Echocardiographic evaluation of left ventricular function in ischemic heart disease

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Chapter 2

Prognostic value of echocardiography after acute myocardial infarction

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ABSTRACT

Echocardiography is useful for risk stratification and assessment of prognosis after myocardial infarction, which is the focus of this review. Various traditional echocardiographic parameters have been demonstrated to provide prognostic information, such as left ventricular volumes and ejection fraction, wall motion score index, mitral regurgitation and left atrial volume.

The introduction of tissue Doppler imaging and speckle-tracking strain imaging has resulted in additional prognostic parameters, such as left ventricular strain (rate) and dyssynchrony. Also, (myocardial) contrast echocardiography provides valuable information particularly about myocardial perfusion (as a marker of myocardial viability), which is strongly related to prognosis after myocardial infarction. Stress echocardiography provides information on ischemia and viability, coronary flow reserve can be obtained by Doppler imaging of the coronary arteries, and finally, 3-dimensional (3D) echocardiography provides optimal information on left ventricular volumes, function, and sphericity which are also important for long-term outcome.

INTRODUCTION

At present, 2D echocardiography is a frequently used imaging modality in the management of patients with acute myocardial infarction. It is a low-cost and safe modality, which can be easily applied at bedside and is valuable for patient follow-up. Important benefit of echocardiography has been demonstrated in establishing the diagnosis, location, and extent of myocardial infarction, and in detection of mechanical complications after myocardial infarction. In particular, echocardiography is useful for assessment of prognosis and risk stratification.

The main focus of this review is the value of transthoracic 2D echocardiography for prognosis after acute myocardial infarction. A variety of prognostic parameters can be derived from routine and more sophisticated echocardiographic approaches, including tissue Doppler imaging (TDI) and speckle-tracking strain imaging (Table 1). The use of contrast echocardiography for prognosis is also discussed extensively, followed by a brief discussion on the prognostic value of other echocardiographic techniques.

Table 1. Echocardiographic parameters related to prognosis after myocardial infarction

Traditional parameters	· LV volumes · LVEF · MR · WMSI · Diastolic function · LA volume · RV function
Novel parameters	· Strain · Strain rate · LV dyssynchrony
Intravenous contrast	· Endocardial border detection · Thrombus detection · Assessment of perfusion / viability
Stress echocardiography	· Ischemia · Contractile reserve
Coronary artery flow	· Coronary flow reserve
3D echocardiography	· LV volumes, LVEF and sphericity indices

LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; RV: right ventricular; WMSI: wall motion score index.

TRADITIONAL PROGNOSTIC PARAMETERS

Left ventricular volumes and ejection fraction

Traditionally, left ventricular (LV) function has been described as an important predictor of outcome after acute myocardial infarction. The prognostic importance of LV ejection fraction (LVEF) after myocardial infarction, mostly assessed with contrast ventriculography, has been demonstrated in several large studies (1). In addition, the value of LVEF quantified by echocardiography for prognosis after myocardial infarction was confirmed. Moller et al. examined a group of 767 patients with acute myocardial infarction and demonstrated that echocardiographically determined LVEF at 1 day after admission for acute myocardial infarction was a powerful predictor of all-cause mortality during a median follow-up of 19 months (2).

Although LVEF has commonly been used to describe LV function, the prognostic value of LVEF after myocardial infarction has been questioned. Low LVEF may be the result of reduced contractile function due to extensive myocardial damage or continuing ischemia or, on the other hand, as a result of LV dilatation caused by infarct expansion and stretching of the myocardial scar. Furthermore, assessment of LVEF early after myocardial infarction can be misleading due to the presence of myocardial stunning. It has been advocated that LV end-systolic volume (LVESV) or LV end-diastolic volume (LVEDV) may be more meaningful predictors of prognosis than LVEF. In a group of 605 patients with acute myocardial infarction, White et al. demonstrated that LVESV was the primary predictor of survival after myocardial infarction (Figure 1) (3). It was observed that LVESV was superior to LVEF in patients with depressed LVEF (<50%) or small LVESV (<100 ml).

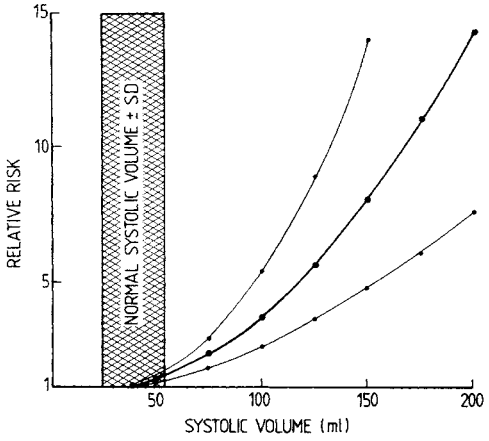

Figure 1. Relationship between LVESV and relative risk of cardiac death during follow-up. A significant relation is demonstrated between LVESV and cardiac death during follow-up after acute myocardial infarction. The fine lines indicate the 95% confidence limits of the relative risk. LVESV: left ventricular end-systolic volume; SD: standard deviation. Reprinted from White et al. (3) with permission.

Wall motion score index

It has been advocated that optimal assessment of LV function in patients after myocardial infarction is performed by evaluating the segmental function of the left ventricle rather than evaluation of global LV function. A practical approach is to divide the ventricle into a number of segments and to evaluate wall motion in each segment. A regional score index, the wall motion score index (WMSI), can be derived and provides powerful prognostic information. After myocardial infarction extensive regional wall motion abnormalities may be present but when compensated by regional hyperkinesis of the normal segments, LVEF will be (almost) normal; in these patients, WMSI could more correctly reflect the magnitude of myocardial damage (4).

The prognostic value of WMSI after acute myocardial infarction has been described in few, relatively small studies. Galasko et al. studied 120 consecutive patients with acute myocardial infarction treated with thrombolysis (5). The authors demonstrated that WMSI independently predicted cardiac events during a mean follow-up of 13 months. Compared with LVEF, echocardiographic WMSI was described as a cheaper and more readily available technique, which is more discriminatory in cases of mild LV dysfunction following acute myocardial infarction. In a study performed by Carluccio et al., 144 patients with a first acute myocardial infarction treated with thrombolytic therapy were followed for a mean period of 18 months (6). Patients with cardiac events during follow-up had a higher WMSI at pre-discharge than patients without events. During multivariate analysis, a WMSI >1.50 was the most powerful predictor of a subsequent event (chi-square 17.8, $p<0.0001$). Furthermore, Moller et al. demonstrated in a larger population of patients with acute myocardial infarction that WMSI was an independent predictor of death (hazard ratio 1.15 per 0.2-unit increase) (2). In addition, WMSI also proved to be an independent predictor of hospitalization for heart failure (hazard ratio 1.21 per 0.2-unit increase). In the same study, LVEF demonstrated to be a powerful predictor of all-cause mortality after myocardial infarction, but did not provide incremental prognostic information over WMSI. Furthermore, LVEF was not predictive for heart failure hospitalization.

Mitral regurgitation

The presence of mitral regurgitation after acute myocardial infarction is often asymptomatic and systematic evaluation using echocardiography should be performed in post-myocardial infarction patients. Standard color Doppler imaging is a highly sensitive method to detect even mild degrees of mitral regurgitation. Furthermore, echocardiography permits accurate quantification of the severity of mitral regurgitation by measuring the effective regurgitant orifice area and the regurgitant volume using Doppler technique (7).

The incidence of acute mitral regurgitation is high among patients with acute myocardial infarction and is an independent predictor of late cardiovascular and all-cause mortality. Lehmann et al. studied 206 patients within 7 hours after first myocardial infarction using contrast left ventriculography and demonstrated the presence of mitral regurgitation in 13% of patients (8). In a substudy from the Survival And Ventricular Enlargement (SAVE) investigators, Lamas et

al. studied a cohort of 727 patients who underwent left ventriculography up to 16 days after myocardial infarction. Mitral regurgitation was present in 141 patients (19%). The presence of mitral regurgitation was related to the risk of occurrence of a cardiovascular event during 3.5 years of follow-up. Patients with mitral regurgitation had a higher cardiovascular mortality (29% versus 12%, p<0.001; Figure 2) and a higher prevalence of severe heart failure (24% versus 16%, p<0.05) compared to patients without mitral regurgitation. The presence of mitral regurgitation demonstrated to be an independent predictor of cardiovascular mortality with a relative risk of 2.00 (9). In addition, Feinberg et al. described the value of echocardiography for assessment of mitral regurgitation and demonstrated mild mitral regurgitation in 29% and moderate-severe mitral regurgitation in 6% of 417 patients with acute myocardial infarction using color Doppler echocardiography within 48 hours of admission (10). Both mild mitral regurgitation and moderate-severe mitral regurgitation were independently associated with increased 1-year mortality with hazard ratios of 2.31 and 2.85, respectively. The prognostic value of mitral regurgitation assessed by echocardiography was further confirmed by Perez de Isla et al. who studied 300 consecutive patients admitted for non-ST-segment elevation myocardial infarction. During echocardiography in the first week after myocardial infarction, mitral regurgitation was detected in 42%. Only mitral regurgitation was an independent predictor of long-term outcome during a mean follow-up of approximately 14 months (11).

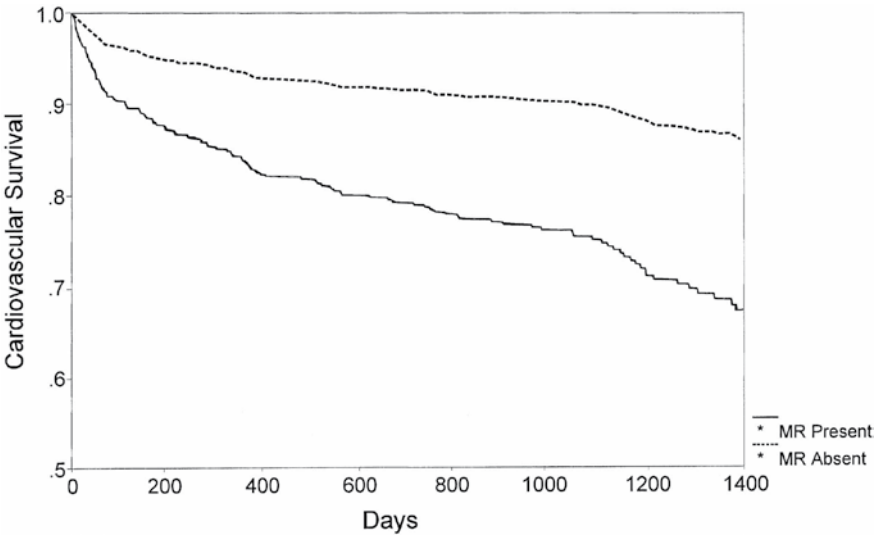

Figure 2. Kaplan-Meier curves of cardiovascular survival in patients with and without mitral regurgitation. After acute myocardial infarction, cardiovascular survival was significantly better in patients without mitral regurgitation (p=0.0022). MR: mitral regurgitation. Reprinted from Lamas et al. (9) with permission.

Diastolic function

Since the availability of Doppler echocardiography, reliable measures of diastolic function in patients with acute myocardial infarction can be obtained. Determination of the LV filling pattern provides important information about LV diastolic function in this patient group (Figure 3) (12,13). Specifically a restrictive filling pattern demonstrated to be a powerful independent predictor of late LV dilatation and cardiovascular mortality in patients with acute myocardial infarction (14). In a study by Nijland et al., short deceleration time of the early filling wave (E wave) was described as the best predictor of cardiac death in hospital survivors after acute myocardial infarction (15). A 1-year survival rate of 100% was observed in the patients without a restrictive filling pattern (peak velocity of early diastolic filling wave (E)/peak velocity of late filling wave (A) ratio ≤1 or between 1 and 2 with a deceleration time >140 ms) as compared to only 50% in the restrictive group (E/A ratio ≥2 or between 1 and 2 and deceleration time ≤140 ms). Moreover, 3-year survival rates were 100% and 22%, respectively.

In addition to this higher mortality, patients with a restrictive filling pattern have a higher risk for development of heart failure after myocardial infarction. During 1-year follow-up, Poulsen et al. reported an incidence of heart failure during hospitalization of 71%, with a hospital readmission rate for heart failure of 21% in patients with a restrictive LV filling pattern after myocardial infarction (16). Conversely, no patient with normal LV filling at baseline had heart failure during hospitalization or follow-up. In addition, Cerisano et al. studied 104 patients and obtained echocardiograms 3 days after acute myocardial infarction (17). Survival rate at a mean follow-up of 32 months was 79% in patient with a restrictive filling pattern (deceleration time ≤130 ms) versus 97% in patients without a restrictive filling pattern (deceleration time >130 ms;

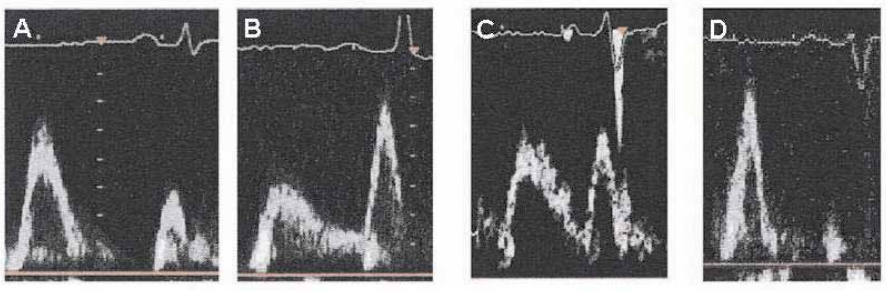

Figure 3. Pulsed-wave Doppler recordings of transmitral LV filling. Diastolic (dys)function can be categorized using the ratio of the peak velocities of early (E wave) and late (A wave) diastolic filling (the E/A ratio), and the deceleration time of the E wave. Examples of the different grades of diastolic dysfunction, as assessed by pulsed-wave Doppler echocardiography, are shown. *Panel A*: normal inflow pattern (E>A, normal deceleration time of E wave); *panel B*: impaired relaxation (E<A, prolonged deceleration time of E wave); *panel C*: pseudonormal filling pattern (E=A, normal deceleration time of E wave); *panel D*: restrictive filling pattern (E>>A, shortened deceleration time of E wave). LV: left ventricular. Reprinted from Moller et al. (12) with permission.

p=0.003). Multivariate analysis showed that, besides age, restrictive filling was an independent predictor of event-free survival.

In a recent meta-analysis of 12 prospective studies (including 3,396 patients), the presence of a restrictive filling pattern after acute myocardial infarction was an important independent predictor of mortality regardless of LVEF, LVESV and Killip heart failure class (18).

Left atrial volume

Doppler variables reflecting diastolic function are influenced by several factors (importantly loading conditions) and may change rapidly after myocardial infarction. In contrast, left atrial (LA) volume is less influenced by acute changes and reflects subacute or chronic diastolic function. The prognostic value of LA size and volume after myocardial infarction has been addressed in several studies. Moller et al. assessed LA volume during admission for acute myocardial infarction in 314 patients and corrected for body surface area (LA volume index) (19). During a mean follow-up period of 15 months, 46 patients (15%) died. LA volume index was a powerful and independent predictor of mortality (hazard ratio 1.05 per 1 ml/m^2 change). The importance of LA volume for clinical outcome after myocardial infarction was confirmed by Beinart et al. (20). In 395 consecutive patients with acute myocardial infarction, the authors demonstrated that LA volume index, determined within the first 48 hours of admission, was an independent predictor of 5-year mortality with incremental prognostic information over clinical and echocardiographic data (Figure 4). Patients with LA volume index >32 ml/m^2 had a significantly higher mortality compared to patients with LA volume index ≤32 ml/m^2 (34.5% versus 14.2%, respectively).

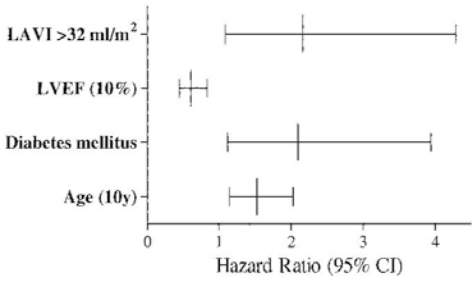

Figure 4. Overview of the independent predictors for 5-year mortality of patients with first myocardial infarction (hazard ratio [95% confidence interval]). Besides the presence of diabetes, age and LVEF, LAVI is an independent predictor of mortality after acute myocardial infarction. LAVI: left atrial volume index; LVEF: left ventricular ejection fraction. Reprinted from Beinart et al. (20) with permission.

Right ventricular function

It is clear that the extent of LV dysfunction is associated with an adverse prognosis in survivors of acute myocardial infarction. In contrast, the significance of right ventricular (RV) dysfunction after myocardial infarction is less clear and data are scarce. In the SAVE echocardiographic substudy, Zornoff et al. analyzed 2D echocardiograms from 416 patients with LV dysfunction (LVEF ≤40%) at a mean of 11 days after myocardial infarction and related RV function to clinical outcome (21). On multivariate analysis, the percentage of change in RV cavity area from end-diastole to end-systole (the fractional area change) on the apical 4-chamber view was an independent predictor of total mortality, cardiovascular mortality and heart failure.

In contrast, Gadsboll et al. failed to show a relationship between RV function and 1-year mortality in 423 patients after acute myocardial infarction, but many of the patients had normal LV function (22). Furthermore, in the Thrombolysis In Myocardial Infarction (TIMI)-II trial, in which all patients received reperfusion (n=1,110), RV wall abnormalities were observed in only 5% of patients after myocardial infarction and were not associated with increased mortality during 1-year follow-up after hospital discharge (23). However, this population existed only of patients with an inferior myocardial infarction. Obviously, more data on the precise value of RV dysfunction after myocardial infarction are needed.

NOVEL PROGNOSTIC PARAMETERS

More recently, the prognostic value of LV strain (reflecting tissue deformation) and strain rate (tissue deformation per time period) after myocardial infarction have been evaluated. Strain and strain rate can be quantified using tissue Doppler imaging (TDI) or with the more recently introduced technique of speckle-tracking imaging. The TDI based measurements of strain and strain rate are relatively simple to perform. The technique of speckle-tracking imaging makes use of natural acoustic markers, or speckles, that are present on standard ultrasound tissue images. This novel technique is able to discriminate between active and passive myocardial contraction and is angle-independent as it does not use the Doppler technique (Figure 5) (24,25). Speckle-tracking imaging has recently been validated using microcrystals and magnetic resonance imaging (MRI) (26-28).

After myocardial infarction, the extent of transmurality of infarcted tissue is a determinant of functional recovery of myocardium and contains prognostic importance. Traditionally, sophisticated imaging modalities as delayed-enhancement MRI are used for assessment of the extent of transmurality. However, Vartdal et al. demonstrated that strain can be a valuable predictor of the transmural extent of myocardial infarction as well and may therefore be an important clinical tool for risk stratification in the acute phase of myocardial infarction (29). The authors studied 30 patients with acute anterior myocardial infarction who underwent longitudinal strain assessment with TDI at 1.5 hours after revascularization. After a 9-month

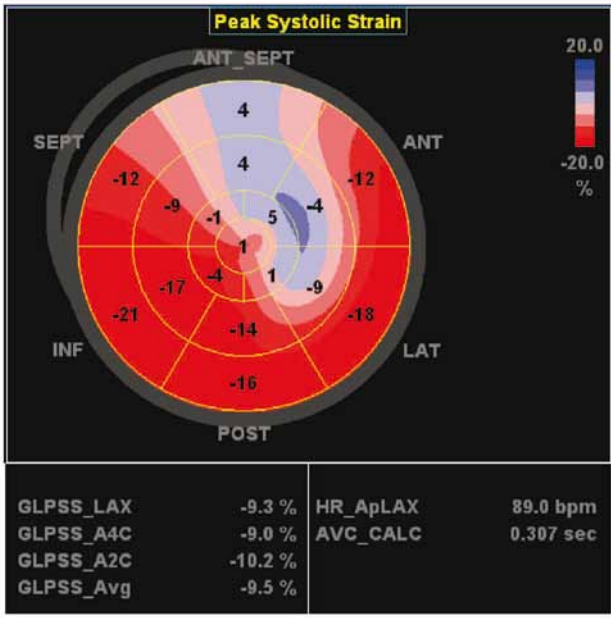

Figure 5. Bull's-eye plot providing peak systolic longitudinal strain for all 17 LV segments of a patient with an acute myocardial infarction (48 hours old). LV segments with normal strain are presented in red and those segments with decreased strain are presented in blue. In this patient, the left anterior descending coronary artery was the infarct-related artery. Decreased peak systolic longitudinal strain is observed in the anteroseptal LV segments (blue) consistent with the region of infarction. In addition, global peak systolic longitudinal strain (GLPSS_Avg) was severely reduced (normal values range from -20.3% to -24.1%) (24,25). LV: left ventricular.

follow-up period, MRI was performed to assess the precise extent of myocardial scar formation in 16 corresponding myocardial segments. To obtain a global LV strain value, the 16 segmental strain values were averaged. A good correlation was found between global strain and total infarct size (r=0.77; Figure 6). Multivariate analysis demonstrated that global peak LV strain was independently related with infarct size measured by MRI. Furthermore, a clear inverse relation was observed between segmental strain and the transmural extent of scar tissue in individual segments (r=0.67).

In another study, Zhang et al. studied 47 patients with first acute myocardial infarction and 60 healthy controls (30). Within a few days after myocardial infarction, all subjects underwent TDI with quantification of strain rate and contrast-enhanced MRI to determine the extent and transmurality of scar tissue. Peak systolic strain rate of the transmurally infarcted segments was significantly lower compared to normal myocardium or with non-transmurally infarcted segments (Figure 7). A cutoff value of peak systolic strain rate of -0.59/s detected transmural scar tissue with high sensitivity (90.9%) and specificity (96.4%), and peak systolic strain rate between -0.98/s and -1.26/s distinguished subendocardial scar tissue from normal myocardium with a sensitivity of 81.3% and a specificity of 83.3%. Accordingly, the authors concluded that

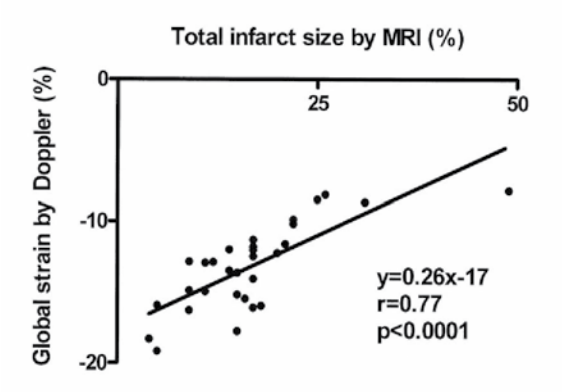

Figure 6. Relation between global strain (assessed by echocardiography) and infarct size (assessed with MRI). Infarct size assessed with MRI is inversely related with global strain assessed with echocardiography. MRI: magnetic resonance imaging. Reprinted from Vartdal et al. (29) with permission.

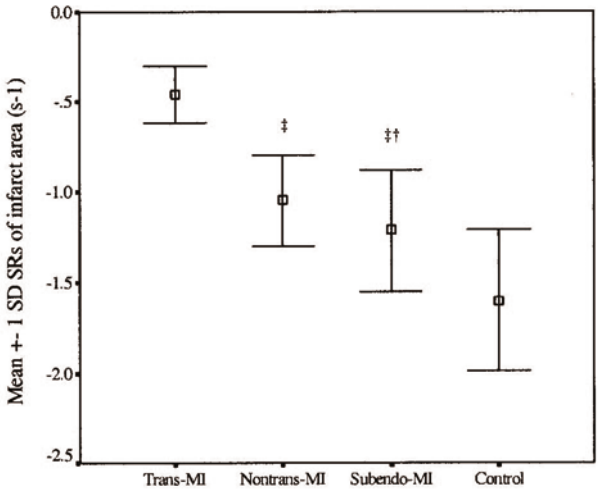

Figure 7. Mean peak systolic strain rate (SRs) in different infarcted segments. A relation was demonstrated between strain rate and the extent of myocardial infarction. The lowest strain rate values were observed in patients with transmural myocardial infarction. MI: myocardial infarction. Reprinted from Zhang et al. (30) with permission.

peak myocardial deformation assessed by strain rate imaging can differentiate between transmural and non-transmural myocardial infarction, and it permits non-invasive determination of transmurality of scar tissue after myocardial infarction (reflecting the extent of non-viable myocardium).

Where the traditional prognostic parameters demonstrated to be directly related to survival, strain and strain rate have mostly been associated with only surrogates of clinical outcome. However, Park et al. studied 50 patients with acute anterior myocardial infarction and primary

reperfusion (percutaneous coronary intervention [PCI] in 44 patients and thrombolysis in 6 patients) and assessed longitudinal strain by both TDI and speckle-tracking imaging in 7 LV segments related to the vascular territory of the left anterior descending coronary artery territory (31). A total of 22 patients showed LV remodeling (LV dilatation with an increase in LVEDV ≥15% during follow-up); these patients had significantly lower baseline longitudinal strain, assessed by the 2 echocardiographic techniques. Both strain assessed by TDI and assessed by speckle-tracking imaging were independent predictors of LV remodeling (odds ratio 1.430 and 1.307, respectively) during 18-month follow-up. Importantly, in this relatively small study, both strain parameters were independently predictive of death or development of congestive heart failure during follow-up (odds ratio 1.436 and 1.455, respectively). Furthermore, Hung et al. recently demonstrated in a group of more than 600 patients from the Valsartan In Acute Myocardial Infarction (VALIANT) trial that both strain and strain rate (by speckle-tracking imaging) were independent predictors for death. In particular, strain rate imaging provided incremental prognostic information beyond LVEF after acute myocardial infarction (32).

Left ventricular dyssynchrony

The clinical importance of LV remodeling, i.e. an increase in LV volumes with a decrease in LVEF, after myocardial infarction was already emphasized by White et al. (3). Patients who died during follow-up after myocardial infarction had significantly larger LV volumes and lower LVEF than survivors. Furthermore, the authors identified LVESV as the primary predictor of survival after myocardial infarction. Therefore, early identification of patients who will experience LV remodeling late after acute myocardial infarction is important for risk stratification and optimization of (medical) therapy.

Mollema et al. recently studied 124 patients presenting with acute myocardial infarction who underwent primary PCI. Within 48 hours of intervention, 2D echocardiography was performed and LV dyssynchrony was quantified using color-coded TDI. The authors observed that the presence of LV dyssynchrony at baseline (≥65 ms) was strongly related (r=0.73) to the extent of LV dilatation at 6-month follow-up (33). In a subsequent study, the same authors introduced LV dyssynchrony, as assessed by speckle-tracking radial strain analysis, as early predictor of LV remodeling (increase in LVESV ≥15%) at 6-month follow-up after acute myocardial infarction (Figure 8) (34). A total of 178 consecutive patients presenting with acute myocardial infarction who underwent primary PCI were included. Within 48 hours of intervention, 2D echocardiography was performed and LV dyssynchrony was quantified. Patients showing LV remodeling at 6-month follow-up (20%) had comparable baseline characteristics to patients without LV remodeling (80%), except for higher peak troponin T levels, peak creatine phosphokinase levels, WMSI, mitral inflow peak early velocity (E)/mitral annular peak early velocity (E'), or E/E' ratio, and a larger extent of LV dyssynchrony. Multivariable analysis demonstrated that LV dyssynchrony was independently predictive for LV remodeling. Receiver-operating characteristic curve analysis demonstrated that a cutoff value of 130 ms for LV dyssynchrony

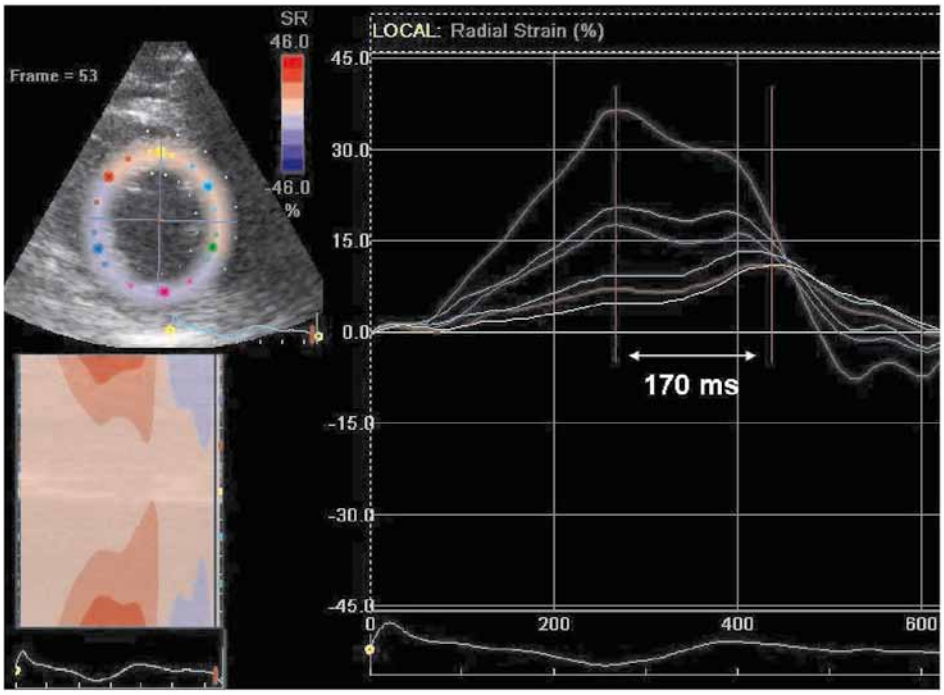

Figure 8. Time-radial strain curves of a patient at 2 days after acute myocardial infarction with the left anterior descending coronary artery as the infarct-related artery. On the X-axis the time is provided. The Y-axis provides the extent of radial strain for the individual segments. Most decreased radial strain was observed in the anteroseptal LV segments (light-blue, yellow and red curves). In addition, substantial LV dyssynchrony was demonstrated with the anteroseptal segments as the latest activated segments. LV dyssynchrony was defined as the time difference between the first segments and last segments that reach peak radial strain. In this example, the extent of LV dyssynchrony was 170 ms for the earliest versus the latest activated segments. LV: left ventricular.

yields a sensitivity of 82% and a specificity of 95% to predict LV remodeling at 6-month follow-up (Figure 9). Despite the lack of a survival analysis, the importance of LV dyssynchrony >130 ms within 48 hours after admission for clinical outcome (LV remodeling) after acute myocardial infarction was emphasized.

In a recent study, Ng et al. studied 122 healthy volunteers and 40 patients with non-ST-segment elevation myocardial infarction. The authors compared LV dyssynchrony assessment using speckle-tracking with LV dyssynchrony assessment with TDI. A good correlation (r=0.75) was demonstrated between the derived dyssynchrony indexes between the 2 imaging modalities. However agreement between the techniques was suboptimal, as LV dyssynchrony assessed with speckle-tracking was significantly lower compared to LV dyssynchrony quantified with TDI. In addition, speckle-tracking had lower coefficients of variation than TDI. Importantly, only speckle-tracking was able to identify significant differences in systolic dyssynchrony in patients with non-ST-segment elevation myocardial infarction versus healthy subjects (35).

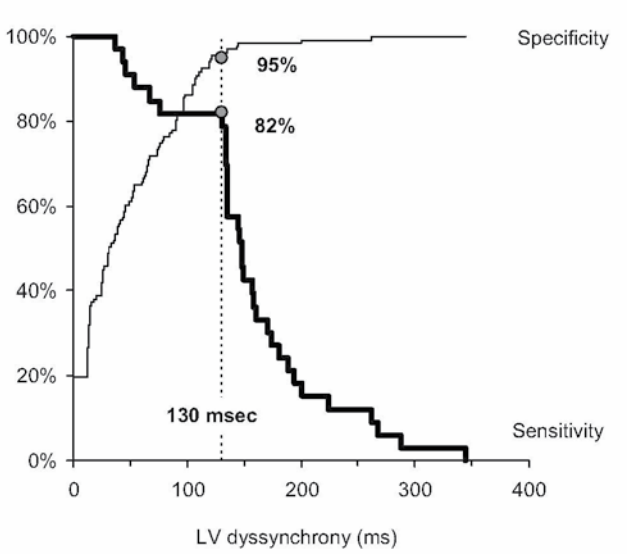

Figure 9. Receiver-operating characteristic curve analysis to determine the optimal cutoff value for LV dyssynchrony to predict LV remodeling. Using a cutoff value of 130 ms, a sensitivity of 82% and a specificity of 95% were obtained to predict LV remodeling at 6-month follow-up. LV: left ventricular. Reprinted from Mollema et al. (34) with permission.

Additional large studies are needed to confirm the prognostic value of the presence of substantial LV dyssynchrony in the early phase after myocardial infarction and to evaluate the effect on survival.

CONTRAST ECHOCARDIOGRAPHY

Initially, clinical use of contrast echocardiography was directed to detection of intracardiac shunts. Nowadays, the use of intravenous contrast in combination with echocardiography is increasingly applied and is of prognostic importance in patients with acute myocardial infarction. In those patients, contrast echocardiography can be used to improve endocardial border detection for better assessment of global and regional systolic LV function and to identify LV thrombi (Figure 10). Furthermore, myocardial contrast echocardiography enables evaluation of myocardial perfusion and microvascular integrity (and thus myocardial viability), providing valuable information about myocardial viability which is important for clinical outcome after acute myocardial infarction.

Because of recent safety considerations, the possible interaction between ultrasound and tissue has received much attention (36,37). Recently, the Food and Drug Administration (FDA) has declared that echo contrast agents should not be administered in patients with unstable

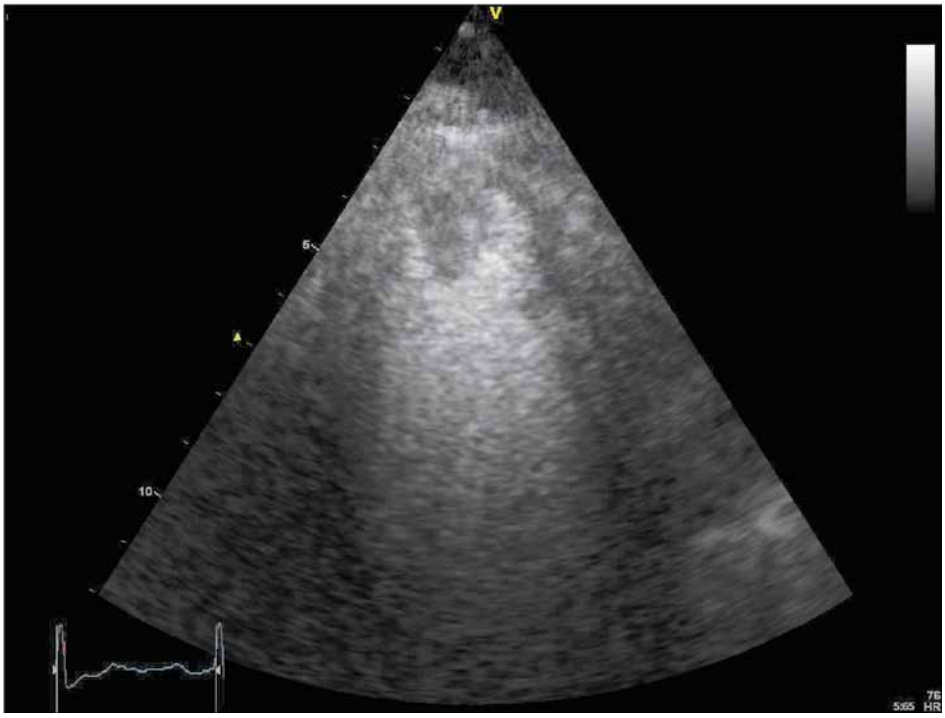

Figure 10. Example of the use of myocardial contrast echocardiography for better detection of LV thrombus after acute myocardial infarction. This patient had a recent anterior myocardial infarction with apical involvement. The echocardiographic images (2-chamber view) are suboptimal due to limited acoustic window; the presence of an LV thrombus was suspected. With the use of intravenous contrast the presence of the thrombus was confirmed. LV: left ventricular.

coronary disease in view of deaths observed in such patients in post-marketing surveillance. However, more recently, the FDA recalled this so called black box warning (38). It seems that the usefulness of contrast echocardiography in ST-segment elevation myocardial infarction is such that the benefit far outweighs the potential risk certainly in comparison with other competing techniques. In fact, large-scale phase III studies of more than 1,700 patients leading to product approval revealed no safety concerns (39,40). Furthermore, no adverse events have been reported in large human studies performed in patients with ST-segment elevation myocardial infarction. Recently, Kusnetzky et al. retrospectively analyzed 18,671 hospitalized patients undergoing clinically indicated echocardiography (41). Of those patients who underwent echocardiography without the use of intravenous contrast, 46 died within 24 hours (0.37%). Of patients receiving intravenous contrast, 26 died within 24 hours (0.42%, p=0.60). No patient died within 1 hour of echocardiography. More specifically, Nucifora et al. recently studied the safety of contrast echocardiography in 115 consecutive patients within 24 hours after ST-segment elevation acute myocardial infarction. All patients were admitted to the coronary care unit and underwent clinically indicated contrast echocardiography to assess LV size, shape and function,

but also to exclude thrombus formation. Administration of intravenous contrast did not lead to any significant change in vital signs, nor were abnormalities on physical examination or on the ECG detected. No major adverse events occurred and only minor events (hypersensitivity at the injection site and transient back pain) were observed in 4% of patients (42).

Endocardial border detection

The use of contrast echocardiography for opacification of the LV cavity enhances endocardial border delineation, thereby decreasing the variability in the assessment of LV volumes and LVEF, and improving the interpretation of regional wall motion abnormalities (43-47). Malm et al. evaluated the accuracy and reproducibility of contrast echocardiography versus tissue harmonic imaging for measurements of LV volumes and LVEF in 110 consecutive patients; MRI was used as an independent gold standard (43). A volume underestimation by echo was described, which was less pronounced when contrast was used. Limits of agreement between echo and MRI for assessment of LV volumes and LVEF narrowed significantly with the use of echo contrast (Figure 11).

Reilly et al. examined the value of contrast echocardiography in the assessment of LV wall motion in 70 intensive care unit patients, with a poor acoustic window (47). Wall motion (16-segment model) was evaluated on standard echocardiography, harmonic echocardiography, and after intravenous contrast administration. Uninterpretable wall motion was present in 5.4 segments/patient on standard echocardiography, 4.4 on harmonic echocardiography ($p=0.2$), and 1.1 on contrast echocardiography ($p<0.0001$). An average of 7.8 segments were read with surety on standard echocardiography, 9.2 on harmonic echocardiography ($p=0.1$), and 13.7 on contrast echocardiography ($p<0.0001$). Therefore, particularly in patients with a poor acoustic

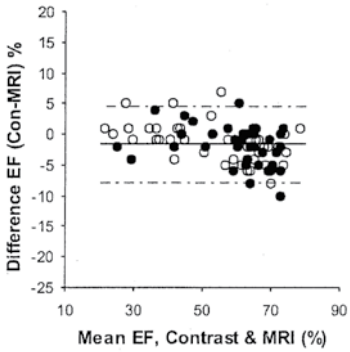

Figure 11. Bland-Altman diagram for assessment of LVEF, demonstrating mean difference (solid lines) and limits of agreement (dashed lines) between contrast echocardiography and MRI. Limits of agreement between echo and MRI for assessment of LVEF narrowed significantly when intravenous contrast was used. Closed circles indicate poor baseline image quality (n=36) and open circles indicate good baseline image quality (n=51). LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging. Reprinted from Malm et al. (43) with permission.

window, contrast echocardiography appears to have incremental value for assessment of LV function and wall motion.

Assessment of myocardial perfusion (viability)

Besides improved endocardial border detection and identification of LV thrombi, myocardial contrast echocardiography allows non-invasive evaluation of myocardial perfusion and microvascular integrity (viability). Initial animal studies demonstrated the feasibility of assessment of perfusion defects with contrast echocardiography (48-51). Cheirif et al. studied 15 open chest dogs after transient coronary artery occlusion, and detected perfusion defects on contrast echocardiography in 14 dogs (48). Good agreement between contrast echocardiography and nuclear imaging with thallium-201 was shown for detection and sizing of perfusion defects ($r=0.58$, $p<0.03$). Moreover, the extent of perfusion defects on contrast echocardiography correlated with post-mortem histology. The authors concluded that myocardial contrast echocardiography can be used to visualize and quantify the amount of myocardium at risk during coronary occlusion.

Kaul et al. studied 30 patients with known or suspected coronary artery disease who underwent myocardial contrast echocardiography and technetium-99m sestamibi SPECT (52). Agreement between the 2 techniques was 92% on a segmental basis, 90% on a vascular territory basis, and 86% on a patient basis. Meza et al. subsequently performed a head-to-head comparison between contrast echocardiography and technetium-99m sestamibi SPECT imaging in 41 patients referred for coronary angiography (50). The overall agreement for detection of perfusion defects was 78% on a patient basis, and a good correlation for defect size between both techniques was noted ($r=0.62$, $p<0.001$; Figure 12).

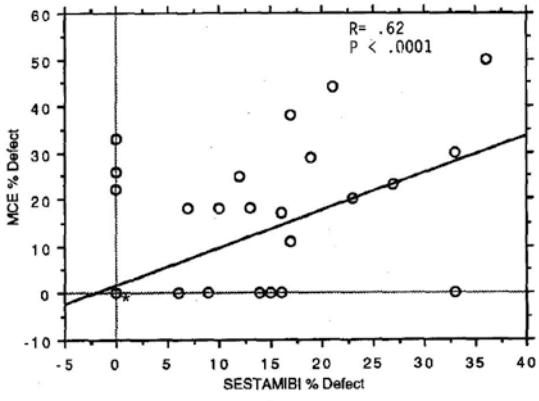

Figure 12. Relation between perfusion defect size on contrast echocardiography and technetium-99m sestamibi SPECT. A good correlation for perfusion defect size between both techniques was observed ($r=0.62$, $p<0.001$). MCE: myocardial contrast echocardiography; SPECT: single photon emission computed tomography. Reprinted from Meza et al. (50) with permission.

Prediction of functional recovery after acute myocardial infarction

The extent and severity of perfusion defects after acute myocardial infarction have been shown to correlate (inversely) with the likelihood of functional recovery at follow-up (36,53-55). Patients with large perfusion defects (indicating non-viable tissue) appear to have a low likelihood of functional recovery after acute myocardial infarction, whereas dysfunctional regions with preserved perfusion (indicating viable myocardium) frequently exhibit improvement of function during follow-up (Figure 13) (36,53). Main et al. studied 34 patients with recent acute myocardial infarction (54). Two days after myocardial infarction, patients underwent resting 2D echocardiography to assess wall motion, followed by contrast echocardiography to assess perfusion; 2 months later recovery of function was evaluated. Ninety percent of dysfunctional segments with preserved perfusion improved in function at follow-up.

In addition, Janardhanan et al. demonstrated that myocardial contrast echocardiography is able to predict functional recovery after reperfusion therapy for acute myocardial infarction (56). Fifty patients underwent myocardial contrast echocardiography 7 to 10 days after acute myocardial infarction. Myocardial perfusion, wall thickening and wall thickening index (scores

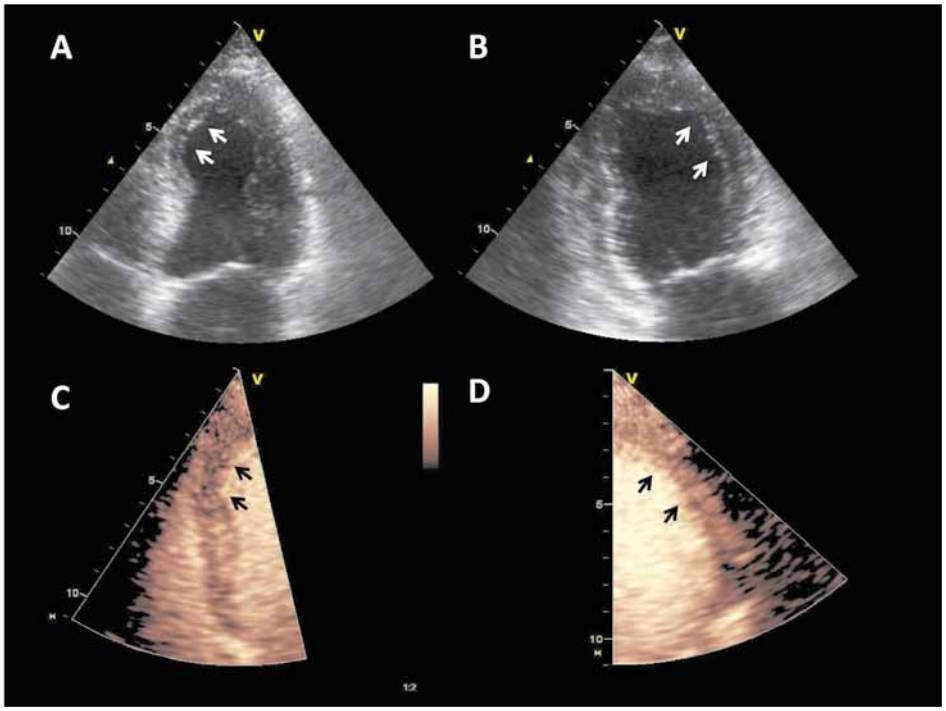

Figure 13. Example of a patient with acute anterior myocardial infarction. On standard 2D echocardiography the apical part of the septum *(panel A)* and the mid and apical parts of the anterior wall *(panel B)* are akinetic. Myocardial contrast echocardiography revealed normal perfusion of both the septum *(panel C)* and the anterior wall *(panel D)*. At 6-month follow-up, functional recovery of these akinetic segments was observed.

of all segments divided by the number of segments, marker of global LV function) were assessed at baseline. Wall thickening and systolic wall thickening index were re-assessed at 3-month follow-up. Improvement in function was observed in 84% with preserved perfusion, whereas 93% of segments with perfusion defects did not recover in function ($p<0.05$). Moreover, the extent of LV myocardium with preserved perfusion was related to global LV function at 3 months ($r=-0.91$, $p<0.001$). Multivariate analysis demonstrated that the findings on contrast echocardiography contributed independently to the prediction of functional recovery.

Ito and colleagues studied 39 patients with acute anterior myocardial infarction who were treated with primary PCI (57). Myocardial contrast echocardiography was performed immediately after successful PCI. LVEF was measured sequentially at 1 day and 1 month after PCI. Myocardial contrast echocardiography showed preserved perfusion of the infarct-related segments in 30 (77%) patients. The remaining 9 patients (23%), however, showed impaired perfusion in the infarct zone. The baseline LVEF was higher in the patients with preserved perfusion; during follow-up, the improvement in LVEF was significantly larger in the patients with preserved perfusion (from 42.3 ± 11.0% at baseline to 56.4 ± 13.4% at follow-up, $p<0.001$) compared to patients with reduced/absent perfusion (from 34.7 ± 8.9% at baseline to 42.7 ± 8.9% at follow-up, p=NS). Myocardial contrast echocardiography demonstrated that the extent of perfusion defects after successful PCI is predictive for global functional recovery in patients with acute myocardial infarction. Pooled analyses of 23 previously published studies (with more than 1,100 patients) showed high sensitivity (approximately 85%) but lower specificity (approximately 74%) of myocardial contrast echocardiography to predict recovery of regional and/or global function after acute myocardial infarction (36,53).

The extent and severity of myocardial perfusion defects (non-viable myocardium) after acute myocardial infarction are also related to the development of LV dilatation (remodeling) over time (58-62). In the Acute Myocardial Infarction Contrast Imaging (AMICI) study, Galiuto and coworkers evaluated 110 patients with first successfully reperfused ST-segment elevation myocardial infarction (61). After primary PCI, peak creatine kinase, ST-segment resolution, TIMI flow grade and myocardial blush grade (on angiography) were assessed. Perfusion defects (non-viable tissue) were evaluated with myocardial contrast echocardiography on day 1 after reperfusion. WMSI, the extent of wall motion abnormalities, LVEDV, and LVEF were assessed after reperfusion and at 6-month follow-up. Over that 6-month period, 27 (25%) patients developed LV remodeling. At multivariate analysis, only TIMI flow grade <3 and the extent of perfusion defects on contrast echocardiography were independently associated with LV remodeling (Figure 14). Main et al. studied 50 patients with recent anterior wall myocardial infarction and regional akinesia (63). All patients underwent myocardial contrast echocardiography 2 days after myocardial infarction. At 6-month follow-up, LV remodeling (defined as an increase >15% in LVEDV index) occurred in 19 patients (38%). Both the transmural extent of infarction and the number of abnormally perfused segments predicted LV remodeling; all patients with >5 myocardial segments with reduced perfusion exhibited LV remodeling.

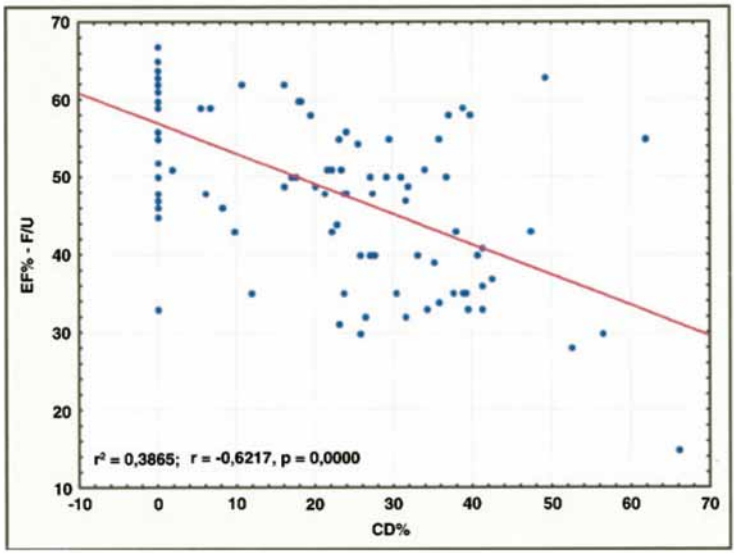

Figure 14. Correlation between the extent of perfusion defects and LVEF at follow-up. On the X-axis the extent of the perfusion defect (expressed as the length of the contrast defect [CD]) assessed with myocardial contrast echocardiography on day 1 after reperfusion is provided. The Y-axis provides the LVEF at follow-up. A strong relation was observed between both parameters. LVEF: left ventricular ejection fraction. Reprinted from Galiuto et al. (61) with permission.

Prognostic value after acute myocardial infarction

The prognostic value of contrast echocardiography after acute myocardial infarction has been addressed in various studies. Reduced myocardial perfusion (scar tissue, but also no-reflow after acute myocardial infarction) is associated with poor outcome (64-67).

Khumri and colleagues demonstrated that patients with first anterior myocardial infarction are at high risk of death during long-term follow-up in the presence of abnormal perfusion (Figure 15) (65). The authors evaluated 167 patients with anterior acute myocardial infarction with contrast echocardiography 2 days after admission, and a perfusion score index was calculated; mean follow-up was 39 months. The perfusion score index was a strong predictor of mortality (odds ratio 3.2 for each 1.0 increase in perfusion score index, p=0.04) and provided incremental value over clinical and angiographic variables.

The prognostic value of myocardial contrast echocardiography was further addressed by Dwivedi et al. (66) who investigated 95 stable patients with contrast echocardiography at 7 ± 2 days after acute myocardial infarction. During follow-up of 46 ± 16 months, there were 15 (16%) events (8 cardiac deaths and 7 non-fatal acute myocardial infarctions). Among the clinical, biochemical, electrocardiographic, echocardiographic, and coronary angiographic markers of prognosis, the contrast echo results were independently predictive of cardiac death (p=0.01) and cardiac death or acute myocardial infarction (p=0.002). Similarly, Sakuma et al. evaluated 50 patients with first myocardial infarction and thrombolytic therapy, using contrast

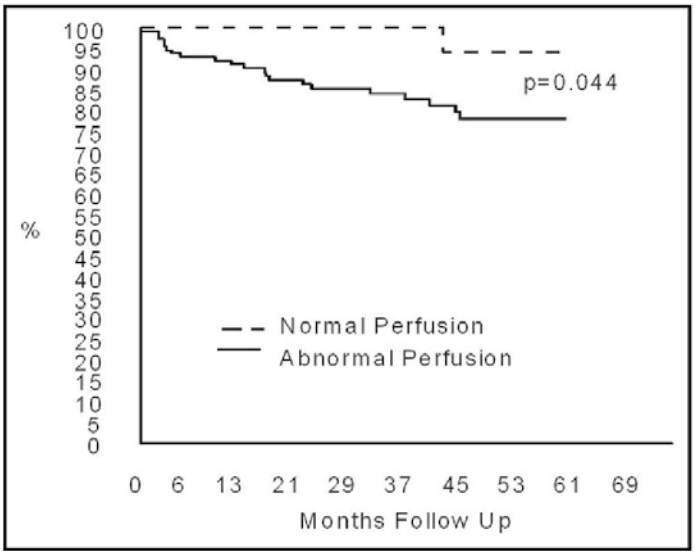

Figure 15. Kaplan-Meier curve showing event-free survival for the combined end point of death and new-onset heart failure in patients with normal perfusion (dashed line) or abnormal perfusion (solid line) on contrast echocardiography. Patients with abnormal perfusion had a lower survival as compared to those patients with normal perfusion during follow-up after acute myocardial infarction. Reprinted from Khumri et al. (65) with permission.

echocardiography on day 2 post-infarction. The presence of reduced perfusion on myocardial contrast echocardiography, was predictive of major cardiac events (death, nonfatal myocardial infarction, or admission for heart failure) during a mean follow-up of 22 months (event rate 28% in patients with reduced perfusion versus 4% in those with preserved perfusion, $p<0.05$) (67).

OTHER ECHOCARDIOGRAPHIC TECHNIQUES

Stress echocardiography

In patients with acute myocardial infarction, stress (exercise or pharmacologic) echocardiography can be used to assess ischemia and viability. Worsening of wall motion during high-dose dobutamine infusion is related to the presence of ischemia, whereas improvement of wall motion during low-dose dobutamine infusion (contractile reserve) indicates the presence of viable (stunned) myocardium. Extensive reviews have been previously published on the prognostic value of stress echocardiography (68,69).

Picano et al. studied the value of dipyridamole stress echocardiography in predicting re-infarction in 1,080 patients assessed early (10 ± 5 days) after uncomplicated acute myocardial infarction. Patients were followed for 14 ± 10 months. The results of stress echocardiography were positive for ischemia in 475 patients (44%). During follow-up, re-infarction occurred in 30

patients with positive and 20 with negative results (6.3% versus 3.3%, p<0.01). Re-infarction was fatal in 5 of 30 patients with positive and in none of 20 with negative results (16.6% versus 0%, p=0.07). Therefore, it was concluded that dipyridamole stress echocardiographic positivity identifies patients at higher risk of re-infarction, especially fatal re-infarction, early after acute myocardial infarction (70).

Next, Sicari et al. assessed the value of stress-induced ischemia early after infarction (12 ± 5 days) using dobutamine-atropine stress echocardiography in 778 patients. Dobutamine-atropine stress echocardiographic findings were positive for myocardial ischemia in 436 of patients (56%) and negative in 342 (44%). During follow-up (9 ± 7 months), there were 14 cardiac-related deaths (1.8% of the total cohort), 24 (2.9%) non-fatal myocardial infarctions and 63 (8%) hospital re-admissions for unstable angina. One hundred seventy-four patients (22%) underwent coronary revascularization (PCI or coronary artery bypass grafting). Spontaneous events occurred in 61 of 436 patients with positive and 40 of 342 patients with negative findings on dobutamine-atropine stress echocardiography (14% versus 12%, p=0.3). When only hard cardiac events were considered, age was the strongest predictor (chi-square 3.6, p=0.056), followed by WMSI at peak dose (chi-square 3.3, p=0.06) and remote ischemia (chi-square 2.25, p=0.1). When cardiac death was considered, WMSI at peak dose was the best predictor (hazard ratio 9.2, p<0.0001) (71).

Bigi et al. evaluated the prognostic value of dobutamine stress echocardiography performed in the early post-infarction period; 406 patients underwent dobutamine stress echocardiography within 10 days of uncomplicated myocardial infarction and were prospectively followed for almost 9 months. The change in WMSI between rest and stress (p<0.001) was an independent predictor for cardiac events (72).

Pierard et al. were among the first to use low-dose dobutamine echocardiography to detect the presence of contractile reserve indicative of stunned, viable myocardium. The authors showed that patients with contractile reserve after acute myocardial infarction exhibited spontaneous improvement in function (73).

Picano and coworkers evaluated the prognostic value of residual viability, as assessed by low-high dobutamine stress echocardiography performed at 12 ± 6 days after acute myocardial infarction, in 314 patients (mean age 58 ± 9 years) with global LV dysfunction (74). Over a mean follow-up of 9 ± 7 months there were 12 cardiac deaths (3.8%). The presence of myocardial viability was related to good outcome, whereas the presence of ischemia was related to poor outcome.

In addition, Swinburn et al. evaluated 212 patients who underwent dobutamine stress echocardiography at a mean of 4.8 ± 1.5 days after acute myocardial infarction (75). Viability in the infarct zone was detected by low-dose dobutamine echocardiography in 44% of patients. During follow-up (803 ± 297 days), 27 (13%) patients died and 16 (8%) experienced a non-fatal re-infarction. Independent predictors of both mortality and combined mortality and non-fatal acute myocardial infarction were age, resting LV function and the absence of viability (Figure 16).

In general, the presence of ischemia on dobutamine stress echocardiography is associated with poor outcome when patients are treated conservatively; patients with viability however have good outcome which is possibly related with the presence of stunned myocardium, which improves spontaneously in function after acute myocardial infarction.

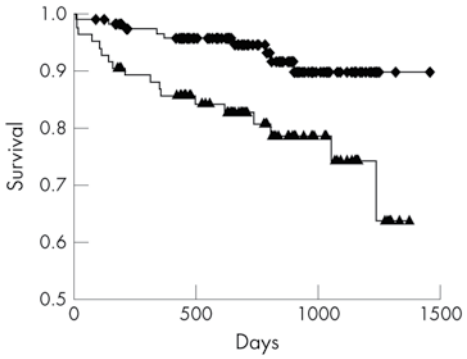

Figure 16. Kaplan-Meier curves demonstrating the impact on mortality of a WMSI at low-dose dobutamine of ≤1.6 (diamonds) compared with a score of >1.6 (triangles). Survival was higher in patients with WMSI ≤1.6 compared to those with WMSI >1.6 (p=0.005). WMSI: wall motion score index. Reprinted from Swinburn et al. (75) with permission.

Coronary flow reserve

Advances in color Doppler technology permit assessment of flow (and flow reserve, CFR) in the coronary arteries, particularly in the left anterior descending coronary artery (76,77). Coronary flow reserve was defined as the ratio between the hyperemic diastolic flow velocity (after intravenous adenosine infusion) and the resting diastolic flow velocity (78).

Voci and colleagues demonstrated the feasibility of transthoracic Doppler echocardiography for assessment of CFR in both the left anterior descending and posterior descending coronary arteries in 44 subjects with varying degrees of coronary artery disease (79). Based on coronary angiography, patients were divided into 3 groups: group 1 (0% to 29% stenosis), group 2 (30% to 69% stenosis), and group 3 (≥70% stenosis). Mean CFR of the left anterior descending coronary artery was 3.31 ± 0.54 in group 1 (n=15), 2.49 ± 0.71 in group 2 (n=10), and 1.12 ± 0.49 in group 3 (n=19, p<0.0001). CFR of the posterior descending coronary artery was 2.62 ± 0.25 in group 1 (n=17), 2.33 ± 0.32 in group 2 (n=9), and 1.40 ± 0.54 in group 3 (n=18, p<0.0001). A cutoff value for CFR <2 identified ≥70% stenosis in both the left anterior descending and posterior descending coronary arteries. Pizzuto et al. used transthoracic Doppler echocardiography during venous adenosine infusion to measure CFR of the left anterior descending coronary artery in 45 patients before and 3.7 ± 2.0 days after successful PCI, as well as in 25 subjects with an angiographically normal left anterior descending coronary artery

(control group) (78). CFR before PCI was significantly lower in patients than in control subjects (1.45 ± 0.50 versus 2.72 ± 0.71, p<0.01) and increased towards the normal range after PCI (2.58 ± 0.70 versus 2.72 ± 0.75, p=NS).

Rigo et al. assessed the prognostic value of CFR in patients with known or suspected coronary artery disease and negative stress echocardiography (80). All 329 patients underwent dipyridamole stress echocardiography with CFR evaluation of the left anterior descending coronary artery. During follow-up (28 ± 10 months), 22 events occurred: 1 cardiac death, 6 non-fatal infarctions, 5 patients with unstable angina, and 10 late (>6 months) coronary revascularizations. CFR ≤1.92 was the best predictor of future events (77% sensitivity, 85% specificity) and was used as criterium for reduced CFR accordingly. Sixty-three (19%) patients had reduced and 266 (81%) had normal CFR of the left anterior descending coronary artery. The 36 months event-free survival was higher in patients with normal and lower in patients with reduced CFR (98% versus 64%, p<0.0001, Figure 17). CFR of the left anterior descending coronary artery provided additional prognostic information over clinical, resting echo, and angiographic findings. Therefore, in patients with known or suspected coronary artery disease and negative stress echocardiography by wall motion criteria, CFR provides independent information for prognostic stratification. A reduced CFR is associated with worse long-term outcome.

These results were recently confirmed by the same authors in a prospective, multicenter, observational study (81). The authors evaluated 1,145 patients who underwent high-dose dipyridamole stress echocardiography with assessment of CFR of the left anterior descending coronary artery. Stress echocardiography was positive for regional wall motion abnormalities

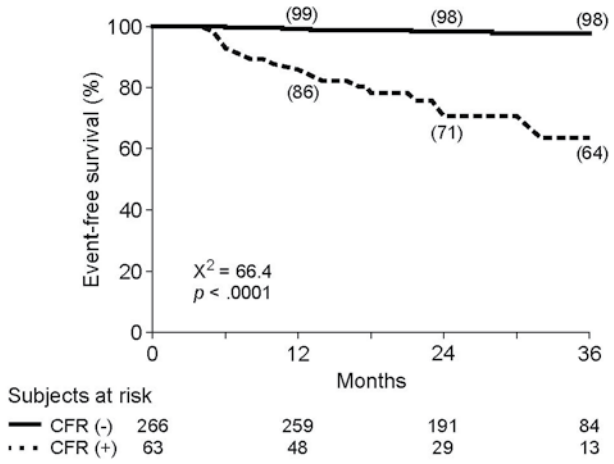

Figure 17. Kaplan-Meier event-free survival curves illustrating the group with preserved (CFR-, solid line) and reduced CFR (CFR+, dotted line). Number of patients examined each year is shown. The 36-month event-free survival was higher in patients with preserved CFR and lower in patients with reduced CFR (98% versus 64%, p<0.0001). Reprinted from Rigo et al. (80) with permission.

in 291 (25%) and negative in 854 (74%) patients. Mean CFR was 2.2 ± 0.5. At individual patient analysis, 702 patients had normal (CFR >2.0) and 443 had abnormal CFR of the left anterior descending coronary artery. During a median follow-up of 27 months, 109 events occurred: 16 deaths, 17 non-fatal infarctions and 76 re-hospitalizations for unstable angina. At multivariable analysis, CFR of the left anterior descending coronary artery (hazard ratio 2.4, p=0.030) and stress echocardiography positivity for regional wall motion abnormalities (hazard ratio 3.6, p=0.000) were independent prognostic predictors of cardiac events.

Few data is available about the value of CFR in patients early after acute myocardial infarction. However, CFR of the left anterior descending artery in patients with acute myocardial infarction has been associated with long-term viability of the jeopardized myocardium. Ueno et al. studied 29 patients with acute anterior myocardial infarction who underwent successful PCI (82). Transthoracic Doppler echocardiography was used to quantify coronary flow velocities in the distal left anterior descending artery at rest and after adenosine triphosphate. Coronary flow velocity reserve was calculated immediately and 24 hours after revascularization. Regional wall motion was analyzed to calculate the anterior WMSI before revascularization and at discharge (20 ± 4 days after infarction). Coronary flow velocity reserve immediately and 24 hours after revascularization correlated significantly with anterior WMSI at discharge (r=-0.58, p<0.001, and r=-0.80, p<0.0001, respectively). The optimal cutoff ratio for predicting viable myocardium was 1.5 for coronary flow velocity reserve 24 hours after revascularization yielding a sensitivity of 94% and specificity of 91%.

In a study by Saraste and coworkers, 15 patients with a first acute anterior myocardial infarction who underwent successful PCI were analyzed (83). Coronary flow velocity was measured from the mid left anterior descending artery 3 days after PCI. Myocardial viability of the region of the left anterior descending artery was quantified 3 months after acute myocardial infarction using F18-fluorodeoxyglucose and positron emission tomography. Diastolic deceleration time of left anterior descending artery flow velocity correlated with myocardial viability on positron emission tomography in the region of the left anterior descending artery; a diastolic deceleration time <190 ms was always related with non-viable myocardium.

Montisci et al. tested whether preserved CFR 2 days after reperfused acute myocardial infarction is predictive of myocardial viability (84). The authors assessed CFR in the left anterior descending coronary artery in 24 patients with acute anterior myocardial infarction. Low-dose dobutamine echocardiography was performed 6 ± 3 days after acute myocardial infarction and follow-up echocardiography at 3 months. An inverse correlation was found between CFR and anterior WMSI at dobutamine and follow-up echocardiography (r=-0.49, p=0.016, and r=-0.55, p=0.005, respectively). The authors concluded that CFR early after acute myocardial infarction is correlated with myocardial viability at follow-up.

Accordingly, noninvasive measurement of CFR has been shown to provide important prognostic information both in patients with stable coronary artery disease and in patients with acute myocardial infarction.

Three-dimensional echocardiography

The use of 3D echocardiography in clinical cardiology has increased over the recent years, particularly for the assessment of LV volumes and LVEF (85). Particularly in patients with myocardial infarction, the LV shape can be distorted and 3D echocardiography provides superior information on LV volumes and LVEF.

Jenkins et al. studied 50 patients (mean age 64 ± 8 years) presenting for evaluation of LV function with 2D echocardiography, 3D echocardiography and MRI as the gold standard (86). The average LVEDV by MRI was 172 ± 53 ml. LVEDV was underestimated by 2D echocardiography (mean difference -54 ± 33 ml; $p<0.01$) but only slightly by 3D echocardiography (-4 ± 29 ml; $p=0.31$). Similarly, LVESV by MRI (91 ± 53 ml) was underestimated by 2D echocardiography (mean difference -28 ± 28 ml; $p<0.01$) and by 3D echocardiography (mean difference -3 ± 18 ml; $p=0.23$). LVEF by MRI was similar by 2D echocardiography ($p=0.76$) and 3D echocardiography ($p=0.74$).

Preliminary data have shown the use of 3D echocardiography for prediction of LV dilatation after acute myocardial infarction. Mannaerts et al. evaluated 33 acute myocardial infarction patients with 3D echocardiography at baseline (6 ± 4 days after myocardial infarction) and at 6 and 12 months follow-up. LV remodeling was defined as an increase in LVEDV by 20% or more at 6- or 12-month follow-up. The sphericity index derived from 3D echocardiography (LVEDV divided by the volume of a sphere whose diameter is the LV end-diastolic long-axis) was the best predictor for LV dilatation (Figure 18) (87).

Li and colleagues evaluated 62 acute myocardial infarction patients with 3D echocardiography at baseline (72 ± 5 hours after myocardial infarction) and 6 months later (88). LV remodeling was defined as a 20% increase in LVEDV from baseline to 6-month follow-up. The LV conic index (LVEDV divided by the volume of a cone whose bottom diameter is the internal diameter of the mitral annulus and height is the LV long-axis) at baseline appeared the best predictor of LV remodeling.

CONCLUSION

In clinical practice, echocardiography has become an important component in the evaluation of patients with acute myocardial infarction. Various parameters derived from 2D echocardiography have been demonstrated to provide prognostic information, including LV volumes, LVEF, WMSI, and E/E' ratio. These parameters focus on LV function, but additional information on cardiac performance such as mitral regurgitation, LA size, and RV function is also important for prognostification. This has been confirmed in several large clinical studies. Moreover, novel technology including strain (rate) imaging based on TDI and speckle-tracking can also provide prognostic information; particularly the prognostic value of LV dyssynchrony appears of interest. These more sophisticated parameters appear promising, but thus far only small patient

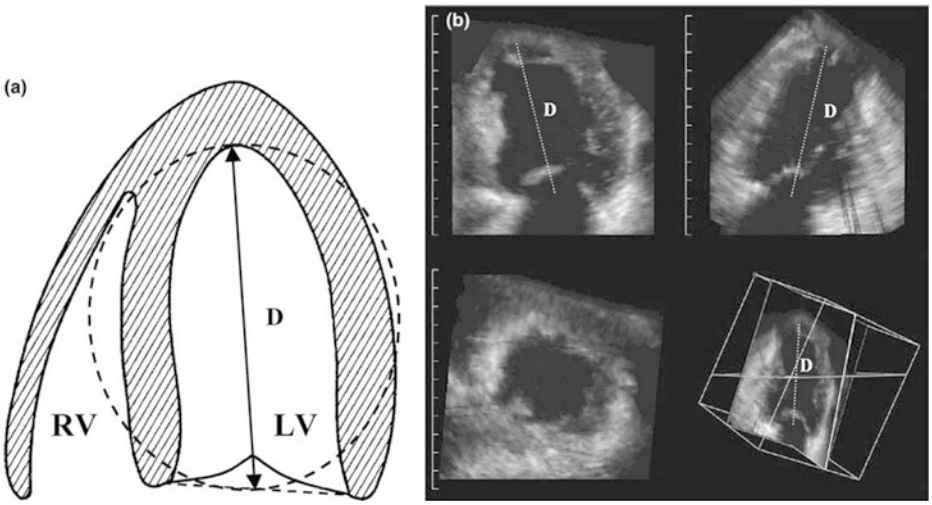

Figure 18. Schematic overview of the 3D sphericity index *(panel A)*. The LV cavity is shown with *D* as the LV end-diastolic major long-axis. Overview of the dynamic 3D dataset with 2 near perpendicular long axes *(panel B, top)*, a short-axis *(panel B, lower left)*, and a cubical display with corresponding cutplanes *(panel B, lower right)*. The measurement of *D* is shown. LV: left ventricular. Reprinted from Mannaerts et al. (87) with permission.

cohorts were reported, and surrogate end points such as LV remodeling were used, rather than long-term survival; accordingly long-term outcome studies in large patient cohorts are needed to confirm the initial findings.

Contrast echocardiography is able to improve endocardial border detection, including optimized detection of LV thrombus. In addition, contrast echocardiography provides information on myocardial perfusion; dysfunctional segments with reduced/absent perfusion relate to scar tissue, whereas dysfunctional segments with perfusion are viable. Based on this information, contrast echocardiography permits prediction of functional recovery after myocardial infarction, and identifies patients with a high likelihood of LV dilatation after myocardial infarction. This information may guide the clinician in therapeutic decision making. Moreover, contrast echocardiography (based on identification of scar tissue and viable myocardium) provides important prognostic information, and various studies have shown that patients with large perfusion defects after myocardial infarction have poor outcome.

Stress echocardiography can be used after acute myocardial infarction to detect residual ischemia, which is associated with poor outcome if treated conservatively; viability (contractile reserve) can also be assessed, and is associated with spontaneous recovery of function and good outcome. Various studies have employed Doppler imaging of the coronary arteries, yielding flow velocities and flow reserve; preserved flow reserve portends good outcome, whereas outcome is poor when flow reserve is reduced. 3D Echocardiography has not been used much

after acute myocardial infarction, but yields excellent information on LV volumes, LVEF and LV sphericity indices, which may predict future LV dilatation.

In conclusion, echocardiography provides strong prognostic information in patients with recent myocardial infarction and should be integrated in the routine evaluation of these patients.

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