance, indicate disease of the ventricular myocardium and, like those of valvular disease, they may not come and go in the same way. The traditional clinical use of the term cardiac failure makes no pathophysiological assumptions and is not disease specific.

This traditional usage contrasts with the definition of congestive failure implicit in the patient selection criteria for many of the recent large therapeutic trials and epidemiological studies [1-8]. In these reports, congestive cardiac failure could be described as the combination of impaired effort tolerance with reduced left ventricular contractility and, sometimes, reduced maximal oxygen consumption. The condition is attributed to ischemic heart disease or nonspecific myocardial disease, usually in a proportion of about three to one, although patients with valve disease and hypertensive heart disease are often included. In such series, patients with the traditional features of cardiac failure may be in a minority. When these patients are present, they may be described as being "decompens-
ated” or showing “overt” heart failure, while, after therapeutic remission they are described as “compensated.” There is little to distinguish patients with “non-overt heart failure” [8] from patients with “heart disease.”

While it may be clear to those in the field that the epidemiological, clinical, and prognostic features of what is being described as congestive cardiac failure are actually those of chronic ischemic left ventricular myocardial disease, this may not always be clear to the general physician or internist, or to the marketing department of the pharmaceutical house. Many forms of heart disease represent latent heart failure, but their natural histories and response to drugs can differ. For this reason they are better described as “ischaemic heart disease,” “hypertensive heart disease,” “mitral valve disease,” and so on, rather than as “compensated,” “asymptomatic,” “latent,” or “early” cardiac failure.

Pathophysiology

The pathophysiological features associated with cardiac failure can be divided into

1. Disorders of the pump function of the heart, including ventricular dysfunction and various forms of overload of previously normal ventricles and atria.
2. Disorders of the function of the heart and circulation as sensory and endocrine organs, in which roles they play a central part in the elaborate system for the regulation of body fluid volume, which is gradually coming to light.

The so-called neuroendocrine activation or response to heart failure is best placed in this second category. Not enough is known about the whole system of volume homeostasis to attribute all the neuroendocrine changes to reduced cardiac output. In particular, the natriuretic factor synthesized and secreted by the atria [9], together with their neural afferent output, influence renal function, alter renin and aldosterone production, interact with the vascular system, and possibly modify the effect of natriuretic factors produced by other organs [10]. This system responds to the many alterations in atrial hemodynamics that may accompany heart disease rather than to changes in cardiac output. While changes in volume regulation may represent self-preserving short-term adaptations to exercise and hemorrhage, there is little evidence that their purpose is to “compensate” for heart disease. As much of the system of volume homeostasis still remains hidden from view, it cannot be predicted that restoring the measurable components to normal will necessarily be beneficial. The value of such manipulations can only be determined by trial and error. Interference with renal tubular function by diuretic drugs effectively combats fluid retention, but measures to correct abnormal levels of noradrenaline, aldosterone, natriuretic peptide, and other neuroendocrine components have, individually, been disappointing. The benefits of angiotensin-converting enzyme inhibition are not confined to patients with high circulating levels of renin or angiotensin [11].

Epidemiology and Prognosis

In the developed world, ischemic heart disease and hypertensive heart disease are responsible for a high proportion of congestive cardiac failure in the population [12]. In these conditions, the development of fluid retention is associated with high morbidity and mortality and carries a poor short-term prognosis [13]. This does not necessarily apply to other patients with ischemic heart disease and left ventricular dysfunction, whose condition may remain static for long periods. Left ventricular dysfunction, particularly when it is regional rather than global, correlates poorly with effort tolerance and prognosis [14]. The situation is complicated in ischemic heart disease by effort intolerance due to angina, which may be difficult to separate from effort intolerance due to dyspnea. The prognosis in ischemic heart disease is also influenced largely by the state of the coronary circulation, which is likely to be the important determinant of sudden death associated with myocardial infarction and ventricular arrhythmias.

The development of peripheral edema may carry an equally grave prognosis in other forms of heart disease but should be viewed in the light of the natural history of the particular heart disease involved. Congestive failure in this sense occurs much later in the course of, for example, aortic stenosis than it does in mitral valve disease. Similarly, some forms of idiopathic myocardial disease progress very slowly, whereas the appearance of congestive failure in hypertrophic cardiomyopathy signifies early mortality. For this reason, in epidemiological reviews and in trials of treatment aimed at improving the prognosis, it is important to consider carefully the precise etiology of congestive cardiac failure. Precise etiological classification is made difficult in such studies because, without coronary arteriography, it is frequently impossible to confirm or exclude coronary artery disease in patients with chronic left ventricular myocardial disease. Absence of previous angina or myocardial infarction alone does not exclude ischemic heart disease. It is likely that some patients classified as idiopathic dilated cardiomyopathy suffer from coronary artery disease. The patients involved in many of the large recent therapeutic trials include a much higher proportion of congestive cardiomyopathy than is found in ordinary practice in the United Kingdom [15]. These and similar differences should be kept in mind when comparing the results of controlled clinical trials so that recommendations based upon their conclusions