Eligibility for and Benefit of Thrombolytic Therapy in Inferior Myocardial Infarction: Focus on the Prognostic Importance of Right Ventricular Infarction

MANFRED ZEHENDER, MD, WOLFGANG KASPER, MD, ELISABETH KAUDER, MD, ANNETTE GIEBEL, MD, MARTIN SCHÖNTHALER, MD, MANFRED OLSCHEWSKI, PhD,* HANJÖRG JUST, MD

Freiburg, Germany

Objectives. This study was undertaken to determine eligibility for and benefit of thrombolytic therapy in patients with acute inferior myocardial infarction with or without right ventricular involvement.

Background. Right ventricular involvement commonly complicates acute inferior myocardial infarction and is considered to have prognostic relevance. We hypothesized that the presence of right ventricular infarction, diagnosed early by ST segment elevation in the right precordial lead (V4R), may be of clinical importance in identifying patients who will benefit most from thrombolytic therapy.

Methods. We studied 200 consecutive patients with acute inferior myocardial infarction to assess the prognostic impact of right ventricular infarction in those considered eligible or ineligible for reperfusion therapy. Prognostic analyses were based on the in-hospital period and a 1- to 6-year follow-up (mean ±SD 37 ± 12 months).

Results. ST segment elevation in lead V4R was a reliable marker of right ventricular infarction (sensitivity 88%, specificity 78%, diagnostic efficiency 83%) in 107 patients (54%) with inferior myocardial infarction. Seventy-one eligible patients (36%) received thrombolytic therapy and had a lower mortality (8% [6 of 71]) and complication (31% [22 of 71]) rate than ineligible patients (mortality rate 25% [32 of 129], p < 0.001; complication rate 56% [72 of 129], p < 0.01). However, the overall benefit of thrombolysis was restricted to patients with right ventricular infarction complicating acute inferior myocardial infarction (with vs. without thrombolysis, respectively: mortality rate 10% vs. 42%, p < 0.005; complication rate 34% vs. 54%, p < 0.05). In the absence of right ventricular infarction, no difference was observed in the mortality (7% vs. 6%, p = NS) and major in-hospital complication (27% vs. 29%, p = NS) rates, whether or not the patient underwent thrombolytic therapy. Posthospital course over 37 ± 12 months was not different in patients with and without right ventricular infarction but was best in all patients considered for reperfusion therapy.

Conclusions. During acute inferior myocardial infarction, the right precordial electrocardiogram is a simple but promising variable to identify a subgroup of patients with an unfavorable course who will benefit most from thrombolytic therapy.

(J Am Coll Cardiol 1994;24:362-9)
(25) showed that improvement of right ventricular function was similar in patients with and without reopening of the right coronary artery by thrombolytic therapy. At present it is uncertain whether the presence or absence of right ventricular involvement during acute inferior myocardial infarction has any influence on the in-hospital course of patients considered eligible or ineligible for thrombolytic therapy (W,26).

ST segment elevation >0.1 mV in the right precordial lead V4 has recently been recognized to be a simple, reliable and widely available marker of right ventricular infarction when assessed during acute inferior myocardial infarction (27-33). In addition, ST segment elevation in lead V4R was also found to be of prognostic relevance, identifying a subgroup of patients with acute inferior myocardial infarction and an increased in-hospital mortality and complication rate (20,34,35).

In a prospective study in 200 consecutive patients with acute inferior myocardial infarction, the prognostic impact of right ventricular infarction in patients found eligible and ineligible for thrombolytic therapy (20,26).

ST segment elevation >0.1 mV in the right precordial lead V4R has recently been recognized to be a simple, reliable and widely available marker of right ventricular infarction when assessed during acute inferior myocardial infarction (27-33). In addition, ST segment elevation in lead V4R was also found to be of prognostic relevance, identifying a subgroup of patients with acute inferior myocardial infarction and an increased in-hospital mortality and complication rate (20,34,35).

In a prospective study in 200 consecutive patients with acute inferior myocardial infarction, the prognostic impact of right ventricular infarction in patients found eligible and ineligible for reperfusion therapy was evaluated during the in-hospital and long-term course.

**Methods**

Patients. In a prospective study from August 1985 to January 1990 we included 200 consecutive and consenting patients admitted to the University Hospital of Freiburg with acute inferior myocardial infarction. The study was approved by the local ethics committee. Inferior myocardial infarction was diagnosed by typical chest pain lasting >30 min, ST segment elevation >0.1 mV in two or more leads of II, III and aVF and an increase in creatine kinase (CK) above twice normal (>140 U/liters) <24 h after admission. Patients were included in the study when symptoms of chest pain lasted <24 h before admission (mean [±SD] 6.1 ± 4.6 h, range 0.5 to 23 h). Clinical data of the patients are presented in Table 1.

**Study protocol.** In all patients a standard 12-lead electrocardiogram (ECG) (leads I to III, aVL, aVF, V1 to V6) and right precordial ECG (leads V3 to V6R) were recorded immediately after admission to the hospital. ST segment deviations were assessed 0.04 s after the J point in all 18 leads. Three consecutive QRS complexes were measured using the PQ level as the isoelectric line. Only ST segment elevations >0.1 mV were evaluated. All prognostic analyses were made by a cardiologist unaware of the clinical status of the patient by using the ST segment elevation in lead V4R >0.1 mV as a marker of right ventricular infarction (29).

The diagnostic accuracy of ST segment elevation in lead V4R indicating right ventricular infarction was determined by 1) autopsy findings (27,33); 2) left/right ventriculography and coronary angiography (the criterion was wall motion abnormalities or occlusion or severe stenosis of the right coronary artery >80% proximal to the right ventricular branch [36]); 3) technetium-99m pyrophosphate imaging (15 mCi of technetium-99m coupled with 5 mg of stannous pyrophosphate; the criterion was focal uptake of the right ventricle [15,37]); and 4) invasive hemodynamic measurements (the criterion was a right atrial pressure equal to the pulmonary capillary pressure or a severe noncompliant pattern [33,38]).

Hemodynamic measurements and technetium-99m pyrophosphate imaging were considered only when performed within the acute phase of myocardial infarction (<24 h). Sensitivity (percent of patients with right ventricular infarction correctly identified by ST segment elevation in lead V4R), specificity (percent of patients without right ventricu-

---

| Table 1. Clinical Characteristics and Hospital Outcome in 200 Consecutive Patients With Acute Inferior Myocardial Infarction, With or Without Thrombolytic Therapy |
|--------------------------------------------------|--------------------------------------------------|
| Patients With | Patients Without |
| Thrombolysis (n = 129) | Thrombolysis (n = 71) |
| **Clinical characteristics** | **Clinical characteristics** |
| Gender (male/female) | 58/13 | 95/34 |
| Mean (±SD) age (yr) | 61 ± 7 | 67 ± 11 |
| Previous myocardial infarction | 8 (11%) | 25 (19%) |
| Max CK >1,000 U/liter | 27 (38%) | 34 (26%) |
| Shock on admission | 7 (10%) | 15 (12%) |
| ST segment elevation on ECG lead V4R >0.1 mV | 41 (58%) | 66 (51%) |
| **Hospital outcome** | **Hospital outcome** |
| Mortality | 6 (9%) | 32 (25%) |
| Cardiogenic shock | 8 (11%) | 23 (18%) |
| Ventricular fibrillation | 9 (13%) | 22 (17%) |
| Sustained VT | 10 (14%) | 14 (13%) |
| Complete AV block | 7 (10%) | 15 (12%) |
| Pacing requirement | 4 (5%) | 15 (12%) |
| Myocardial rupture, tamponade | 8 (12%) | 15 (12%) |

AV = atrioventricular; CK = creatine kinase; ECG = electrocardiogram; Max = maximal; VT = ventricular tachycardia.
lary infarction without ST segment elevation in lead V4R and diagnostic efficiency of ST segment elevation in lead V4R (patients correctly identified by the presence or absence of ST segment elevation in lead V4R) were calculated for each of the four diagnostic tests. Thus, ST segment elevation in lead V4R showed a high diagnostic efficiency for right ventricular infarction compared with autopsy findings [18 patients] sensitivity 88% [14 of 16], specificity 50% [1 of 2], diagnostic accuracy 83% [15 of 18]; coronary angiography/ right ventriculography ([118 patients] sensitivity 89% [55 of 62], specificity 77% [43 of 56], diagnostic accuracy 83% [98 of 118]); technetium-99m pyrophosphate imaging ([92 patients] sensitivity 92% [48 of 52], specificity 80% [32 of 40], diagnostic accuracy 87% [80 of 92]); and hemodynamic measurements ([68 patients] sensitivity 76% [28 of 37], specificity 81% [25 of 31], diagnostic accuracy 78% [53 of 68]). Overall diagnostic accuracy was calculated by using the results of the first test in each patient according to the previous sequence (autopsy findings [18 patients], angiographic/ventriculographic findings [112 patients], technetium-99m pyrophosphate imaging [37 patients], hemodynamic findings [20 patients]). In 13 patients none of the four tests could be adequately performed (e.g., early death, technical reasons), and they were excluded from this analysis.

Thrombolytic therapy. Thrombolytic therapy was used in all eligible patients. Eligibility was defined before beginning the study as follows: infarct symptoms lasting ≤6 h; age ≤75 years; patient consent; no contraindications, including poorly controlled hypertension (>180 mm Hg systolic or >110 mm Hg diastolic blood pressure); active bleeding; recent surgery or significant trauma; and any cerebrovascular accident or neoplasm (1.39). Thrombolytic therapy was performed using either intravenous streptokinase (1.5 MIU in 1 h), anisoylated plasminogen streptokinase (30 mg in 5 min) or recombinant tissue-type plasminogen activator (100 mg in 3 h). Postthrombolytic therapy consisted of heparin (500 to 1,000 U/h intravenously), adjusted to keep the partial thromboplastin time at 1.5 to 2 times the control level for >24 h, and aspirin (100 mg/day). Coronary balloon angioplasty was not performed routinely after thrombolytic therapy.

Prognostic evaluations. The in-hospital and long-term course was determined in all patients. The prognostic impact of ST segment elevation in lead V4R was evaluated in patients eligible or ineligible for thrombolysis with regard to mortality and the occurrence of major in-hospital complications, including ventricular fibrillation, sustained ventricular tachycardia (>30 s or causing hemodynamic intolerance), cardiogenic shock (systolic blood pressure <90 mm Hg for >30 min, together with signs of impaired peripheral circulation or necessity of catecholamine administration), myocardial rupture, third-degree AV block and asystole requiring temporary or permanent cardiac pacing and reinfarction. All complications were analyzed by whether they occurred <24 h after admission or during the remaining in-hospital period. In patients with evidence of right ventricular infarction, volume loading was the therapy of choice; nitrates were given only in the presence of pulmonary capillary wedge pressure ≥15 mm Hg.

All patients were followed up for >1 year. At the end of follow-up, 141 patients were still alive. The observation period ranged from 12 to 76 months (mean 37 ± 12 months). Information about vital status, including mode of death and follow-up events (e.g., reinfarction, cardiac pacing, aortocoronary artery bypass, coronary angioplasty), was obtained from each patient or the general practitioner by means of a standardized questionnaire.

Statistical analysis. Mean values ± SD were calculated for continuous variables and absolute and relative frequencies for discrete variables (40). Differences between groups were examined for statistical significance by use of a two-sample t test for continuous variables and the chi-square test for discrete variables. The distribution of the patient survival times, allowing for examination of long-term survival after hospital discharge, was estimated using the Kaplan-Meier method. The independent prognostic relevance of selected clinical variables with respect to long-term survival was assessed by applying the Cox proportional hazards multiple regression model to patient survival times and included the following clinical variables: gender, age, history of myocardial infarction, time to treatment, comorbid disease, CK >1,000 U/liter on admission, cardiogenic shock on admission and presence of ST segment elevation in lead V4R >0.1 mV on admission. The statistical significance of these variables within the multivariate models was evaluated using the Wald test (40). All tests of significance were two tailed and used a significance level of p ≤ 0.05.

Results

ST segment elevation in lead V4R during the first ECG on admission was observed in 107 patients (54%). When compared with autopsy findings, left/right angiography/ventriculography, technetium-99m pyrophosphate imaging and hemodynamic measurements, ST segment elevation ≥0.1 mV in lead V4R had an overall sensitivity of 88%, a specificity of 78% and a diagnostic efficiency of 83% for demonstrating right ventricular infarction.

Prognostic impact of right ventricular infarction during acute inferior myocardial infarction. During the in-hospital period, 38 (19%) of 200 patients with acute inferior myocardial infarction died, and 94 (47%) had major complications. When acute inferior myocardial infarction was complicated by right ventricular infarction, the in-hospital mortality rate increased from 6% (6 of 93) to 31% (33 of 107) (p < 0.0001), and the complication rate increased from 28% (26 of 93) to 64% (68 of 107) (p < 0.0005).

Thrombolytic therapy during acute inferior myocardial infarction. Seventy-one patients (36%) with acute inferior myocardial infarction were considered eligible for thrombolytic therapy and underwent this form of treatment. The
clinical data of patients with and without reperfusion therapy are summarized in Table 1.

Patients who underwent thrombolytic therapy had a lower in-hospital mortality (6% [6 of 71]) and complication (31% [22 of 71]) rate than those considered ineligible for thrombolysis (25% [32 of 129], p < 0.001; 56% [72 of 129], respectively, p < 0.01). In the two groups deaths (<24 h 13 patients; >24 h 25 patients) and major complications (<24 h 58 patients; >24 h 36 patients) were highest during the 1st 24 h after admission. However, in multivariate analysis when age, gender, peak CK, comorbid disease, time to treatment, previous myocardial infarction and shock on admission were considered, reperfusion therapy was of independent prognostic importance only for in-hospital mortality (Table 2). Survival analysis for patients found eligible or ineligible for reperfusion therapy is presented in Figure 1.

Prognostic impact of right ventricular infarction in patients eligible or ineligible for thrombolysis. Right ventricular infarction was present in 41 (58%) of 71 patients with and 66 (51%) of 129 patients without thrombolysis. In the presence of right ventricular infarction, patients undergoing thrombolysis showed a 4.2-fold lower mortality (10% vs. 42%, p < 0.001) and 2.4-fold lower complication (34% vs. 54%, p < 0.05) rate than those considered ineligible for thrombolysis. In the absence of right ventricular infarction there was no difference in mortality (7% [2 of 30] vs. 6% [4 of 63], p = NS) and complication (27% [8 of 30] vs. 29% [18 of 63], p = NS) rate regardless of whether the patient underwent reperfusion therapy or not.

ST segment depression in the left precordial leads (≥0.1 mV in two or more leads V1 to V5) was observed in 87 (43%) of 200 patients. In these patients the mortality rate was higher (22% [19 of 87] vs. 11% [13 of 113], p < 0.05) when the patient was considered ineligible for thrombolytic therapy. In patients undergoing thrombolysis, no difference in in-hospital mortality rate was observed (3% [3 patients] vs. 3% [3 patients], p = NS). Adding patients with left precordial ST segment depression and right precordial ST segment elevation did not have superior prognostic impact compared with right precordial ST segment elevation alone.

When each major complication was analyzed separately, patients with right ventricular infarction showed a lower incidence of cardiogenic shock (p < 0.05), asystole (p < 0.05), third-degree AV block and pacing requirement when reperfusion therapy was used. In patients without right ventricular infarction there was an inverse but nonsignificant trend for the majority of major complications (Fig. 2). Similar observations for the overall benefit of thrombolysis were made when any of the criteria evidencing right ventricular infarction during angiographic, scintigraphic or hemodynamic measurements replaced ST segment elevation in the right precordial leads.

Figure 1. Kaplan-Meier analysis of cumulative survival rates for all 200 patients with acute inferior myocardial infarction during a follow-up of 1 to 6 years (mean 3.1 ± 1 years). Survival rates are stratified by the presence or absence of reperfusion therapy. Level of significance describes the hospital and follow-up periods.
The prognostic impact of right ventricular infarction in patients with and without reperfusion therapy verified by multivariate analysis was visualized using Kaplan-Meier analyses. In patients found eligible for thrombolytic therapy, survival was very similar whether or not the patient had right ventricular infarction (Fig. 3 (top)). However, when the patient was ineligible for thrombolysis, the presence of right ventricular infarction markedly determined the patient's prognosis (Fig. 3 (bottom)). In addition to eligibility for thrombolysis, Kaplan-Meier graphics were influenced by other clinical variables that were different in patients with and without thrombolysis. After discharge from hospital, the long-term prognosis was somewhat better in patients who underwent thrombolytic therapy (2 [3%] of 65 patients with vs. 18 [19%] of 97 patients without thrombolysis died, p < 0.01; 5 [8%] of 65 patients with vs. 9 [9%] of 97 patients without thrombolysis had a reinfarction, p = NS) independent of the presence or absence of right ventricular infarction. This effect is mainly the result of the lower mean age of the patients who underwent thrombolytic therapy.

**Discussion**

In a consecutive series of 200 patients with inferior myocardial infarction, 36% were found eligible for thrombolysis. Right ventricular infarction was reliably evidenced from ST segment elevation in the right precordial leads and was present in 57% of patients. In the presence of right ventricular infarction, thrombolytic therapy was associated with a lower in-hospital mortality (4.2-fold, p < 0.001) and complication (1.6-fold) rate (p < 0.01). In patients without right ventricular infarction, the in-hospital mortality and complication rates were similar whether or not the patient underwent thrombolysis.

**Prognosis of inferior myocardial infarction and use of thrombolytic therapy.** The use of thrombolytic therapy after acute inferior myocardial infarction remains controversial. Bates (41) recently reviewed the effect of thrombolysis on left ventricular function and observed a beneficial effect of reperfusion therapy. Other studies (42,43) demonstrated a significant improvement in infarction zone function after reperfusion therapy for inferior infarction. In a recent meta-analysis by Grines and DeMaria (1) in 12,014 patients with
Acute inferior infarction, thrombolysis reduced the 2-week to
1-year mortality rate from 8.7% to 6.8% (p < 0.0001). 
However, data were collected from nine studies, of which 
six smaller studies failed to prove a significant benefit of 
 thrombolysis.
To improve the overall benefit of thrombolytic therapy in 
inferior myocardial infarction, additional criteria have been 
evaluated to identify subgroups of patients who would 
benefit most from this form of therapy (6,44-48). Right 
ventricular infarction, present in 40% to 50% of patients with 
inferior myocardial infarction, has been suggested most 
recently to identify patients with an unfavorable course 
(14-20). However, data on the benefit of thrombolytic ther-
apy in these patients are limited. In the TIMI II trial, 
thrombolytic therapy reduced the risk for right ventricular 
dysfunction from 42% to 13% (23). In two smaller studies 
(24,25) improvement in right ventricular function as a result 
of reperfusion therapy remained controversial.
Diagnostic assessment of right ventricular infarction during 
acute inferior infarction. To guide thrombolytic therapy, 
diagnostic assessment of right ventricular infarction must be 
simple, reliable and widely and rapidly available after the 
patient is admitted to the hospital. These criteria are best and 
only met when the right precordial surface ECG is used to
diagnose right ventricular infarction (33). In a recent review 
by Rohalino et al. (29), ST segment elevation ≥0.1 mV in the 
right precordial lead V4R showed a diagnostic accuracy 
>80% and thus was superior to all other ECG criteria. In the 
present study, 54% of patients with inferior infarction 
showed ST segment elevation in lead V4R on admission. 
In comparison with invasive, scintigraphic and autopsy find-
ings, ST segment elevation in lead V4R had a sensitivity of 
88% and a diagnostic accuracy of 83% for evidencing right 
ventricular infarction. ST segment elevation in lead V4R 
evidencing right ventricular infarction was also shown by 
our (49) and other working groups (20,34,35) to be a strong 
and independent prognostic variable.
Importance of right ventricular infarction for the benefit of 
thrombolytic therapy. On the basis of previous recommenda-
tions (1,39), 36% of patients with acute inferior infarction 
were found eligible for reperfusion therapy. Patients under-
going thrombolysis showed a 3.1-fold lower mortality and a 
1.8-fold lower complication rate during the in-hospital 
course. This effect was considered to be a result of the 
benefit of thrombolysis, as well as the better overall prog-
nosis of patients considered eligible for thrombolytic therapy 
(1,2).
The prevalence of right ventricular infarction was similar 
in patients considered eligible or ineligible for reperfusion 
therapy. In patients with right ventricular infarction, the use 
of thrombolytic therapy was associated with a 4.2-fold lower 
in-hospital mortality and a 2.4-fold lower complication rate. 
In particular, the incidence of cardiogenic shock and brady-
cardic rhythm disturbances was significantly lower in pa-
patients undergoing reperfusion therapy, whereas ventricular 
tachyarrhythmias were similar in the two groups. Thus, in 
in patients undergoing thrombolysis, due to rapid reperfu-
sion to minimize myocardial damage, right ventricular infarction 
diagnosed on admission lost its prognostic relevance for 
immediate and long-term survival. In contrast, when the 
patient was ineligible for thrombolysis, right ventricular 
infarction was associated with a significant worsening of the 
prognosis. The same observation was made when the pre-

cence of right ventricular infarction was demonstrated by 
scintigraphic, hemodynamic or angiographic measurements.
Because multivariate analysis had shown that right ven-
tricular infarction was an independent prognostic value, 
these data strongly argue for a superior beneficial effect on 
prognosis in patients who present with right ventricular 
infarction complicating acute inferior myocardial infarction 
and are considered for thrombolysis. These data may also 
question the overall benefit of thrombolysis in patients with 
inferior infarction not complicated by right ventricular in-
farction and may help to settle the earlier controversy 
surrounding the general benefit of thrombolytic therapy. 
These data are also of interest for the 60% to 80% of patients 
with contraindications for thrombolysis who are known to 
have a worse prognosis (1). When relative contraindications 
may limit the use of reperfusion therapy, right ventricular
infection should be a strong argument for the use of thrombolytic therapy or for the early use of direct percutaneous transluminal coronary angioplasty.

After discharge from hospital, the long-term course of patients with and without right ventricular myocardial infarction was similar. Patients who underwent reperfusion therapy showed better long-term survival in both groups because of the benefit of thrombolysis as well as selection criteria (e.g., age <75 years).

**Study limitations.** Our analyses were not based on a randomized study design. However, in a multivariate analysis of thrombolytic therapy none of the clinical variables were found to independently reduce the prognostic impact of right ventricular infarction. Therefore, our data appear to have clinical relevance, particularly because, at present, data with respect to the prognostic impact of right ventricular infarction during thrombolytic therapy are very limited or not available. In addition, on the basis of our present knowledge of the benefit of thrombolytic therapy and clinical outcome in patients with right ventricular infarction, it is no longer possible to study patients with and without right ventricular infarction randomized to receive either thrombolytic therapy or placebo because of substantial ethical considerations. Therefore, our data represent the largest group of patients with right ventricular infarction studied for prognostic reasons and may provide an important basis for further studies addressing the importance of right ventricular infarction in thrombolytic therapy.

**Clinical implications.** Involvement of the right ventricle during acute inferior myocardial infarction is common, and its early and reliable recognition by ST segment elevation in lead V5R has important therapeutic implications. Thirty-six percent of patients presenting with inferior myocardial infarction were considered eligible for reperfusion therapy. In patients with right ventricular infarction complicating inferior myocardial infarction, thrombolytic therapy was associated with a significantly lower in-hospital mortality and complication rate. Patients without right ventricular involvement have a better prognosis overall after inferior myocardial infarction that seems to be independent of whether reperfusion therapy is used. During clinical routine, the presence of right ventricular infarction should be considered as an additional argument for treating the patient with thrombolytic therapy or direct coronary angioplasty, especially when only relative contraindications, such as borderline age or time after onset of symptoms, are present.

**References**


25. Verani MS, Tortoledo FE, Batty JW, Raizner AE. Effect of coronary


