Echocardiographic assessment of the incidence of mechanical complications during the early phase of myocardial infarction in the reperfusion era: a French multicentre prospective registry

Evaluation échocardiographique de l’incidence des complications mécaniques à la phase aiguë d’un infarctus du myocarde à l’ère de la reperfusion


a Département de cardiologie, Hôpital Henri Mondor (AP-HP), Créteil, France.
b Département de cardiologie, Hôpital du Bon Secours, Metz, France.
c Département de cardiologie, Centre Hospitalier Universitaire du Morvan, Brest, France.
d Département de cardiologie, Centre Hospitalier Universitaire, Caen, France.
e Département de cardiologie, Centre Hospitalier Universitaire, Hôpital Nord, Saint Etienne, France.
f Département de cardiologie, Centre Hospitalier Universitaire de Rangueil, Toulouse, France.
g Département de cardiologie, Centre Hospitalier Universitaire Gabriel Montpied, Clermont-Ferrand, France.
i Département de cardiologie, Hôpital Cochin (AP-HP), Paris, France.

Summary
Background. — Since the early reports on the incidence of mechanical complications of acute myocardial infarction (AMI) assessed by echocardiography published in the 1980s, the management of patients with AMI has changed considerably, in particular with the progressive development of early revascularisation.

Methods. — The aim of this multicentre study was to assess the incidence of mechanical complications of AMI in the reperfusion era. Nine-hundred and eight consecutive patients were included. Echocardiography was performed on admission and at discharge. Seventy-eight percent of patients were revascularised at the acute phase.

Results. — The following incidence rates of mechanical complications were observed: mitral regurgitation 28%, secondary to left ventricular (LV) remodelling (43%) or papillary muscle dysfunction (57%); pericardial effusion 6.6%, more frequent after anterior AMI and associated...
with a lower ejection fraction (EF); LV thrombus 2.4%, mainly after anterior AMI and associated with a lower EF (38±10% vs. 48±12%; p<0.001); early infarct expansion 4%; septal rupture 0.6%; and acute free wall rupture 0.8%. The following factors were independently associated with the occurrence of mechanical complications by multivariate logistic regression analysis: lack of early revascularisation (OR 3.48, 95%CI 1.36-8.95; p<0.001), LV-EF <50% (OR 1.95, 95%CI 1.42-2.67; p<0.001), Killip class >II (OR 1.91, 95%CI 1.27-2.87; p<0.002) and age ≥70 years (OR 1.42, 95%CI 1.03-1.97; p=0.03).

Conclusion. — This study demonstrates the favourable prognostic influence of early revascularisation as shown by the low incidence of mechanical complications after AMI, and underlines the persistent relationship between the development of these complications and depressed LV function.

© 2008 Published by Elsevier Masson SAS.

Over the past two decades, the widespread availability of echocardiography in coronary care units (CCUs) has had a major impact on the early diagnosis of mechanical complications of acute myocardial infarction (AMI). The ability of echocardiography to detect these complications, in particular those that cause haemodynamic instability, has largely obviated the need for cardiac catheterisation.

The majority of prospective studies of echocardiography investigating the incidence of complications including pericardial effusion (1,2), left ventricular (LV) thrombus (3-5) and mitral regurgitation (6-8) were performed in the 1980s. A detailed description of echo Doppler signs of septal and free wall ruptures was published during the same period (9-15). However, as these complications are rare no longitudinal echo studies have been performed to assess their incidence.

Since the 1980s, the management of patients with AMI has changed considerably, in particular with the progressive development of early revascularisation by thrombolysis and/or primary coronary angioplasty, contributing to the preservation of LV function and hopefully to a decrease in incidence of these complications. Furthermore, the technical characteristics of Doppler echocardiographic machines has also improved dramatically (wide band transducers, harmonic imaging, etc), yielding better quality images and increasing diagnostic accuracy.

The aim of this prospective study was to assess the current incidence of complications of AMI, in the reperfusion era, using modern echocardiographic technology. The study cohort consisted of consecutive patients admitted to a CCU with a ST-segment elevation AMI.

Methods

Study population

All consecutive patients with AMI admitted to the CCU of the participating centres between April 1 and June 30, 2004, were included in this prospective study. Fifty-five
French hospital centres took part (30 academic and 25 general hospitals or private clinics) in the study.

AMI diagnosis was based on established criteria: 1) elevated serum markers of myocardial necrosis greater than twice the upper limit for creatine kinase or troponins; and 2) symptoms compatible with AMI for ≥30 min and/or electrocardiographic changes on at least two contiguous leads with a pathological Q wave (>0.04 sec) and/or persistent ST elevation ≤0.1 mV.

Cardiovascular history, risk factors, in-hospital clinical course including Killip class and initial therapeutic management (revascularisation by thrombolysis and/or coronary angioplasty) were recorded for each patient.

**Echocardiographic evaluation**

Since the majority of mechanical complications usually occur within the first week after an acute event, echocardiographic studies were performed at the bedside for all patients as soon as possible after admission to the CCU (median 4 h after the onset of symptoms) and at the end of the hospitalisation period (median 6 days). Echocardiograms were obtained using various recent ultrasound systems all equipped with harmonic imaging and Doppler modalities including colour flow imaging. Images were obtained in the standard transthoracic parasternal long- and short-axis, apical and subcostal views, as well as in unconventional views produced by angulation of the transducer on- and off-axis to visualise any potential abnormalities when indicated. Image quality was classified as good, fair or poor by the investigators.

LV ejection fraction (EF) was calculated using the 2D echo biplane or single plane modified Simpson’s rule, or estimated visually whenever image quality impeded accurate calculation.

Echocardiography was aimed at detecting the following mechanical complications of AMI: mitral regurgitation (quantification and mechanism), pericardial effusion (location, abundance and tolerance), LV thrombus (location and morphology), wall ruptures (septal and/or free wall rupture) and early infarct expansion.

The diagnosis of mitral regurgitation was based on the presence of regurgitation demonstrated by colour flow Doppler echocardiography. Mitral regurgitation severity was evaluated semi-quantitatively from the area of the regurgitant jet by colour Doppler (16). Regurgitation was classified as absent, trivial, mild, moderate or severe, and was considered as ischaemic regurgitation when the mitral valve was anatomically normal and regurgitation was secondary to LV abnormalities (papillary muscle rupture, chordal rupture, papillary muscle asynergy, LV remodelling).

The echocardiographic diagnosis of pericardial effusion required the presence of an echo-free space posterior to the left ventricle on the parasternal long and short-axis views throughout the cardiac cycle. Effusion was classified as mild/moderate or large and circumferential. When pericardial effusion was demonstrated, echocardiography was performed to detect evidence of cardiac tamponade.

The diagnosis of LV thrombus was based on the presence of an echo dense mass contiguous but distinct from the endocardium, located in an area of advanced asynergy (akinesia or dyskinesia), that was seen in both systole and diastole in at least two echocardiographic views and, as a result of multiple sector orientations, was distinguishable from muscle trabeculations, chordal structures or false masses resulting from tangential views of the LV wall (17). The shape of the thrombus was classified as protruding or mural.

Infarct expansion was defined as an outward definite bulging and alteration in curvature of the LV infarcted segment with hinge points persistent during both systole and diastole (18).

The presence of ventricular septal rupture was identified either by interventricular septum discontinuity seen by 2D echocardiography and/or by flow disturbance seen as turbulent flow across the interventricular septum and exiting into the right ventricle during Doppler colour flow mapping. The site of the defect was classified as apical/anterior or posterior.

Acute LV free-wall rupture is recognised as one of the most common causes of mortality in AMI; diagnosis is most often made by the presence of sudden electromechanical dissociation followed by syncope and death impeding echocardiography. In some sub-acute forms, patients can survive for several hours allowing time for diagnosis and immediate surgical intervention. In the current study, the diagnosis was primarily based on the demonstration of a haemopericardium suggested by visualisation of a pericardial effusion with high acoustic echoes indicating the presence of clotted blood in the pericardial sac (19) and cardiac tamponade by echocardiography. Although the myocardial tear itself is rarely identified, infarct expansion, whenever associated, was shown to increase the specificity of echocardiography for wall rupture (20,21).

**Statistical analysis**

Time to admission (h) and time to 1st and 2nd echocardiograms (h and days, respectively) are expressed as median time with 25th and 75th percentiles. All other continuous variables are given as the mean±SD. Comparisons between groups were made by 1-way ANOVA, with the unpaired t-test for continuous variables and X² test for discrete variables. Multivariate stepwise logistic regression analysis was used to calculate the risk ratio (95% confidence intervals (CI)) and to identify the independent predictors of mechanical complications detected by echocardiography. Variables with a value of p<0.1 on univariate analysis were included in the model. For all tests, a value of p<0.05 was considered to be statistically significant. All analyses were performed using the SAS 8.2 statistical analysis programme.

**Results**

Nine-hundred and eight consecutive patients were included in the study. The baseline demographic and clinical characteristics of the study population are summarised in Table 1. Early revascularisation (<6 h) was performed successfully in 78% of patients.

With the use of modern echocardiography machines, image quality was considered to be good in 46%, fair in 41% and poor in 13% of cases by the investigator. The 1st and 2nd echo examinations were performed 4 h (1.00-6.00) and 6 days (3.00-8.00) after admission, respectively. Out of 902 patients, 749 (82%) underwent the two scheduled echocardiograms.

LV-EF was available in 97% of cases: the mean value at admission was 48±12% (median 50; 40-55). It was significantly
lower in patients with anterior AMI compared to those with inferior AMI (42±12% vs. 52±10%, respectively; p<0.0001).

The incidence of mechanical complications is summarised in Table 2. Mitral regurgitation was observed in 28% of patients (250/908): mainly trivial (67%) or mild (26%), and rarely moderate (4%) or severe (3%), secondary to LV remodelling after anterior AMI (43%) or to papillary muscle dysfunction after inferior AMI (57%, among them seven papillary muscle ruptures).

Pericardial effusion was observed in 6.6% (60/908) of patients: either moderate and inferior (72%) or large and circumferential (28%) (six cases of cardiac tamponade due to LV free wall rupture). Pericardial effusion was more frequent after anterior AMI (63%) than after inferior AMI (37%), and was significantly associated with a lower LV-EF (44±13% in the presence vs. 51±12% in the absence of pericardial effusion, respectively; p<0.004).

LV thrombus was detected in 2.4% (22/908, 10 protruding and 12 mural), located mainly in the antero apical region (21/22) and associated with a significantly lower LV-EF (38±10% vs. 48±12%, respectively; p<0.0001).

Early infarct expansion was seen in 4% of patients (37/908), more frequently after anterior AMI (29/37 cases) with a low LV-EF (37±13%) than after inferior AMI (8/37; LV-EF 51±12%).

Septal rupture was rare (0.6%, 5/908: three anterior and two posterior) as was acute free wall rupture (0.8%, 7/908).

After adjusting for clinical variables, univariate regression analysis identified six parameters associated with the development of mechanical complications (Table 3); multivariate logistic regression analysis showed that lack of early revascularisation, LV-EF at admission <50%, Killip class at admission >II and age ≥70 years were independently associated with the occurrence of at least one mechanical complication (Table 4).

Discussion

The present study was carried out to assess the current incidence of mechanical complications of AMI, detected by echocardiography, in the reperfusion era. The principal findings of this analysis are: 1) the favourable prognostic influence of early revascularisation as shown by a low inci-

Table 1 Baseline demographic and clinical characteristics of the study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AMI (n = 908)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 ± 14</td>
</tr>
<tr>
<td>Males</td>
<td>77%</td>
</tr>
<tr>
<td>Previously treated hypertension</td>
<td>32%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17%</td>
</tr>
<tr>
<td>Time to admission (h)</td>
<td>4 (3.00-9.00)</td>
</tr>
<tr>
<td>First AMI</td>
<td>91%</td>
</tr>
<tr>
<td>Infarct location (anterior/inferior)</td>
<td>44% / 47%</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>48±12%</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>Performed during acute phase 78%  vs. 2 and 3 vessel disease 73% vs. 27% Early revascularisation 78% Killip class at admission (I+II/III/IV) 76% / 20% / 4% Mortality during acute phase 6.2%</td>
</tr>
</tbody>
</table>

Values are the mean±SD or numbers (percentage). Time to admission is expressed as median time with 25th and 75th percentiles.

Table 2 Comparison of the incidence of mechanical complications after AMI before and in the reperfusion era.

<table>
<thead>
<tr>
<th></th>
<th>Before reperfusion era (average)</th>
<th>In reperfusion era (current study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial effusion</td>
<td>25%</td>
<td>6.6%</td>
</tr>
<tr>
<td>LV thrombus (anterior MI)</td>
<td>35-40%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>53%</td>
<td>28%</td>
</tr>
<tr>
<td>Infarct expansion</td>
<td>30%</td>
<td>4%</td>
</tr>
<tr>
<td>Septal rupture</td>
<td>1-3%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Free wall rupture</td>
<td>2%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Table 3 Univariate regression analysis of risk factors associated with mechanical complications in AMI.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of revascularisation</td>
<td>4.15</td>
<td>1.65-10.47</td>
<td>0.002</td>
</tr>
<tr>
<td>Killip class at admission &gt;II</td>
<td>2.66</td>
<td>1.82-3.88</td>
<td>0.0001</td>
</tr>
<tr>
<td>LV ejection fraction &lt;50%</td>
<td>2.41</td>
<td>1.79-3.24</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age ≥70 years</td>
<td>1.75</td>
<td>1.29-2.38</td>
<td>0.0004</td>
</tr>
<tr>
<td>Time to admission &gt;6 h</td>
<td>1.71</td>
<td>1.25-2.34</td>
<td>0.0008</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.47</td>
<td>1.03-2.11</td>
<td>0.003</td>
</tr>
<tr>
<td>Risk factors (hypertension, diabetes)</td>
<td>1.47</td>
<td>1.09-1.97</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 4 Multivariate logistic regression of risk factors independently associated with the occurrence of echo-detected mechanical complications.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of revascularisation</td>
<td>3.48</td>
<td>1.36-8.95</td>
<td>0.001</td>
</tr>
<tr>
<td>LV ejection fraction &lt;50%</td>
<td>1.95</td>
<td>1.42-2.67</td>
<td>0.001</td>
</tr>
<tr>
<td>Killip class at admission &gt;II</td>
<td>1.91</td>
<td>1.27-2.87</td>
<td>0.002</td>
</tr>
<tr>
<td>Age ≥70 years</td>
<td>1.42</td>
<td>1.03-1.97</td>
<td>0.03</td>
</tr>
<tr>
<td>Time to admission &gt;6 h</td>
<td>1.37</td>
<td>0.98-1.91</td>
<td>0.06</td>
</tr>
</tbody>
</table>

© 2019 Elsevier Masson SAS. Tous droits réservés. - Document téléchargé le 30/01/2019 Il est interdit et illégal de diffuser ce document.
recently, Nakatani et al. (29) documented the beneficial reduction in the incidence of mechanical complications of AMI in the reperfusion era when compared with the previous period (Table 2), and underlines the importance of medical care, especially early revascularisation, on the occurrence of these complications. In multivariate analysis, lack of reperfusion appeared to be the most powerful independent predictor of the occurrence of mechanical complications (OR 3.48, 95% CI 1.36–8.95). These observations agree with those of previous reports which specifically addressed the issue of the beneficial effect of thrombolysis on some of these complications, whereas similar information after primary coronary angioplasty is scarce. In the study of Pizzetti et al. (22), patients receiving thrombolytics had a lower incidence of LV thrombosis, particularly when the left anterior descending coronary artery was patent, whereas a meta-analysis (23) suggested that thrombolytic therapy may prevent mural thrombus formation. GISSI investigators demonstrated that the incidence of peri-cardial effusion in patients treated with thrombolytic agents was approximately half of that in the control group (24). A reduced incidence of significant mitral regurgitation after thrombolysis was reported by Tenenbaum et al. (25). Crenshaw and GUSTO-1 investigators (26) documented the decreased incidence of ventricular septal rupture in the thrombolytic era, most likely because of improved reperfusion and myocardial salvage. Kinn (27), Moreno (28) and coworkers demonstrated that primary coronary angioplasty reduces the risk of post infarction cardiac rupture. More recently, Nakatani et al. (29) documented the beneficial effect of successful late reperfusion by angioplasty on mechanical complications. Furthermore, these authors showed that age $\geq 70$ years, Killip class $\geq 1$, absence of collateral vessels and failed reperfusion were independently associated with an increased risk of complications. However, only free wall rupture, septal rupture and mitral regurgitation were taken into consideration whereas infarct expansion, LV thrombus and pericardial effusion were not. Furthermore, patients were excluded if they were treated with angioplasty and thrombolysis or if mechanical complications occurred before angioplasty. In our study, all consecutive hospitalised patients with AMI were included whether or not reperfusion therapy by angioplasty and/or thrombolysis was performed. Finally, two echocardiographic examinations were carried out, the first soon after admission (median 4 h) and the second at the end of the hospitalisation period (median 6 days). Serial examinations throughout this period increased the chances of documenting these complications since they occur most often during the first week after AMI onset.

**Mitral regurgitation**

The relatively high incidence of mitral regurgitation is surprising and may be due to several factors: 1) the broad range of underlying mechanisms of post-AMI mitral regurgitation, including papillary muscle dysfunction or rupture, changes in LV shape and regional function, may play an important role (30), but also slight modifications of geometry (remodelling) may contribute to the increased frequency of mitral regurgitation after AMI (7,31,32); 2) current colour Doppler echocardiography provides highly sensitive detection of sub-clinical or mild regurgitation. However, the essential point remains the major prognostic impact of mitral regurgitation, even when mild (33-35), on long term survival (36,37), and hence the importance of detecting mitral regurgitation during the acute phase of myocardial infarction to assess risk stratification and apply appropriate therapy according to the presence of symptoms and the severity/mechanism of regurgitation (38).

**Influence of LV function**

The second important finding of our study is that the development of mechanical complications remains strongly associated with reduced systolic LV function as demonstrated by multivariate logistic regression analysis (LV-EF <50% was associated with an OR = 1.95 (95% CI 1.42–2.67). LV-EF was significantly lower in subgroups of patients with pericardial effusion, LV thrombus and infarct expansion. There is now clear evidence that the salvage of at risk myocardium and subsequent improvement of LV function are the mechanisms by which early reperfusion therapy is effective in reducing infarct size and consequently the incidence of these complications. Conversely, in cases of failure or lack of reperfusion, the conditions are set for the development of complications just as they were before the reperfusion era.

**Limitations of the study**

It can be argued that the data were collected through a declarative registry with no analysis of echo recordings in a core laboratory. However, all investigators were experienced physicians well trained in echocardiography. Our study reflects the current practice of performing echocardiography in daily practice in a relatively large cohort of consecutive patients who had recent AMI from multiple centres. Despite some degree of difference in performance and interpretation between centres, the overall data gathered by echocardiography has strong informative power.

Although relatively rare with current echo machines, which yield continuously improved diagnostic accuracy, possible diagnostic errors cannot be eliminated. Because of usual lack of direct tear visualisation, false positive aspects of free wall rupture may be misinterpreted. False positive or negative diagnoses for LV thrombus also remain possible, even though investigators were asked to pay special attention to potential errors and to follow the published guidelines (17, 39). Diagnostic errors for pericardial effusion, mitral regurgitation and infarct expansion are less likely to occur with current echo machines.

Lack of quantitative assessment of mitral regurgitation is also a limitation. Although a quantitative approach is cur-
rently recommended, especially in mitral regurgitation of ischaemic origin, data were not available for all patients. For logistic reasons, the study period was limited to the acute phase of myocardial infarction with no further follow-up, impeding prognostic long-term information. Finally, although the use of coronary intervention procedures has increased over time (40), the high proportion of early hospitalisations and revascularisation rates from which three-quarters of patients benefited may not reflect the current situation in other countries. However, the number of patients included was large enough to afford sufficient power to the study and clearly identify lack of reperfusion as a major determinant in the incidence of mechanical complications.

Conclusion

This prospective multicentre study provides recent data on the value of echocardiography to detect mechanical complications of AMI. This non-invasive imaging technique is carried out routinely by many hospital teams affording great feasibility and good image quality for the majority of patients examined at the bedside. Permanent technological improvements allow high diagnostic performance.

The present study demonstrates the current low incidence of mechanical complications of AMI in the reperfusion era and underlines the importance of medical care, especially early revascularisation, in reducing the incidence of these complications. It also demonstrates the persistent relationship with LV dysfunction.

References

[30] Moore CA, Nygaard TW, Kaiser DL, Cooper AA, Gilson RS. Post-infarction ventricular septal rupture: the importance of loca-

© 2019 Elsevier Masson SAS. Tous droits réservés. - Document téléchargé le 30/01/2019 Il est interdit et illégal de diffuser ce document.
Echocardiographic assessment of the incidence of mechanical complications during the early phase of myocardial infarction in the reperfusion era: a French multicentre prospective registry

APPENDIX

The following persons and centres participated in the study; centres are listed in order of patients recruited and principal investigators indicated by *
