Effects of Spontaneous and Streptokinase-induced Recanalization on Left Ventricular Function After Myocardial Infarction

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SUMMARY  The effect of recanalization of the “infarct vessel” on left ventricular (LV) function was assessed 6–8 weeks after acute myocardial infarction (MI) in two groups: patients who had streptokinase-induced recanalization during the acute phase and control patients who had spontaneous recanalization. The ejection fraction and severity of LV wall motion abnormalities in 100 patients with recanalization were compared with those in 78 patients with persistent occlusion of the infarct vessel. Among patients with inferior MI, LV function was significantly better in those with spontaneous (n = 41, p < 0.05) and streptokinase-induced recanalization (n = 15, p < 0.02) than in those with persistent occlusion of the infarct vessel (n = 40) in the control group. The LV function was equally good in patients with spontaneous and streptokinase-induced recanalization. Among anterior MI patients, LV function was significantly better in those with streptokinase-induced recanalization (n = 10) than in those with spontaneous recanalization (n = 34, p < 0.01) or persistent occlusion in the control group (n = 28, p < 0.001). We conclude that recanalization has a beneficial effect on LV function in patients with MI.

AFTER the initial attempt of Boucek et al.11 in 1960 to lyse the thrombus by application of fibrinolysin in the aortic root of patients with acute myocardial infarction (MI), nonsurgical coronary artery reperfusion has attracted renewed interest and has recently become a feasible procedure in patients with evolving MI.1-4 Intracoronary infusion of a thrombolytic agent can reestablish antegrade coronary flow in 73–95% of the patients.1-4 To what extent this intervention leads to myocardial salvage has not been fully evaluated. DeWood et al.4 showed that total coronary occlusion of the infarct vessel is frequent during the early hours of transmural infarction and decreases in frequency during the initial 24 hours, suggesting subsequent recanalization in the evolution of infarction. The effects of this spontaneous recanalization on LV function are unknown. Documentation of a possible beneficial effect of spontaneous recanalization on infarct size would be relevant in evaluating the technique of intracoronary fibrinolytic therapy.

In this study we assessed the effect of streptokinase-induced recanalization and spontaneous recanalization on LV function. The left ventriculograms of a consecutive series of patients treated with intracoronary streptokinase were compared with the ventriculograms of a control group, matched for age, history of infarction, site of infarction and site of associated coronary occlusion (“infarct vessel”). Ventriculography was performed 6–8 weeks after infarction in both groups.

Methods

Streptokinase Group

All patients under 65 years of age whose history suggested acute MI were considered candidates for intracoronary thrombolysis. Further inclusion criteria were admission within 3 hours from onset of chest pain, ST-segment elevations of at least 0.2 mV and no pathologic Q waves in corresponding leads, no history of MI and no contraindication for thrombolytic therapy. Between November 1980 and December 1981, 48 of 98 consecutive patients admitted with a first MI fulfilled these criteria. Three refused treatment; technical difficulties prevented the procedure in three others. Lysis was attempted in 42 patients; 35 patients were eligible for this study (table 1). Successfully reperfused patients were those in whom reestablishment of antegrade flow was proved angiographically both at the time of lysis and 6–8 weeks after infarction. Thrombolysis was considered unsuccessful if the patient had no antegrade flow at the time of lysis after 2 hours of attempted reperfusion or had early reocclusion of the infarct vessel (within 6–8 weeks).

Control Group

The control group consisted of 143 patients (all younger than 65 years of age) who survived a first transmural MI. As part of a separate research protocol, all survivors had coronary angiography and left ventriculography 6–8 weeks after the acute event. These 143 patients were eligible from a consecutive series of 171 patients who were admitted with a transmural MI between January 1979 and November 1980, the period before thrombolytic treatment was attempted. Twelve of these 171 patients died during the acute phase and 16 refused investigation. Eleven patients died in the hospital, seven with severely impaired LV function
and four with rupture of the left ventricle. One patient died suddenly 1 week after discharge. Excluded were two patients with serious other disease and all five patients who were referred from other hospitals because of complications of the infarctions. Transmural MI was diagnosed if all of the following criteria were present: typical history, evolution of pathologic Q wave (> 0.04 second) and specific cardiac enzyme rise.

**Protocol**

**Streptokinase Group**

Nonsurgical recanalization was performed on a 24-hour basis. Informed consent was obtained from the patient and a relative. Before angiography, 600 mg of aspirin were given orally. Coronary angiography in the acute phase was performed with the Judkins technique. After the infarct vessel was visualized, 10 mg of sublingual nifedipine were given to exclude spasm. In no patient with total occlusion did the vessel show antegrade flow after nifedipine. The same catheter used for coronary angiography was used to infuse streptokinase. A bolus of streptokinase (10,000–20,000 U) was injected into the infarct vessel. Thereafter, streptokinase, 2000 U/min, was constantly infused into the infarct vessel.

The effect of streptokinase infusion was checked angiographically every 20 minutes or after a decrease of the ST-segment elevation. If occlusions persisted for more than 1 hour, the streptokinase infusion rate was increased to 4000 U/min. As a rule, infusion was not given for more than 2 hours. After successful reperfusion, the streptokinase infusion was continued for a further 10–30 minutes. After the procedure, the catheter tip was left in the descending aorta and the patients were monitored in the coronary care unit. The catheter was removed 6–12 hours after lysis.

Analgesics and sedation were given as appropriate during the acute phase. All patients were given aspirin, 200 mg/day and nifedipine 30 mg/day. During recovery, β blockers were added if the patient had angina pectoris. None of the patients were given anticoagulants.

**Control Group**

Analgesics and sedatives were given as necessary. In the acute phase, no patient received nifedipine, aspirin, other vasodilator agents or β blockade. From the first day of admission all patients received oral anticoagulation (coumarin), which was continued until a few days before angiography. After mobilization (48 hours after admission), patients were given β blockers if angina pectoris occurred.

**Investigation**

Six to 8 weeks after acute infarction, all patients were readmitted for coronary angiography and left ventriculography using the Judkins technique. All
medication was stopped at least 2 days before ventricu-
lography in all patients; digitalis was stopped 14 days
before investigation. Left ventriculograms were fil-
ed at 50 frames/sec in the 30° right anterior oblique pro-
jection and in the 60° left anterior oblique projection.
Left ventriculography was performed before angiog-
raphy using 30-40 ml of contrast material (Isoopaque
Coronair) injected at a rate of 15 ml/sec. Only the
ventriculograms of normally conducted beats without
preceding extrasystoles were analyzed.

Segmental wall motion of the left ventricle was
qualitatively assessed according to the criteria of the
American Heart Association committee. Each ven-
triculogram was divided into seven segments (fig. 1).
Each segment was assigned a score as follows: normal
= 0, hypokinesia = 1, akinesia = 2, dyskinesia = 3.
For each patient, the scores of the seven segments were
added to yield a total score, representing the severity of
left ventricular damage. The range from normal to a
maximally damaged ventricle is thus represented by a
score range of 0–21. Ejection fraction was calculated
using the area-length method.8

The coronary arteries were filmed in multiple axial
and hemiaxial views. Only obstructions of left anterior
descending, circumflex and right coronary arteries
were included. Obstructions of diagonal branches of
the left anterior or descending coronary artery and the
obtuse marginal branch of the circumflex coronary
artery were excluded. It was assumed that anterior
infarction was caused by obstruction of the left anterior
descending and that inferior infarction was caused by
obstruction of the circumflex or right coronary artery.
If both arteries were obstructed, the more severely
obstructed vessel was selected as the infarct vessel.

The angiographic data were analyzed without
knowledge of the clinical details of the patient by two
independent observers. The ventriculograms were ana-
yzed first without knowledge of the coronary anatomy.

Statistical Methods

Each statistical test was performed at a two-sided
5% level of significance; a result was considered sig-
nificant when the two-tailed p value was 5% or less.
The ejection fraction in the groups was compared using
the t test and the total score with the test of Yates.9

Results

Clinical Characteristics

Streptokinase Group

The eligible streptokinase-treated group consisted of
14 patients with an acute anterior wall MI and 21
patients with an acute inferior wall infarction. In 10 of
the 14 patients with an anterior MI, successful recana-
lization resulted in an open infarct vessel; in four pa-
tients streptokinase had no effect and the infarct vessel
remained occluded. Fifteen of the 21 patients with
inferior MI had a successful recanalization. The time
interval from onset of symptoms to successful recana-
lization was 2–4 hours. The mean total doses of strep-
tokinase was 120,000 U (range 60,000–300,000 U).
The mean age was 53 years (range 37–64 years).

LV Function in Inferior MI

The ejection fraction and the severity of LV damage
were similar in patients with spontaneous and strepto-
kinase-induced recanalization. The ejection fraction
was lower and the LV damage more severe in patients
with persistent occlusion of the infarct vessel (table 2,
fig. 2A). The number of patients in whom streptokinase
induced treatment was unsuccessful was too small for sta-
tistical analysis. The presence of multivessel disease
and the distribution of circumflex or right coronary
ttery infarct vessel were comparable in the groups.

LV Function in Anterior MI

The ejection fraction was higher and LV damage
less in patients with streptokinase-induced recanaliza-
tion than in those with spontaneous recanalization or
persistent occlusion of the infarct vessel (table 3, fig.
2B). The ejection fraction was higher and LV damage
less severe in patients with spontaneous recanalization
than in those with persistent occlusion of the infarct
vessel. These differences were not statistically signifi-
 cant, at least partly because of the small number of
patients. The number of patients in whom streptokinase
induced treatment was unsuccessful was too small for sta-
tistical analysis. The presence of multivessel disease
was comparable in the study groups.

Discussion

Functional impairment after acute MI is related to
the extent of myocardial ischemic injury.10–12 Massive
myocardial ischemia produces pump failure and seri-
ous ventricular arrhythmias11, 13, 14 and is the most com-
mon cause of death and morbidity among patients hos-
pitalized with acute MI. Both early and late prognosis
are worse with larger infarcts.13, 14 Therefore, methods
that reduce left ventricular damage may improve prognosis.

The presence of a zone of cells with reversible myocardial injury after coronary artery occlusion has been recognized. Interventions that either reduce the oxygen demand or increase oxygen supply may salvage this zone. In animals, the amount of reversible ischemic tissue is largest immediately after coronary occlusion and becomes smaller with time until it disappears, 6–9 hours after occlusion. Myocardial salvage intervention should therefore be instituted as soon as possible, probably within 6 hours. For this reason, only patients admitted to the hospital within 3 hours after onset of symptoms were treated with streptokinase.

Little is known about the natural history of occluded infarct vessels and the subsequent left ventricular damage. Acute MI results from an acute imbalance between oxygen supply and demand. The severity of reduction of blood flow during the acute phase of MI has recently been established by acute angionography. In the early hours of transmural MI, the prevalence of a totally occluded infarct vessel is 72–95%, all other lesions being subtotal. DeWood et al. showed the existence of spontaneous recanalization during the first hours of MI. To prove reversal of a total to a subtotal occlusion requires serial studies in a given patient; but comparison of the studies of prevalence of total occlusion early after onset of symptoms (72–95%) with the study of DeWood et al. 24 hours after the acute event (65%) and with those of Bertrand et al. and Betriu et al. 2–4 weeks after the acute event (45–53%) and our own study at 6–8 weeks (47%) highly suggest this to be the case. Therefore, it may be assumed that for some time during the acute phase of

![Graph A](image1.png)

![Graph B](image2.png)

**Figure 2.** (A) Ejection fraction and severity of left ventricular (LV) damage in inferior myocardial infarction. (B) Ejection fraction and severity of LV damage in anterior infarction.
TABLE 2. Ejection Fraction and Severity of Left Ventricular Damage in the Streptokinase-treated and Control Patients with Inferior Myocardial Infarction

<table>
<thead>
<tr>
<th>Infarct vessel open*</th>
<th>Controls</th>
<th>Streptokinase</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>41</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>54.4 +/− 10.1</td>
<td>57.5 +/− 10.3</td>
<td>NS</td>
</tr>
<tr>
<td>Severity of LV damage‡</td>
<td>2.8 +/− 2.3</td>
<td>2.6 +/− 2.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Statistics

Ejection fraction | p < 0.05 | p < 0.02 |
Severity of LV damage | p < 0.03 | p < 0.02 |

Infarct vessel occluded‡

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>40</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction (%)</td>
<td>48.9 +/− 12.0</td>
<td>52.8 +/− 10.3</td>
</tr>
<tr>
<td>Severity of LV damage‡</td>
<td>4.5 +/− 2.5</td>
<td>4.7 +/− 2.3</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

*Open = stenosis < 99% 6 weeks after MI (untreated patients: open = spontaneous recanalization; treated patients: open = streptokinase-induced recanalization).

†Occluded = no antegrade flow 6 weeks after MI (untreated patients: occluded = persistent occlusion; treated patients: occluded = no effect of streptokinase).

‡Severity = total score (normal = 0, hypokinesia = 1, akinesia = 2, dyskinesia = 3).

Abbreviations: LV = left ventricular; MI = myocardial infarction.

TABLE 3. Ejection Fraction and Severity of Left Ventricular Damage in the Streptokinase-treated and Control Patients with Anterior Myocardial Infarction

<table>
<thead>
<tr>
<th>Infarct vessel open</th>
<th>Controls</th>
<th>Streptokinase</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>34</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>46.1 +/− 13.5</td>
<td>60.3 +/− 10.3</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Severity of LV damage</td>
<td>6.5 +/− 2.8</td>
<td>3.3 +/− 2.7</td>
<td>p &lt; 0.0005</td>
</tr>
</tbody>
</table>

Statistics

Ejection fraction | NS | p < 0.001 |
Severity of LV damage | NS | p < 0.002 |

Infarct vessel occluded

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>28</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction (%)</td>
<td>40.0 +/− 13.2</td>
<td>46.8 +/− 13.9</td>
</tr>
<tr>
<td>Severity of LV damage</td>
<td>7.3 +/− 3.0</td>
<td>6.8 +/− 1.9</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Definitions and abbreviations are as in Table 2.

transmural MI, there is a complete absence of ante-
grade blood flow in the diseased artery in the majority
of patients. The underlying mechanism is not known,
but it appears that in some patients this occlusion
persists and in others spontaneous recanalization occurs.
The same studies suggest that spontaneous recanalization
is an ongoing process, starting in the early hours
after the onset of symptoms and continuing for well
over 24 hours.

In survivors of MI, angiographic assessment of LV
wall motion and ejection fraction is a means of estab-
lishing the severity of postinfarction LV damage. The
severity of asynergy, depicted ventriculographically,
and the amount of muscle loss determined histopatho-
logically are related. Hypokinetic segments show a
small degree of muscle loss, akinetic segments show
more significant amounts of muscle destruction, and
dyskinetic segments show the most extensive muscle
loss and subsequent replacement by fibrous tissue. Our
angiographic scoring system takes account of these
degrees of segmental asynergy and should therefore
reflect the severity of LV damage.

Little agreement exists about the natural history of
LV function after acute MI. Some investigators have
demonstrated no improvement in the LV per-
formance 2–6 weeks after the acute event, whereas
others claim improvement in some patients studied 2
weeks to 6 months and 6–14 months after the acute
event. Studies of coronary occlusion and reperfusion
have shown that a potentially reversible zone may take
1–4 weeks to regain normal contractility. WE
therefore evaluated our patients 6–8 weeks after acute
infarction.

We analyzed the effects of spontaneous recanaliza-
tion and persistent occlusion on LV function and com-
pared these with the effect of streptokinase-induced
recanalization. We found a definite beneficial effect in
patients with inferior MI and spontaneous recanaliza-
tion; the same trend was present in patients with anteri-
or MI and spontaneous recanalization. Patients who
had an anterior MI and successful recanalization with
intracoronary streptokinase had significantly better LV
function than the control patients with spontaneous
recanalization or persistent occlusion. In patients with
inferior MI and successful recanalization, LV function
was not different from that in patients with spontane-
ous recanalization, but was better than that in patients
with persistent occlusion. Although the number of pa-
tients with thrombolysis was too small for statistical
analysis, no worsening of LV function was shown
compared with patients who had persistent occlusion.

Experimental and clinical experience suggests that
reperfusion is beneficial only early after the onset of ischemia. We do not know why and how sponta-
neous recanalization has a favorable effect. Reopen-
ing of the artery may increase the flow to the border zones and thus limit extension of infarction.

Inferior wall MI usually causes a smaller degree of
myocardial necrosis than anterior MI. This was
also shown in our study. The potential for a beneficial
effect in inferior wall MI may therefore be smaller.
Also, in inferior MI, only differences in LV performance were measured, although right ventricular damage occurs in 38–50%. We may therefore have seriously underestimated the potential for improvement in inferior MI.

All patients treated with intracoronary streptokinase also received nifedipine and aspirin. We do not know the extent to which these drugs affected salvage of ischemic myocardium. Experimental studies of the effect of nifedipine on infarct size are conflicting. Some showed a reduction, whereas others showed no effect on infarct size.

Definite conclusions regarding reduction of infarct size with intracoronary streptokinase and subsequent improvement of prognosis for morbidity and mortality must be drawn from carefully designed randomized studies. At this stage, we do not recommend widespread use of intracoronary streptokinase in acute MI.

Acknowledgment

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References


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