The clinical syndrome of congestive heart failure has become a major cause of morbidity and mortality. Physiologists and clinicians distinguish many causes and manifestations. In the past decades the importance of the diastolic function of the heart was recognised in the genesis of this syndrome. Although the prevalence of diastolic left ventricular dysfunction as a manifestation of congestive heart failure varies widely between the majority of studies, it is generally estimated between 30 and 40% (Kitzman 1991, Bonow 1992, Vasan 1995).

Diastolic dysfunction is the result of a diversity of structural and/or physiologic abnormalities of myocardial relaxation and/or ventricular compliance that increase resistance to ventricular inflow, e.g. constrictive pericarditis, amyloidosis, hypertrophic cardiomyopathy and, more commonly hypertension and myocardial ischaemia (Grossman 1991). Similar to patients with systolic heart failure, signs and symptoms of patients with diastolic heart failure are related to increased pulmonary venous pressure and/or decreased cardiac output, and include (exertional) dyspnoea, fatigue, gallop sounds, lung crepitations and pulmonary oedema, (Goldsmith 1993, Vasan 1996). In patients with congestive heart failure and systolic left ventricular dysfunction, diastolic function parameters are consistently found to correlate significantly to symptom status (Franciosa 1985, Szlachcic 1985, Rihal 1994, Lapu-Bula 1999). This contrasts with the finding that the severity of systolic dysfunction, i.e. left ventricular ejection fraction, only correlates weakly with exercise capacity or symptom status (Franciosa 1981, Rihal 1994).

Despite the similarity between the clinical symptoms of diastolic and systolic dysfunction, the reported mortality rate for patients with heart failure and predominantly diastolic dysfunction is considerably lower (Cohn 1990, Vasan 1995). In addition to the strong correlation between the severity of systolic dysfunction and prognosis in patients with heart failure with left ventricular systolic dysfunction, the common finding of diastolic dysfunction, a restrictive filling pattern in particular, also appears to correlate with increased cardiac mortality (Pinamonti 1993, Rihal 1994, Temporelli 1998).

Diastolic heart failure is a common clinical entity with similar signs and symptoms as systolic heart failure, but with different prognosis. Isolated diastolic dysfunction is
often believed to be present in patients with heart failure in whom no systolic dysfunction can be found (Cohn 1990, Goldsmith 1993). Therapy depends on the type and phase of the disease and the underlying mechanisms (Brutsaert 1993). It is therefore of clinical importance to establish criteria for the diagnosis of diastolic heart failure.

To date, diastolic left ventricular heart failure is diagnosed in patients with evidence of congestive heart failure by excluding a systolic cause and where possible increasing the plausibility of presence of diastolic dysfunction by various diagnostic tests. Many diagnostic tools are available for the diagnosis of diastolic dysfunction, whether primary or secondary. These tests can make the presence or absence of diastolic dysfunction more likely. None of the tests however can diagnose diastolic dysfunction unambiguously. The European study group on diastolic heart failure recently proposed guidelines for the diagnosis of diastolic heart failure (European study group on diastolic heart failure 1998). In order to diagnose diastolic heart failure, signs or symptoms of congestive heart failure together with normal or mildly abnormal systolic function, and evidence of abnormal left ventricular diastolic function must simultaneously be present. Independent predictive values of each technique and each index for the diagnosis of diastolic heart failure are however not yet available.

Radionuclide angiography of left ventricular systolic function at rest and during exercise has proven to be of great value for diagnosis and prognosis in patients with coronary artery disease, valvular heart disease, and congestive heart failure (Bonow 1991). Although left ventricular ejection fraction is the most important variable derived from radionuclide angiography, numerous variables describing diastolic left ventricular function may also be obtained. They may provide clinically relevant additional information in selected patients, and give insight into pathophysiologic processes of various cardiac diseases (Bonow 1991).

**AIM OF THE THESIS**

The present thesis was conducted in order to outline the value of radionuclide angiography in diagnostic testing and follow-up of diastolic left ventricular function, and to provide insight in the role of diastolic dysfunction of the left ventricle in the pathophysiology of various cardiac disorders.

In **Chapter 2** an introduction is given on “diastology” and its role in cardiac disease. A variety of diagnostic tools which can be used to assess diastolic left ventricular dysfunction will be summarised. Also the therapeutic implications of diastolic dysfunction will be discussed.

**Chapter 3** deals with the normal values and reproducibility of the radionuclide angiography derived diastolic function parameters which are used in the nuclear laboratory of the Martini Hospital in Groningen. These findings are discussed and a comparison with other studies is made.

In **Chapter 4** a specific problem with regard to this technique, the quantification of the atrial contribution to diastolic filling is addressed. The moment of onset of atrial
contraction is mostly derived from the left ventricular volume curve. No external reference point for the onset of atrial contraction, e.g. the P wave on the electrocardiogram, is used. We investigated whether the use of either the left ventricular volume curve or the P wave on the electrocardiogram as starting-point for the atrial contribution phase led to different estimations of the atrial contribution to diastolic filling.

In chapter 5 the unexpected observation of diurnal variation of left ventricular diastolic function in patients with congestive heart failure and decreased left ventricular ejection fraction is discussed. This diurnal variation could have important implications for the timing of diagnostic testing of diastolic left ventricular function in patients with heart failure and left ventricular systolic dysfunction. The diurnal variation of diastolic left ventricular function could play a role in the circadian rhythm of the onset of acute cardiogenic pulmonary oedema in these patients (Kitzis 1999). Treatment regimens should account for increased risk of pulmonary oedema early in the morning.

In chapter 6 the effect of the calcium antagonist mibefradil on left ventricular diastolic function is tested in patients with congestive heart failure and decreased left ventricular ejection fraction. Although the administration of calcium antagonists in patients with decreased systolic function is potentially hazardous because of their negative inotropic action, some representatives of this group are (practically) safe in this respect. Because some investigators described a beneficial effect of calcium antagonists on diastolic function in patients with depressed systolic function, it was of interest to test this hypothesis with mibefradil. During this investigation mibefradil did not affect diastolic function.

Our haemodynamic findings in patients with atrial fibrillation are discussed in chapters 7 and 8. The beat-to-beat variation of haemodynamics is the point of interest in chapter 7. In this study we used a nuclear stethoscope to collect data of the left ventricular time activity curve in order to assess independent determinants of beat-to-beat variations in left ventricular performance during atrial fibrillation. The short-term and long-term left ventricular diastolic function after electrocardioversion in patients with chronic atrial fibrillation is discussed in chapter 8.

In chapter 9 the results of this thesis are summarised.

References


