Reversible Myocardial Dysfunction, A Possible Complication in Critically Ill Patients Without Heart Disease

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Purpose: Reversible myocardial dysfunction or myocardial stunning is frequently described in patients with episodes of acute coronary syndrome and has recently been reported in critically ill patients without ischaemic heart disease. This article presents a study and description of the possible existence of myocardial dysfunction in critically ill patients in our setting who present no acute episode or history of cardiovascular disease.

Design: Prospective, descriptive study.

Setting: The intensive care unit of a district hospital.

Patients and Participants: The study included all patients admitted to the intensive care unit between March 1998 and March 2001 for noncardiac causes and who underwent echocardiographic examination for electrocardiographic changes, signs of cardiac insufficiency, persistent arrhythmias, or any other indication. Patients with sepsis or other critical illness known to be associated with myocardial dysfunction were excluded from the study. The study was carried out on those selected patients who developed myocardial dysfunction.

Measurements and Results: Transthoracic and transoesophageal echocardiography were carried out to assess the left ventricular ejection fraction and any segmental contractility disturbances. These investigations were carried out within 24 hours of admission, during the first week, during the second or third week, after one month and after three to 6 months. The electrocardiogram was assessed on admission and the changes over time were studied. Thirty-three patients were included in the study after detecting myocardial dysfunction; the median age of these patients was 63 years [range, 23-82 years]. Seven patients died. The median initial left ventricular ejection fraction was 0.34 [range, 0.16-0.48] and improved with time. Segmental contractility disturbances were detected initially in all patients and also normalized with time. All patients presented electrocardiogram changes that normalised in line with the echocardiographic changes.

Conclusions: Reversible myocardial dysfunction can develop in critically ill patients without primary heart disease. This syndrome is associated with systolic dysfunction, segmental contractility disturbances and electrocardiographic changes. © 2003 Elsevier Inc. All rights reserved.

However, despite the considerable clinical implications of this finding for the diagnosis, therapy and prognosis of these patients, this phenomenon has not been fully described. The presence of RMD could also account for the frequent episodes of arrhythmia, acute respiratory insufficiency, or shock that occur in critically ill patients without primary heart disease.

The aim of the present work has been to investigate the presence of myocardial dysfunction in
nonseptic patients admitted to our intensive care unit (ICU) with critical, noncardiac disease.

MATERIALS AND METHODS

A prospective, descriptive study was undertaken of patients admitted to the 9-bed medical/surgical ICU of a provincial hospital from March 1998 to March 2001.

The inclusion criteria were: critically ill patients who underwent echocardiographic examination for: 1) electrocardiographic changes, 2) signs of cardiac insufficiency, 3) persistent arrhythmias, or 4) any other indication considered by the intensivist treating the patient. Those patients in whom myocardial dysfunction was detected in the absence of acute heart disease and with no known history of heart disease were selected for the study. This myocardial dysfunction was determined by the presence of altered segmental contractility or the presence of systolic myocardial dysfunction.

Exclusion criteria were: 1) a history of cardiovascular disease; 2) admission for acute cardiovascular disease; 3) the presence of a critical illness known to be associated with systolic myocardial dysfunction, such as myocarditis, sepsis, septic shock, or postpartum cardiomyopathy; 4) patients suffering cardiorespiratory arrest; and 5) patients with thoracic trauma.

Echocardiographic Study

Echocardiography was performed either to study pre-existing electrocardiographic changes (eg, ST segment or T-wave alterations, bundle branch block, appearance of a Q wave, arrhythmias, QT alterations), or to manage undiagnosed shock or shock with a clinical suspicion of myocardial affection, or because of clinical signs of heart failure. Transthoracic or transoesophageal echocardiography (depending on the sonic window) was performed in the first 24 hours and repeated in the first week, in the second or third week, after one month and after 3 to 6 months. The left ventricular ejection fraction (LVEF) value was the arithmetic mean of a minimum of 3 measurements. The techniques used for this determination were M mode, the modified Simpson’s method and visual estimation when measurements were not feasible. An assessment was also made of possible disturbances of segmental contractility using the recommendations of the American Society of Echocardiography, with the following score: 0 = hyperkinesia; 1 = normal; 2 = hypokinesia; 3 = akinesia; and 4 = dyskinesia.9

Electrocardiography

A 12-lead electrocardiogram (ECG) was routinely performed on all patients on admission and repeated daily, using conventional parameters (paper speed 25 mm/s, calibration 10 mm = 1.0 mV). ST-segment changes, Q waves, T-wave changes and QTc interval were recorded.

Serial serum creatine kinase (CK), including the MB fraction, was measured in all the patients in whom myocardial dysfunction was detected in order to obtain the concentration curve. Data were collected on the classical cardiovascular risk factors and complications, and the degree of severity was quantified using the APACHE III scale.

A Swan-Ganz catheter was inserted according to diagnostic or therapeutic requirements as indicated by the intensivist’s responsible for the patient. Coronary angiography and/or exercise testing was performed when there was suspected acute ischaemic heart disease.

Statistical Analysis

Assuming the non-normal distribution of the variables, the Kruskal-Wallis non-parametric tests were used to study the changes in the LVEF over time. The categorical variables such as the segmental motility score and electrocardiogram were studied using the $\chi^2$ test. The quantitative variables are presented as medians and ranges. Categorical data are expressed as absolute values and percentages. A $P$ value < .05 was considered statistically significant.

RESULTS

During the 3 years of the study, of the total of 1,778 patients admitted to the ICU, 1,160 were admitted for noncardiac disease; 586 of these patients were excluded from the study because of the presence of sepsis or other diseases in which the onset of myocardial dysfunction is classically recognised. Five hundred seventy four critical ill patients without cardiac disease had an echocardiographic study. Of the patients with no history of heart disease who underwent echocardiographic screening, 33 presented myocardial dysfunction. A further 8 patients with acute haemorrhagic stroke presented left ventricular dysfunction, segmental contractility disturbances and electrocardiographic
changes on admission but, since they were transferred to a neurosurgical hospital, they were excluded due to difficulties in follow-up. A further 2 patients with pneumonia but without septic shock developed myocardial dysfunction with segmental contractility disturbances but were excluded from the study because the myocardial dysfunction may possibly have been secondary to sepsis (Fig 1). None of the patients presented chest pain or a clinical picture compatible with angina pectoris. The reasons for admission to ICU are listed in Table 1.

The median age of the final study sample of 33 patients was 63 years (range, 23-82 years); 15 (45.45%) were women (Table 2). The median length of stay was 11 days [range, 3-27]. Seven patients (21.21%) died.

A rise in CK values was detected in 23 patients but an accompanying increase in CK-MB was found only in one trauma patient without thoracic trauma. At the time the myocardial dysfunction was detected, only 9 patients were receiving treatment with catecholamines (dopamine, noradrenaline, dobutamine or adrenaline). A total of 18 patients received catecholamines during the study period.

The frequency of the classical cardiovascular risk factors is shown in Table 3. The most prevalent factor was arterial hypertension.

The median initial LVEF was 0.34 [range, 0.16-

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**Table 1. Primary Disease Causing ICU Admission**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Patients Admitted to ICU</th>
<th>RMD (%)*</th>
<th>Frequency (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>41</td>
<td>7/41 (17.1%)</td>
<td>7/33 (21.2%)</td>
</tr>
<tr>
<td>Postsurgical anoxia</td>
<td>3</td>
<td>1/3 (33.3%)</td>
<td>1/33 (3.1%)</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>56</td>
<td>2/56 (3.6%)</td>
<td>2/33 (6.2%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>17</td>
<td>5/17 (2.9%)</td>
<td>5/33 (15.0%)</td>
</tr>
<tr>
<td>Surgery/haemorrhagic shock</td>
<td>151</td>
<td>2/151 (1.3%)</td>
<td>2/33 (6.2%)</td>
</tr>
<tr>
<td>Heat stroke</td>
<td>6</td>
<td>1/6 (16.7%)</td>
<td>1/33 (3.1%)</td>
</tr>
<tr>
<td>Upper gastrointestinal bleed</td>
<td>78</td>
<td>3/78 (3.8%)</td>
<td>3/33 (9.0%)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>13</td>
<td>4/13 (30.7%)</td>
<td>4/33 (12.4%)</td>
</tr>
<tr>
<td>Trauma patients</td>
<td>204</td>
<td>6/204 (2.9%)</td>
<td>6/33 (18.1%)</td>
</tr>
<tr>
<td>Anaphylactic shock</td>
<td>5</td>
<td>2/5 (40.0%)</td>
<td>2/33 (6.2%)</td>
</tr>
</tbody>
</table>

*Proportion of patients with RMD with respect to different diseases causing ICU admission.
†Proportion of patients with RMD with respect to total number of RMDs detected.
0.48] and showed a progressive improvement to normalisation (\(P < .0001\)) (Fig 2). Left ventricular dilatation was observed in only one patient, with a left ventricular telediastolic diameter axis of 62 mm (parasternal long axis view) that was normal by the sixth month.

Although the contractility of the whole left ventricle was evaluated, contractility disturbances were only observed in apical and basal segments. These disturbances were present in all the patients.

Table 2. Details of Patients Presenting Reversible Myocardial Dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>23-82</td>
<td>63</td>
</tr>
<tr>
<td>Length of stay</td>
<td>3-27</td>
<td>11</td>
</tr>
<tr>
<td>APACHE III</td>
<td>34-158</td>
<td>80</td>
</tr>
<tr>
<td>CK</td>
<td>56-15879</td>
<td>2103</td>
</tr>
<tr>
<td>CK-MB</td>
<td>0-154</td>
<td>21</td>
</tr>
<tr>
<td>LVEF 1</td>
<td>0.16-0.48</td>
<td>0.34</td>
</tr>
<tr>
<td>LVEF 2</td>
<td>0.22-0.60</td>
<td>0.42</td>
</tr>
<tr>
<td>LVEF 3</td>
<td>0.16-0.67</td>
<td>0.46</td>
</tr>
<tr>
<td>LVEF 4</td>
<td>0.42-0.70</td>
<td>0.55</td>
</tr>
<tr>
<td>LVEF 5</td>
<td>0.50-0.73</td>
<td>0.60</td>
</tr>
</tbody>
</table>

LVEF 1: Left ventricular ejection fraction determined within the first 24 hours of the patient’s admission to the ICU.
LVEF 2: Left ventricular ejection fraction determined during the first week of the patient’s admission to the ICU.
LVEF 3: Left ventricular ejection fraction determined during the second or third week of the patient’s admission to the ICU.
LVEF 4: Left ventricular ejection fraction determined approximately one month after admission to the ICU.
LVEF 5: Left ventricular ejection fraction determined between 3 and 6 months after the ICU admission.

The initial echocardiography showed hypokinesia of the septoapical segment in 57% of the patients, akinesia in 28.6% and dyskinesia in 14.3%. Hyperkinesia was observed in the basal wall in 37.0% and hypokinesia in 20.0%. The improvement in the LVEF over time was accompanied by an improvement in the segmental contractility score. Septoapical segments showed a progressive and statistically significant improvement (\(P < .0001\)). Basal segments improved to normalisation, although the differences were statistically significant only between the first and second echocardiograms (Fig 3).

An increase in the left intraventricular gradient observed in the initial echocardiograms of 5 patients had normalised by the second echocardiogram. In 2 trauma patients with fat embolism complications, there was severe right ventricular
failure with severe global hypokinesia; they also presented widespread septobasal and septoapical akinesia of the left ventricle and one developed an apical aneurysm. A further three patients (one asthmatic patient, one patient with acute stroke, and a third patient excluded from the study for presenting pneumonia) developed anterior and inferoapical aneurysms that regressed during the first month. No patient developed intraventricular thrombi. Apart from these contractility disturbances, 8 patients presented global hypokinesia associated with septoapical akinesia-dyskinesia; 5 patients developed mitral insufficiency (2 mild and 3 moderate); and 4 patients presented dilatation of the left atrium. All of these situations normalized during the first month.

**Electrocardiography**

ECG changes included ST depression in 11 patients (1-3 mm), ST elevation in 13 (1-4 mm), the appearance of a Q wave in 6, left bundle branch block in one, T-wave inversion in 15, a peaked T wave in 3 and a lengthening of the QTc interval in 5. The ECG varied with time, with an initial predominance of ST elevation followed by the appearance of a Q wave; later in the course of the study, the predominant change became T-wave inversion. In the survivors, the electrocardiographic changes normalized between the first and 6 months ($P<.0001$) (Fig 4).

Coronary angiography was carried out in seven patients and exercise testing in two for suspected associated ischaemic heart disease; all the results were normal.

The most frequent complication was acute pulmonary oedema, followed by ventricular tachycardia (Table 3). A Swan-Ganz catheter was inserted in 11 patients; the median peak pulmonary wedge pressure was 20 mm Hg (range, 7-31).

**A Typical Case**

A 31-year-old woman with a history of severe asthma was admitted in status asthmaticus refractory to standard medical treatment. Despite endotracheal intubation and mechanical ventilation, optimal ventilation was not achieved and sevoflurane was required. Prior to the initiation of mechanical ventilation, and with no other clinical symptoms, the ECG showed ST elevation in II, III, AVF and V2-V4. There were clinical signs of severe shock during the first 72 hours and the patient required high doses of vasoactive drugs (dopamine and noradrenaline). The ECG changed over time, with ST elevation in II, III, AVF, and V2-V4 and T-wave inversion in V2-V4 at 48 hours. After 1 week, the only alteration was T-wave inversion in V2 and V3 and this showed complete normalization during the first month.

Transthoracic and transoesophageal echocardiography initially showed septoapical akinesia, mild basal hyperkinesias, and an LVEF of 0.32. These changes evolved toward complete normalization over the first month. Six weeks later, a coronary angiography was normal.

**DISCUSSION**

We report the onset of a reversible myocardial dysfunction in critically ill patients with no known...
history of coronary artery or other cardiovascular disease. This dysfunction developed due to alterations primarily affecting the septoapical region. At the same time, disturbances of contractility were observed in the basal wall that may have a compensatory role. However, there was a reduction in the LVEF.

Among the survivors, there was a progressive improvement in the LVEF and segmental contractility until complete normalization had been achieved. Similar findings have been described retrospectively after episodes of acute stroke, asthma, and other critical diseases. In all of these situations, the event of interest is the development of a myocardial dysfunction that is reversible over a variable period of time. It is associated with complications that may modify the prognosis and is accompanied by electrocardiogram changes such as ST elevation, T-wave inversion, or the appearance of a Q wave. RMD may be an uncommon myocardial complication of various critical diseases.

In cases of a clear episode of myocardial ischaemia, we can refer to myocardial stunning. However, the aetiopathology of this syndrome is unknown and other factors apart from the possible imbalance between supply and demand (ischaemia) may be implicated, including the release or administration of catecholamines, tissue hypoxia and reperfusion phenomena, the onset of a systemic inflammatory response with cytokine liberation, or even a direct cytotoxic effect on the myocardium, a theory that could explain the raised troponin levels found in critically ill patients with no previous cardiac pathology. Other authors suggest the possible additive effect of myocardial depression and a cytotoxic lesion.

This myocardial dysfunction could have a similar aetiopathogenesis to that which occurs in the critically ill patient with sepsis or septic shock, being caused by myocardial depression, a myocardial lesion, or a combination of the two. The clinical course and implications of this type of myocardial dysfunction could be similar to the myocardial dysfunction which occurs in sepsis. Supraventricular tachycardia-induced cardiomyopathy should be considered in the differential diagnosis, although most of our patients did not present this arrhythmia in a sustained form and showed no ventricular dilatation or hypertrophy, typical findings in supraventricular tachycardia-induced cardiomyopathy. Hypoxia, ischaemia, and reperfusion phenomena could explain this RMD. However, the normality of all the coronary angiograms we performed (in 7 patients) and the normality or virtual normality of coronary angiograms reported in other studies would suggest a possible alternative or simultaneous mechanism to the reduction in epicardial coronary blood flow.

Of particular interest to this discussion is the specific localization of the dysfunction. This could be explained by a greater liberation of catecholamines in this region, because it is a frontier zone for coronary artery perfusion, or because of a delay in recovery after global affection, or because of a rapid loss of elasticity at the apex of the left ventricle after excessive dilatation. All affected patients showed electrocardiographic changes, with a particular predominance of changes in the ST segment and T wave and the appearance of a Q wave. These electrocardiographic changes appear to be time related, varying in accordance with improvements in the LVEF and in the segmental contractility disturbances. It appears that ST-segment changes develop at onset and the appearance of a Q wave and T-wave inversion occur later, followed by normalisation of the ECG. These electrocardiographic changes are similar to those described by Sharkey. Interestingly, we found no increase in CK-MB, which suggests there was no generation of an acute myocardial infarction but does not rule out myocardial injury. Unfortunately, we had no specific myocardial injury markers available, such as troponin.

The clinical syndrome of RMD in the critical patient may appear as a complication of any critical disease and may have important clinical implications, in particular: 1) Detection and diagnostic suspicion. This dysfunction may have an extremely low incidence. However this incidence may easily be an underestimate due to a lack of clinical suspicion or failure to detect cases. A further factor suggesting the underestimation of this syndrome is the high rate of myocardial lesions detected in critically ill patients based on troponin levels; 2) Differential diagnosis. This clinical syndrome requires us to establish the differential diagnosis with numerous cardiomyopathies and, in particular, with ischaemic heart disease. It is likely that cases of RMD in critically ill patients have been confused with or diagnosed as acute myocardial infarction with normal coronary arteries; 3) Likely
worsening of the prognosis. This syndrome could be responsible for possible complications which have been described by other authors, suggesting a possible worsening of the prognosis. This syndrome could explain frequent complications in critically ill patients that are otherwise poorly explained, such as the onset of acute respiratory insufficiency, arrhythmias or shock. If these complications are induced by an RMD, the patient could benefit from specific techniques to treat left ventricular dysfunction such as the intra-aortic balloon pump or vasoactive drug therapy.

STUDY LIMITATIONS

Despite the interesting results of this study, in which the onset of an RMD appears to have been demonstrated in critically ill patients, there are certain limitations to this work which require the results to be viewed with a degree of caution. The principle limitation comes from the fact that this is a study performed on a case series and, in this paper; therefore, it may only be suggested that a myocardial dysfunction could develop in critically ill patients. This is a descriptive study with no control group, so that the long-term effect of this RMD could not be studied. The sample size is too small to estimate the global incidence of RMD or the incidence associated with each primary disease. Because the echocardiographies were carried out for the prior existence of electrocardiographic changes, for clinical signs of cardiac failure or as part of the investigation of shock, the incidence of RMD may have been underestimated or a selection bias may have been introduced. Very few coronary angiographies were carried out so that the incidence of asymptomatic ischaemic heart disease may have been higher and the clinical picture may sometimes have been due to ischaemic dysfunction. However, the patients presented no clinical symptoms of coronary pain and the coronary angiographies, which were conducted were normal, findings which make the presence of an ischaemic cardiopathy improbable. In fact, if occult or asymptomatic ischaemic heart disease is present, this could be one more cause of the RMD or myocardial stunning that appears in critical patients. Neither diastolic function nor the right ventricle were studied, though they may have been affected in the same way as the left ventricle. We did not monitor troponin levels, an enzyme that is more specific and sensitive and could have enriched our knowledge in this study. We did not study the levels of cytokines, catecholamines or other possible aetiological agents, ie, we did not investigate its aetiopathogenesis.

CONCLUSIONS

A reversible myocardial dysfunction may develop in critically ill patients with no primary cardiac disease. The clinical picture is one of systolic myocardial dysfunction, disturbances of segmental contractility and electrocardiographic changes. Although it may be inferred that this syndrome could worsen a patient’s clinical course, it is not known to what extent it may affect the prognosis of the primary disease. Its aetiopathogenesis is unknown, although it may be due to an inherent physiopathological response in the critical patient.

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