Restrictive Left Ventricular Filling Pattern After Myocardial Infarction: Significance of Concomitant Preserved Systolic Function

Malcolm I. Burgess, M.R.C.P., Paul Atkinson, M.R.C.P., and Simon G. Ray, M.D., F.R.C.P., F.A.C.C.

Department of Cardiology, Wythenshawe Hospital, Manchester, United Kingdom

Restrictive left ventricular (LV) filling identifies a high risk subgroup, following myocardial infarction (MI). The extent and significance of systolic dysfunction in this group is not clear. The aim of our study was to determine the incidence and extent of systolic dysfunction in patients with restrictive filling and nonrestrictive filling examining the prognostic implications. Doppler parameters of LV diastolic function were measured in 102 post-MI subjects within 4 days. Restrictive filling was defined as the presence of E:A ratio > 2 or E:A ratio 1-2 with MDT ≤ 140 msec. Follow-up was to a median of 11 months. Restrictive filling (group A) was found in 19 (19%) of 102 patients. Patients with this pattern were more likely to have systolic dysfunction than those without (group B); 63% and 35%, respectively, P = 0.024. Eight (42%) of 19 patients in group A had relatively preserved systolic function. At 11 months 14 patients had developed heart failure (HF), 6 in group A (32%) and 8 in group B (10%), P = 0.012. There were two deaths (11%) in group A and 7 (8%) in group B, P = ns. Seven (88%) of 8 patients in group A with relatively preserved systolic function were alive and free of heart failure at follow-up compared to 4 of 11 patients (36%) in group A with systolic dysfunction (P = 0.026). Restrictive filling can be associated with relatively preserved systolic function after MI and these patients have a relatively good outcome. Patients with restrictive filling post-MI are a heterogenous group emphasizing the evaluation of both systolic and diastolic function.

Left ventricular diastolic dysfunction is common after myocardial infarction (MI) and the finding of a restrictive type of left ventricular (LV) filling carries important prognostic implications. Previous studies based on pulsed-wave Doppler evaluation of transmirtal flow velocity patterns have demonstrated that patients with this pattern have a particularly poor short- and long-term outcome that is independent of measures of systolic function. Restrictive filling is commonly associated with significant impairment of systolic function where it implies the presence of elevated left ventricular filling pressures and a high likelihood of the presence or subsequent development of symptomatic heart failure. However, in our experience this pattern may occur in some patients in the presence of relatively preserved systolic function, and the clinical implications for this group have not previously been defined. The purpose of this study was to compare the clinical characteristics of patients with and without a restrictive LV filling pattern after MI and determine the incidence and extent of systolic dysfunction in each group. We also examined the prognostic implications of relative preservation of systolic function.
Methods

Study Population

We prospectively studied 102 patients (70 male, aged 66 ± 11 years) with a diagnosis of acute MI who were recruited from the coronary care unit at our hospital. The diagnosis of MI was based on the presence of chest pain characteristic of myocardial ischemia/infarction or conventional electrocardiographic changes together with enzymatic evidence of myocardial necrosis (elevation of serum creatine kinase to at least twice the upper limit of the normal range). Patients with atrial fibrillation were excluded from the study as were patients with severe mitral regurgitation. Patients were also excluded if the mitral flow velocity profile could not be characterized for technical reasons. Follow-up data was collected at a median interval of 11 months. At this point patient symptoms were established from individual case note review and telephone contact. Significant heart failure was defined as New York Heart Association (NYHA) functional class III or IV and assessed without knowledge of the echocardiographic parameters. Cause of death was determined by reviewing hospital records and, when necessary, death certificates. The study was approved by the institutional committee on medical research and full informed consent was given by all study subjects.

Echocardiography

Examination. Within four days of admission transthoracic two-dimensional and Doppler echocardiography were performed. Patients were studied in the left lateral decubitus position with a Hewlett-Packard Sonos 2000 or 2500 machine (Agilent Technologies, Andover, MA, USA) equipped with a 2.5-MHz transducer. All studies were performed by a single experienced operator. Heart rate and blood pressure were recorded at the termination of the procedure. Color flow Doppler imaging was used to quantify mitral regurgitation. M-mode and Doppler recordings were made at a sweep speed of 50 or 100 mm/sec and studies were recorded on 0.75 ins SVHS video tape. In all study subjects echocardiographic parameters were measured offline from video tape recordings with at least three and five consecutive beats averaged each two-dimensional and Doppler parameter, respectively. Ectopic and postectopic beats were not analyzed.

Evaluation of Left Ventricular Systolic Function. Left ventricular end-systolic and end-diastolic dimensions were recorded in the parasternal long-axis view at a level immediately distal to the mitral valve tips from the two-dimensional-guided M-mode image. Left ventricular ejection fraction was calculated from the apical four-chamber and two-chamber views using the apical biplane method of discs. A wall-motion score was calculated for each study based on a nine-segment model that has been extensively validated. Visual assessment of left ventricular function was based on a grading scheme for systolic thickening. The score 3 was used for hyperkinesis, 2 for normokinesis, 1 for hypokinesis, 0 for akinesis, and -1 for dyskinesis. The overall wall-motion score was calculated by dividing the sum of the scores in each segment by nine. An ejection fraction of < 40% was used to represent significant systolic dysfunction.

Evaluation of Left Ventricular Diastolic Function. The transmitral flow velocity profile was recorded from the apical four-chamber view with the pulsed-wave sample volume located at the tips of the mitral valve leaflets in diastole. The maximum E and A wave velocities were recorded. Mitral deceleration time was measured as the time from peak E velocity to the point of intercept of the deceleration slope with the baseline. The mitral deceleration time was not recorded in patients with summation of E and A waves. The isovolumic relaxation time (IVRT) was recorded by pulsed-wave Doppler evaluation with the sample volume midway between the mitral leaflets and the aortic annulus. Using this technique the timing of aortic closure and mitral opening could be identified on the same Doppler trace. Restrictive left ventricular filling was defined as an E:A ratio of > 2 or a ratio of 1-2 and a mitral deceleration time of < 140 msec. This definition has been used previously.

Statistical Analysis. Continuous variables are expressed as mean ± SD. Comparisons between continuous data in patients with and without restrictive filling were made using the paired or unpaired t-test and Mann-Whitney test for parametric and nonparametric data, respectively. Categorical data was compared by the chi-square test.
Results

Baseline Demographic Data

Of 102 patients studied, 19 (19%) had evidence of restrictive filling (group A). Table I shows the age and sex of the two groups in addition to the clinical characteristics. Patients in group A were of a comparable age to those in group B but were more likely to be male. Peak creatine kinase was higher in group A. Pulmonary edema at presentation was more common in group A, but the difference was not statistically significant. There was no difference between the two groups in the proportion presenting with anterior infarction or number with a previous MI. Both systolic and diastolic blood pressure were similar in the two groups. Duration of hospital stay for group A patients was 11.8 ± 10.8 days and for group B, 8.3 ± 4.5 days (P = ns). Within group A there was no significant difference in age between patients with preserved and nonpreserved systolic function (age 65 ± 10 and 62 ± 7 years, respectively; P = ns) and no significant difference in heart rate between these two groups (77 ± 15 and 75 ± 12 beats/min respectively; P = ns).

Echocardiographic Evaluation of Left Ventricular Function

Table II shows the two-dimensional and Doppler echocardiographic data for groups A and B. In addition to MDT, differences in left ventricular filling between the two groups were reflected in significant differences in the E:A velocity ratio and IVRT between the two groups (P < 0.0001 and < 0.001, respectively).

The ejection fraction and wall-motion score were lower in group A than group B (both P = 0.01).

Distribution of Systolic Function in the Two Groups

Figure 1 shows the ejection fraction in each group A patient compared to group B. Eight (42%) patients in group A had preserved systolic function. In four of these patients the ejection fraction was between 40% and 50%. In two patients it was > 55%. In group B, 58 (70%) patients had preserved systolic function. Patients in group A were less likely to have evi-

| TABLE I | Patient Demographic and Clinical Data |
|---|---|---|---|
| | Restrictive (n = 19) | Nonrestrictive (n = 83) | P |
| Age (years) | 64 ± 9 | 66 ± 12 | ns |
| Male | 18 (95%) | 52 (63%) | <0.01 |
| Peak CK (IU/L) | 2184 ± 1337 | 1443 ± 1613 | <0.01 |
| Pulmonary edema | 7 (37%) | 23 (28%) | ns |
| Anterior infarction | 8 (42%) | 35 (42%) | ns |
| Previous infarction | 8 (42%) | 19 (23%) | ns |
| Heart rate (beats/min) | 76 ± 13 | 75 ± 16 | ns |
| Systolic BP (mmHg) | 116 ± 26 | 121 ± 23 | ns |
| Diastolic BP (mmHg) | 63 ± 15 | 65 ± 15 | ns |
| Duration of hospital stay (days) | 11.8 ± 10.8 | 8.2 ± 4.5 | ns |

CK = creatine kinase; BP = blood pressure.

| TABLE II | Echocardiographic Data |
|---|---|---|
| | Restrictive (n = 19) | Nonrestrictive (n = 83) | P |
| E:A | 1.88 ± 0.80 | 0.85 ± 0.32 | <0.0001 |
| MDT | 126 ± 19 | 171 ± 29 | <0.0001 |
| IVRT | 76 ± 20 | 97 ± 21 | 0.0004 |
| EF | 37 ± 13 | 46 ± 13 | 0.01 |
| WMS | 1.03 ± 0.41 | 1.38 ± 0.39 | 0.01 |

E:A = ratio of early to late velocity of ventricular filling; MDT = mitral deceleration time; IVRT = isovolumic relaxation time; EF = left ventricular ejection fraction; WMS = wall-motion score.

Figure 1. Distribution of left ventricular ejection fraction in the two groups. Significantly more patients in group A had significantly impaired systolic function. Solid circles represent patients presenting with pulmonary edema. Empty circles represent those without pulmonary edema.
dence of relatively preserved systolic function ($P = 0.01$).

**Clinical Status at Follow-up**

Follow-up was complete to 11 months. Nine patients died and 14 had developed heart failure (Fig. 2). There had been two deaths (11%) in group A and seven (8%) in group B ($P = ns$). Significantly more patients had developed heart failure in group A (6 [32%]) compared to group B (8 [10%]); $P = 0.012$. Among the eight group A patients with preserved systolic function at presentation, one had developed heart failure and none had died. Of the 11 patients in this group who presented with concomitant systolic dysfunction, five developed heart failure and two had died (Fig. 3). Group A patients with significant systolic dysfunction were more likely to be in heart failure or have died at follow-up compared to those with preserved systolic function ($P = 0.026$).

**Discussion**

**Restrictive Left Ventricular Filling After Myocardial Infarction**

Left ventricular diastolic dysfunction is frequently observed after MI.\(^1\)-\(^7\),\(^11\) Pulsed-Doppler echocardiography is a convenient, noninvasive tool in this setting. Despite well-recognized limitations, evaluation of the transmitral flow velocity profile has been used extensively and provides a means of characterizing left ventricular diastolic properties. A wide spectrum of abnormalities have been described previously. In patients with relatively small infarcts, a pattern of abnormal relaxation is the most frequent finding.\(^4\) A restrictive filling pattern is more common in patients with greater myocardial damage, and in patients with depressed systolic function, it identifies a subgroup at particularly high risk of an adverse outcome.\(^1\)-\(^3\) Previous reports suggest that restrictive filling in the early postinfarction period is not uncommon (13% of all post-MI patients in the study of Nijland et al.\(^1\) and 14% in that by Sakata et al.\(^2\)). In Nijland's study no patient with restrictive filling had evidence of preserved systolic function defined as an ejection fraction of $\geq 45\%$ and a wall-motion score of $\geq 1.76$. Although other studies indicate a low ejection fraction in the group of patients with restrictive filling, these studies do not state how many individual patients had evidence of relative preservation of systolic function. In addition, although it would seem plausible that an

**Figure 2.** Clinical status at follow-up based on the presence or absence of restrictive filling at presentation. $P < 0.05$ for difference in combined endpoint of death and heart failure between the two groups.

**Figure 3.** Clinical status at follow-up in patients with restrictive filling according to the presence or absence of concomitant systolic dysfunction. $P < 0.05$ for difference in combined endpoint of death and heart failure between the two groups.
isolated restrictive filling pattern in the absence of systolic dysfunction would carry different prognostic implications, the outcome for this patient subgroup has not been defined.

**Current Study**

The prevalence of restrictive filling in the post-MI population of our study is comparable to that found by previous investigators. Enzymatic infarct size was significantly greater in patients with restrictive filling in accordance with the study of Nijland et al. and is consistent with the fact that more extensive systolic dysfunction is related to the presence of increased myocardial stiffness. There was a trend toward a higher prevalence of pulmonary edema in patients with restrictive filling, but this failed to reach statistical significance. This is also consistent with increased myocardial stiffness.

We have documented the range of abnormalities of systolic function in patients with restrictive filling after MI. Relative preservation of systolic function was found in 8 (42%) of 19 patients. There is increasing evidence that abnormalities of diastolic function are important contributors to symptoms in patients with congestive cardiac failure, but this is predominantly applicable to those patients with significant systolic dysfunction. This would be consistent with the relatively low incidence of heart failure at follow-up in the subgroup of our patients with isolated restrictive filling. Our findings support the assessment of both systolic and diastolic function in a composite manner after MI. This is likely to provide optimal prognostic information.

**Limitations**

The limitations of transmitral flow velocity patterns in the assessment of diastolic function are widely acknowledged. In addition to the effect of systolic dysfunction, mitral deceleration time can be affected by other factors such as loading conditions and pericardial restraint. However, this method of evaluating ventricular diastolic function is widely available and commonly used in clinical practice. We felt it appropriate to use a technique that was applicable to the routine clinical setting. The mitral deceleration time may appear normal (pseudo-normal) in circumstances where abnormal relaxation and restrictive filling co-exist as they have opposing effects on the transmitral flow velocity profile. This is likely to lead to an underestimation of the prevalence of true diastolic function abnormalities when assessed by this method. However, in the present study we were concerned only with the presence of restrictive filling as it is this pattern alone that has been of prognostic use. The short isovolumic ventricular relaxation time in the patients with restrictive filling suggests that these patients had significantly reduced myocardial compliance compared to the remaining patients. We did not consider the potential effect of drugs such as intravenous nitrates on the parameters of diastolic function. A single Doppler study within 4 days of infarction may not be considered optimal for the reliable evaluation of diastolic function in these patients. It may have been preferable to perform serial studies during the hospital course such as in the study of Nijland. However, in that study it was clearly demonstrated that the presence of restrictive filling at any point during the early post-MI period conferred an adverse outcome. In view of this, we did not repeat the Doppler evaluation.

**Conclusion**

Restrictive filling is frequently associated with relatively preserved systolic function after MI. Although patients with systolic dysfunction and restrictive filling have a poor prognosis, those with isolated restrictive filling have a relatively good outcome. This study emphasizes the composite evaluation of both systolic and diastolic function after MI.

**Acknowledgment:** We wish to thank the staff of the Coronary Care Unit at Wythenshawe Hospital for their assistance in the conduct of the study.

**References**

1. Nijland F, Kamp O, Karreman AJP, et al: Prognostic implications of restrictive left ventricular filling in acute myocardial infarction: A serial Doppler echocardiographic study. *J Am Coll Cardiol* 1997;30:1618-1624.
2. Sakata K, Kashiro S, Hirata S, et al: Prognostic value of Doppler transmitral flow velocity patterns in acute myocardial infarction. *Am J Cardiol* 1997;79:1165-1169.
3. Poulsen SH, Jensen SE, Gotzsche O, et al: Evaluation and prognostic significance of left ventricular diastolic function assessed by Doppler echocardiography in the early phase of a first acute myocardial infarction. *Eur Heart J* 1997;18:1882-1889.
4. Pipilis A, Meyer TE, Ormerod O, et al: Early and late changes in left ventricular filling after acute myocardial infarction and the effect of infarct size. *Am J Cardiol* 1992;70:1397-1401.
5. Pozzolli M, Capomolla S, Opasich C, et al: Left ventricular filling pattern and pulmonary wedge pressure are closely related in patients with recent anterior myocardial infarction and left ventricular dysfunction. *Eur Heart J* 1992;13:1067-1073.

6. Giannuzzi P, Imparato A, Temporelli PL, et al: Doppler-derived mitral deceleration time of early filling as a strong predictor of pulmonary capillary wedge pressure in post-infarction patients with left ventricular systolic dysfunction. *J Am Coll Cardiol* 1994;23:1630-1637.

7. Pozzolli M, Capomolla S, Sanarico M, et al: Doppler evaluations of left ventricular diastolic filling and pulmonary wedge pressure provide similar prognostic information in patients with systolic dysfunction after myocardial infarction. *Am Heart J* 1995;129:16-25.

8. Schiller NB, Shah PM, Crawford M, et al: Recommendations for quantitation of left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358-367.

9. Heger JJ, Weyman AE, Wann S, et al: Cross-sectional echocardiographic analysis of the extent of left ventricular asynergy in acute myocardial infarction. *Circulation* 1980;61:1113-1118.

10. Pfeffer MA, Braunwald E, Moye LA, et al: Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE investigators. *N Engl J Med* 1992;327:669-677.

11. Seals AA, Pratt CM, Mahmarian JJ, et al: Relation of left ventricular dilatation during acute myocardial infarction to systolic performance, diastolic dysfunction, infarct size and location. *Am J Cardiol* 1988;61:224-229.

12. Davies SW, Fussell AL, Jordan SL, et al: Abnormal diastolic filling patterns in chronic heart failure—relationship to exercise capacity. *Eur Heart J* 1992;13:749-757.

13. Sumimoto TS, Jikuhara T, Hattori T, et al: Importance of left ventricular diastolic function on maintenance of exercise capacity in patients with systolic dysfunction after anterior myocardial infarction. *Am Heart J* 1997;133:87-93.