Cardiac function estimated by stroke volume starts to recover just after reperfusion therapy with special reference to stunning of acute myocardial infarction

Toru Yoshida, MD*1, Hitoshi Takehana, MD*1, Hiroshi Imai, MD*1, Masato Machii, MD*1, Yuichi Kataoka, MD*1, Kazui Soma, MD*1, Tohru Izumi, MD*2

Abstract: Background: Considerable parts of the myocardium fall into myocardial stunning just after reperfusion therapy for acute myocardial infarction (AMI). In the present study, the prediction of recovery from myocardial stunning by the change in the stroke volume (SV) with a Swan-Ganz catheter (Stroke Volume with Swan-Ganz, SGSV) just after reperfusion therapy was attempted. Methods: The study consisted of 35 consecutive patients transferred to the Emergency Center of Kitasato University Hospital with a first uncomplicated anteroseptal AMI. Primary percutaneous transluminal coronary angioplasty (primary PTCA) for left anterior descending artery (LAD) was performed in 32 patients. They were divided into a stroke volume-increasing group (SGSV-UP group) or decreasing group (SGSV-DOWN group) according to their SGSV change during the CCU stay. The ejection fraction (EF) and SV on left ventriculography (LVG) (EF on LVG, LVGEF; SV on LVG, LVGSV) in the acute and chronic phase (about 6~8 months later) were compared between the two groups. Results: Twenty-four patients were classified into the SGSV-UP group and 8 patients into the SGSV-DOWN group. LVGEF increased significantly in the SGSV-UP group but not in the SGSV-DOWN group (from 40.8±8.5% to 54.1±9.1%, P=0.0022 vs. from 42.2±10.6% to 43.6±7.7%, N.S.). LVGSV changed similar to LVGEF. In the SGSV-UP group, the relationship between the change in LVGEF (ΔLVGEF) and SGSV (ΔSGSV) was revealed to be ΔLVGEF (%) = 1.4 + 0.5 ΔSGSV (ml) (P=0.0082). Regional asynchrony was significantly reduced in the SGSV-UP group (P=0.034). Conclusion: The increase in SGSV just after reperfusion therapy for AMI was related to the recovery of LVGEF and LVGSV in the chronic-phase. This suggests that recovery from myocardial stunning begins just after reperfusion therapy for AMI. Key words: ① myocardial stunning, ② acute myocardial infarction, ③ Swan-Ganz catheter

Introduction

Generally, considerable parts of the myocardium fall into myocardial stunning just after reperfusion therapy for acute myocardial infarction (AMI). Myocardial stunning was originally reported as the delayed recovery of regional depressed myocardial contractions after transient myocardial ischemia in conscious dogs by Heyndrickx et al. in 1975[3]. In 1982, Braunwald and Kloner defined "the stunned myocardium"[3] and it is now thought to occur in several clinical situations[6~8]. However, prediction of the recovery of cardiac function is difficult because the time course of myocardial stunning recovery is not clear[9~11]. In actual AMI clinical situations, myocardial stunning is retrospectively diagnosed by changes in the myocardial wall motions on left ventriculography (LVG) or echocardiography between the acute and chronic phase[12~15], so it is impossible to predict the recovery of myocardial contractions in the acute phase alone.

A Swan-Ganz catheter, of which use for AMI was originally reported by Swan and Forrester et al. in 1976[20], is now widely used for the management of...
circulatory conditions, as the stroke volume (SV) can be calculated with this catheter. In the case of AMI, especially single vessel lesions, the depression or change in myocardial contraction is limited to a comparatively narrow area, which can be revealed as a depression or change in global left ventricular function. If SV is increased after reperfusion without a positive inotropic agent or mechanical circulatory support, it may reflect the recovery of myocardial wall motion, which indicates recovery from myocardial stunning.

In the present study, the relationship between the recovery of the ejection fraction (EF) / SV on LVEF (EF on LVG, LVEF; SV on LVG, LVGSV) and the change in SV measured with a Swan-Ganz catheter (SV with Swan-Ganz, SGSV) just after the reperfusion therapy for AMI was analyzed.

Methods

Patient profile: The study consisted of 35 consecutive patients transferred to the Emergency Center of Kitasato University Hospital with a first uncomplicated (without the need for mechanical circulatory support or catecholamine) anteroseptal acute myocardial infarction from April 2001 to March 2003. After informed consent was obtained, the emergent cardiac catheterizations (acute-phase catheterization) consisting of coronary angiography (CAG) and LVEF were performed and total obstruction or high-grade stenosis (thrombolysis in myocardial infarction grade, TIMI grade: 0 ~ 2) of the left anterior descending artery (LAD) was recognized in all patients. The right coronary artery (RCA) and circumflex artery (Cx) were intact in all patients. Reperfusion therapy by primary percutaneous transluminal coronary angioplasty (primary PTCA) with coronary stenting was performed and sufficient restoration of coronary flow was achieved (TIMI-3 flow with sufficient lumen) except in 3 patients with peripheral lesions of the LAD. All patients were followed up in the Coronary Care Unit of the Emergency Center 12 ~ 24 hours after reperfusion therapy. ACE-inhibitors and/or isosorbide dinitrate were administered in all cases, and the systemic blood pressure was kept below 140/90. Mean systemic blood pressure (mean BP), heart rate (HR), pulmonary capillary wedge pressure (PCWP), CVP, and the systemic vascular resistance index (SVRI) were measured at the time of admission to CCU and 12 hours post admission. SV measured with a Swan-Ganz catheter (SGSV) was calculated by cardiac output (l·min⁻¹)/HR (times·min⁻¹) in every patient at the time of admission to CCU and 12 hours post admission (Swan-Ganz Combo Edwards Lifesciences Co., USA, and Vigilance Baxter Inc., USA). Cases with obvious valvular diseases were excluded.

Study design: The 32 patients with sufficient reperfusion therapy were classified by the change in SGSV during CCU stay into a stroke volume-increasing group (SGSV-UP group, n = 24) or decreasing group (SGSV-DOWN group, n = 8) and followed up for 6 ~ 8 months. The cut off line between the SGSV-UP group and SGSV-DOWN group was defined as (SGSV at 12 hours post CCU admission)-(SGSV at the time of CCU admission) = 0. The 3 patients that did not undergo reperfusion therapy with primary PTCA and coronary stenting, were excluded from this study. The patients’ backgrounds and prognoses, including the recurrence of myocardial ischemia, were compared between the two groups. Following the obtaining of informed consent, follow-up CAG and LVEF (chronic-phase catheterization) were performed (12 patients in the SGSV-UP group and 6 in the SGSV-DOWN group), and regional wall motion, LVEF, and LVGSV were compared. Regional wall motion was defined as normokinesis = +2, hypokinesis = +1, akinesis = ±0, and dyskinesis = −1 in every AHA’s first-fifth segment of the left ventricle, and was statistically analyzed. LVEF, LVGSV, and regional wall motion were analyzed by independent observers who were blind to the patients’ information.

Statistics: The data were expressed as the mean ± SD. Basic comparisons were performed using the Mann-Whitney U test, the Wilcoxon signed-ranks test or simple regression analysis. P values less than 0.05 were considered statistically significant.

Results

Clinical characteristics of the patients: Twenty four patients were classified into the SGSV-UP group and 8 patients were classified into the SGSV-DOWN group. The patients’ age, gender, basic diseases and use of β-blockers were not significantly different between the SGSV-UP group and the SGSV-DOWN group (Table 1). Angiotensin converting enzyme inhibitors were administered in 19 cases in SGSV-UP group and all 8 cases in SGSV-DOWN group. Both these groups were not significantly different, and no case of both groups was administered angiotensin II receptor blockers. There was no significant difference between the two groups for the duration from the appearance of symptoms to reperfusion (Table 1). The peak CK, and peak CK-MB were not significantly different between the two groups (Table 1). No patient revealed clinical ischemic signs during the follow-up period. There was no significant difference in the duration of chronic phase catheterization between the two groups (Table 1). The radiographic restenotic rate of the culprit lesion was not significantly different between the two groups (Table 1). During the CCU stay, the change in mean BP, PCWP, and CVP did not change significantly, but HR and SVRI were significantly reduced in SGSV-UP group compared to the SGSV-DOWN group (Table 2).

Analysis of LVEF, LVGSV, and regional asynergy: LVEF, LVGSV, and regional asynergy were analyzed by plural blinded investigators with LVEF taken in right anterior oblique view. LVGEF increased significantly in the SGSV-UP group, but not in the SGSV-DOWN
Recovery from stunning

Table 1  Patients' backgrounds

<table>
<thead>
<tr>
<th></th>
<th>SGSV-UP group (n = 24)</th>
<th>SGSV-DOWN group (n = 8)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.4 ± 9.6</td>
<td>57.3 ± 14.6</td>
<td>N.S.</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>19/5</td>
<td>5/3</td>
<td>N.S.</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
<td>2</td>
<td>N.S.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5</td>
<td>4</td>
<td>N.S.</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7</td>
<td>1</td>
<td>N.S.</td>
</tr>
<tr>
<td>Other diseases</td>
<td>6</td>
<td>2</td>
<td>N.S.</td>
</tr>
<tr>
<td>Duration to reperfusion (hours)</td>
<td>7.2 ± 5.2</td>
<td>5.6 ± 3.1</td>
<td>N.S.</td>
</tr>
<tr>
<td>LVGEF just after reperfusion</td>
<td>40.8 ± 8.5</td>
<td>42.2 ± 10.6</td>
<td>N.S.</td>
</tr>
<tr>
<td>Peak CK (IU·L⁻¹)</td>
<td>3.113 ± 2.010</td>
<td>4.189 ± 3.517</td>
<td>N.S.</td>
</tr>
<tr>
<td>Peak CK-MB (IU·L⁻¹)</td>
<td>277 ± 205</td>
<td>336 ± 259</td>
<td>N.S.</td>
</tr>
<tr>
<td>Duration to chronic phase catheterization (months)</td>
<td>6.4 ± 2.2</td>
<td>7.4 ± 1.0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Use of β-blockers</td>
<td>5</td>
<td>2</td>
<td>N.S.</td>
</tr>
<tr>
<td>Re-stenosis rate of culprit lesion of coronary artery (%)</td>
<td>35.7</td>
<td>45.0</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

N.S., not significant.

Table 2  Changes of parameters during CCU stay

<table>
<thead>
<tr>
<th></th>
<th>SGSV-UP group (n = 24)</th>
<th>SGSV-DOWN group (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>On CCU admission</td>
<td>After 12 hours</td>
</tr>
<tr>
<td>Mean BP (mmHg)</td>
<td>92.8 ± 11.5</td>
<td>79.6 ± 13.0</td>
</tr>
<tr>
<td>HR (min⁻¹)</td>
<td>82.6 ± 14.0</td>
<td>78.3 ± 13.9</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>9.5 ± 3.8</td>
<td>7.9 ± 3.3</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>5.1 ± 3.3</td>
<td>4.9 ± 3.0</td>
</tr>
<tr>
<td>CO (l·min⁻¹)</td>
<td>4.8 ± 1.1</td>
<td>5.8 ± 1.3</td>
</tr>
<tr>
<td>SGSV (ml)</td>
<td>590 ± 153</td>
<td>74.8 ± 15.0</td>
</tr>
<tr>
<td>SVRI (dynam·sec·cm⁻³·m⁻³)</td>
<td>2,707 ± 504</td>
<td>1,908 ± 315</td>
</tr>
</tbody>
</table>

*P < 0.05, vs. SGSV-UP group, †P < 0.01, vs. SGSV-UP group.
Mean BP, mean systemic blood pressure; HR, heart rate; PCWP, pulmonary capillary wedge pressure; CO, cardiac output; SGSV, SV with Swan-Ganz; SVRI, systemic vascular resistance index.

group (from 40.8 ± 8.5% to 54.1 ± 9.1%, P = 0.0022 vs. from 42.2 ± 10.6% to 43.6 ± 7.7%, N.S.) (Fig. 1). LVGSV increased significantly in the SGSV-UP group, but not in the SGSV-DOWN group (from 44.0 ± 18.4 ml to 71.4 ± 13.3 ml, P = 0.0024 vs. from 46.7 ± 21.2 ml to 59.2 ± 20.5 ml, N.S.) (Fig. 1). In the SGSV-UP group, the relationship between the changes in LVGEF from acute-phase catheterization to chronic-phase catheterization (Δ LVGEF) and SGSV from admission to CCU to 12 hours post-admission (Δ SGSV) were revealed by simple regression analysis as ΔLVGEF (%) = 1.4 ± 0.5 Δ SGSV (ml) (P = 0.0082) (Fig. 2). The regional wall motion of LVG was significantly improved in the SGSV-UP group (Seg. 1: from 1.6 ± 0.5 to 2.0 ± 0.0, P = 0.0455, Seg. 2: from 0.3 ± 0.6 to 1.0 ± 0.5, P = 0.0027, Seg. 3: from -0.1 ± 0.7 to 0.9 ± 0.7, P = 0.0008, Seg. 4: from 1.4 ± 0.5 to 1.8 ± 0.4, P = 0.0253, Seg. 5: from 1.9 ± 0.3 to 1.9 ± 0.3, N.S.), but not in the SGSV-DOWN group (Seg. 1: from 1.8 ± 0.4 to 1.7 ± 0.5, Seg. 2: from 0.5 ± 0.8 to 0.4 ± 0.5, Seg. 3: from 0.5 ± 0.8 to 0.1 ± 0.4, Seg. 4: from 1.8 ± 0.4 to 1.7 ± 0.5, Seg. 5: from 1.8 ± 0.4 to 1.7 ± 0.5, N.S.) (Fig. 3). Evaluation by echocardiogram in chronic phase showed similar tendency compared with acute phase.

Discussion
The present study evaluating the relationship between the change in SGSV immediately following reperfusion therapy for anteroseptal AMI and the prognosis showed several interesting findings. First, LVGEF and LVGSV were significantly higher in chronic-phase LVG compared to the acute-phase in the SGSV-UP group, but not in the SGSV-DOWN group. Second, anteroseptal regional asynergy was significantly reduced in chronic-phase LVG in the SGSV-UP group compared with the SGSV-DOWN group. Third, in the SGSV-UP group, the relationship between Δ LVGEF and Δ SGSV was revealed by simple regression analy-

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The change in LVGEF and SGSV in each group

The black line indicates the change in the SGSV-UP group and the gray line indicates the change in the SGSV-DOWN group. LVGEF and LVGSV significantly increased in the SGSV-UP group, but not in the SGSV-DOWN group.

N.S., not significant.

The usefulness of SGSV during CCU stay: Transient myocardial dysfunction after ischemia-reperfusion ("myocardial stunning") has been reported in several clinical situations. Although myocardial stunning can be diagnosed by a stress echocardiogram, myocardial contrast echocardiography, myocardial perfusion single photon emission computed tomography (SPECT), positron emission tomography (PET), or MRI, they possess some difficulties and dangers in the period immediately following reperfusion therapy for AMI. A Swan-Ganz catheter, of which use for AMI was originally reported by Swan and Forrester et al. in 1976, is now widely used for the management of circulatory conditions, as SV can be calculated by this catheter. SV is mainly determined by myocardial contractility, but influenced by HR, cardiac pre-load, i.e., PCWP, and after-load, i.e., SVRI. However, HR, pre-load and after-load are not independently determined, and may be influenced by myocardial ischemia-reperfusion and contractility itself through the autonomic nervous system. Moreover, when systemic blood pressure (BP) was decreased under a set point by after-load reduction therapy, SVRI could be decreased by an increase in cardiac output.

So, in the present study, although the decrease in HR and SVRI were significantly larger in the SGSV-UP group than the SGSV-DOWN group, and the decrease in HR and SVRI may have increased SV, the increase in SV may have decreased SVRI and HR. Furthermore, in the case of AMI, particularly single vessel lesions, the depression of myocardial contraction was limited to a comparatively narrow area, which could be a reflection of global left ventricular function. In the present study, the change in SGSV revealed a strong correlation to the recovery of cardiac function and regional left ventricular wall motion in the chronic phase; therefore, SGSV is an excellent tool for the prediction of cardiac function after acute myocardial infarction and a monitor for stunned myocardium.

Time course of myocardial stunning: In clinical situations, several studies have reported the recovery of myocardial contraction days, weeks, and months after the occurrence of AMI, but the initial recovery from myocardial stunning has been unclear. If regional depression of myocardial wall contractions is a reflection of global left ventricular function, a change in SGSV would indicate a change in regional myocardial contraction. If improvement of regional wall motion during CCU stay just after reperfusion were to occur without a positive inotropic agent or mechanical circulatory support, initial recovery from myocardial stunning would be suspected. In the present study, SGSV increased within 12 hours after reperfusion in the SGSV-UP group, so it was sus-
Recovery from stunning

Fig. 3 The change in regional asynergy of LV wall motion in each group

The left graph shows the changes in wall motion in the SGSV-UP group, and the right graph shows the changes in the SGSV-DOWN group. LV wall motion significantly increased in seg. 1-4 in the SGSV-UP group, but not in the SGSV-DOWN group. *P < 0.05.

expected that recovery from myocardial stunning began within 12 hours after reperfusion, earlier than that has ever been expected. Although the change pattern of SGSV during the 12 hours after the reperfusion may be more complex, increased or decreased SGSV (cut off line = 0) at a time point of 12 hours after CCU admission was employed in this study to divide the SGSV-UP and SGSV-DOWN group. Assessment of myocardial stunning in earlier phase than this present study may be an important step to find methods of recovery from myocardial stunning in earlier phase, and it should be evaluated in future studies.

Persistent LV dysfunction in SGSV-DOWN group: Although the clinical situations of the two groups were similar before the admission and the reperfusion therapy was performed similarly in both of two groups in acute-phase catheterization, the LVGEF did not recover significantly in the SGSV-DOWN group. The process of reperfusion may be related not only to myocardial salvage but also reperfusion injury, and it may lead to the expansion of the myocardial infarct area. The larger the myocardial infarct area is the more the left ventricular remodeling occurs, so the LVGEF in the SGSV-DOWN group might be persistently lower compared with the process of the SGSV-UP group.

Relationship to myocardial micro-perfusion: In the present study, TIMI-3 flow with sufficient coronary vascular lumen was achieved by PTCA with coronary stenting, which is considered to be the restoration of myocardial perfusion. However, reperfusion injury includes the damage to the microvasculature, which may lead to myocardial ischemia and dysfunction. The relationship between myocardial stunning and microvasculature damage is unclear, so it should be evaluated in future studies.

Limitations: This study has a few important limitations. First, a general relationship between SGSV and regional wall motion has not been established. Because the subjects of this study were limited to first anteroseptal AMI in the LAD region only, SGSV was related to anteroseptal regional asynergy to a degree, but some uncertainties still exist. Second, the measurement of cardiac output with a Swan-Ganz catheter, the basis of the SGSV calculation, has the possibility of methodological error, especially in the case of valvular disease. To avoid these difficulties, cases of obvious valvular disease were excluded. Third, in the present study, the opportunity for the evaluation of regional myocardial wall motion was limited to only two periods of LVG, and 12 patients of the SGSV-UP group and 2 patients of the SGSV-DOWN group could not undergo chronic-phase catheterization. They did not agree to chronic-phase catheterization for some reason; for example, they had no symptoms. The use of an echocardiogram as an alternative method was considered to add to the evaluation, but the reproducibility of the echocardiogram was unreliable compared with LVG, so it was not employed in this study. The evaluation of myocardial stunning by echocardiography should be performed in future studies. Finally, the measurement of SGSV was performed only at the time of admission to CCU and 12 hours after that. To clarify the characteristics of myocardial stunning, more frequent measurements would be needed. These points should be evaluated in a larger population in a future study.

Conclusion

The increase in SGSV in the early phase after reperfusion therapy for acute myocardial infarction was related to the recovery of EF and SV on LVG. The correlation was expressed with simple regression analysis as the formula: $\Delta$ LVGEF (%) = 1.4 + 0.5 $\Delta$ SGSV (mfr), so the $\Delta$ LVGEF was thought to be predicted by the $\Delta$ SGSV. This suggests that recovery from myocardial stunning begins immediately following the reperfusion therapy for acute myocardial infarction, earlier than that has ever been expected.

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References


