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Influence of Infarct Location on the Prognostic Impact of Thrombolysis in Myocardial Infarction (TIMI) Perfusion Grade of the Infarct-Related Artery after Thrombolysis for Acute Myocardial Infarction

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The influence of the infarct location on the impact of the 90 minute patency status of the infarct vessel on in-hospital mortality was evaluated in 1569 patients treated with thrombolysis for acute myocardial infarction in seven angiographic trials with similar design. Of the 1569 patients 1512 (96.3 %) had a 90-minute angiogram of the infarct-related artery. In 22 patients the infarct vessel could not be determined angiographically. In the remaining 1490 patients the infarct vessel was the left anterior descending coronary artery in 42 %, the right coronary artery in 44 % and the left circumflex coronary artery in 14 %. The in-hospital mortality in the 1490 patients was 4.2 %. The infarct location as determined by the baseline ECG was anterior in 42.6 % and inferior in 57.4 %, while the mortality was 5.5 % and 3.1 % in patients with anterior and inferior infarctions, respectively ($p = 0.035$). The mortality rates in patients with TIMI grade 0/1, 2 and 3 flow were 10.9 %, 6.2 % and 3.0 % anterior infarcts and 5.4 %, 4.1 % and 1.7 % for inferior infarcts, respectively.

This is the first study which demonstrated differences in the prognostic impact of 90-minute TIMI grade 2 flow of the infarct-vessel related to infarct location. While mortality in patients with inferior infarcts and TIMI 2 patency is similar to that with TIMI 0/1 patency, in patients with anterior infarcts, mortality with TIMI 2 flow is better than with TIMI 0/1 patency, but not equivalent to TIMI 3 flow. Therefore although TIMI 3 patency should be the primary aim of any reperfusion therapy, achievement of TIMI 2 patency in patients with anterior infarcts should no longer be considered as therapy failure. *J Clin Basic Cardiol 2000; 3: 43–5.*

Key words: thrombolysis, acute myocardial infarction, prognosis, infarct location

Thrombolytic therapy has been shown to reduce mortality of patients with evolving acute myocardial infarction [1]. The aim of this therapy is the early restoration of blood flow in the infarct related artery. Several studies have shown that complete (Thrombolysis in Myocardial Infarction Grade 3 flow) patency of the infarct vessel 90 minutes after the initiation of thrombolytic therapy is associated with a remarkably low in-hospital mortality of about 3–4 % [2, 3], while mortality in patients with TIMI 2 flow was not statistically better than in patients with occluded arteries (TIMI 0/1 flow). In the Fibrinolytic Therapy Trialists Collaborative Group data base the impact of thrombolysis on survival was most pronounced in the patients with anterior infarctions and considerably lower in patients with inferior infarct location [1]. Therefore we sought to examine if there is any difference in the impact of 90-minute infarct vessel perfusion status on short term mortality between patients with anterior or inferior infarct location.

Methods

Patients aged > 18 years with acute myocardial infarction diagnosed by typical clinical symptoms ≥ 30 min and ≤ 6 h duration and by ST segment elevations in the electrocardiogram (≥ 3 mm in two precordial or ≥ 2 mm in two limb leads) were enrolled in seven multicenter thrombolytic trials with similar design [4–11]. Of the 1584 patients who entered the studies, 473 were treated with front-loaded rt-PA (15 mg bolus, 50 mg over 30 min, 35 mg over 60 min), 124 with 70 mg of rt-PA/90 min, 210 with a bolus of 30 mg of anisoylated plasminogen streptokinase activator complex (APSAC), 121 with urokinase (1.5-million U bolus and 1.5-million over 60 min), 194 with bolus injections of reteplase of 10 million U (n = 43), 15 million U (n = 100) or 10 million U and another 5 million U after 30 min (n = 51) and 447 with 1.5 million U streptokinase over 60 min. Fifteen patients received no thrombolytic treatment because of withdrawal of informed consent or detection of a contraindication after study entry.

The common main endpoint of the seven studies was the 90-minute patency of the infarct related artery as determined by angiography. Each angiogram was evaluated centrally by a core laboratory by at least two independent observers. The perfusion of the infarct-related artery was graded according to the Thrombolysis in Myocardial Infarction (TIMI) study criteria [12].

Of 1569 patients 1512 (96.3 %) had a 90-minute angiogram of the infarct-related artery. In 22 patients the infarct vessel could not be determined angiographically. In the remaining 1490 patients the infarct vessel was the left anterior descending coronary artery in 42 %, the right coronary artery in 44 % and the left circumflex coronary artery in 14 %. The in-hospital mortality in the 1490 patients was 4.2 %. Patients with the left anterior descending coronary artery as infarct vessel had a mortality rate of 5.7 % *versus* 3.3 % and 2.5 %, respectively, in patients with the right and left circumflex coronary artery as the infarct vessel. These differences were not statistically significant in the univariate chi-square test ($p = 0.54$), presumably because the patency rate (TIMI grade 2/3 flow) of the left anterior descending artery was higher than that of the left circumflex or right coronary artery (77.8 % *versus* 73.0 % and 68.6 %, respectively, $p = 0.001$) or because a left circumflex artery needs a larger ischaemic area to achieve the required ST elevations. The influence of the TIMI flow grade on mortality according to the different infarct vessels is shown in Table 1.

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Table 1. In-hospital mortality in patients with thrombolysis for acute myocardial infarction differentiated to 90-minute patency and infarct-related artery

90-min patency	TIMI 0/1	TIMI 2	TIMI 3	p-value
Infarct vessel				
LAD	16/140 (11.4 %)	8/129 (6.2 %)	12/362 (3.3 %)	0.0005
RCA	12/202 (5.9 %)	3/101 (3.0 %)	6/340 (1.8 %)	0.0181
LCX	2/54 (3.7 %)	2/20 (10.0 %)	1/126 (0.8 %)	0.1485

LAD = left anterior descending coronary artery; RCA = right coronary artery; LCX = left circumflex coronary artery

Table 2. Influence of infarct location and early perfusion status of the infarct-related artery on in-hospital mortality after thrombolysis

90 min patency	TIMI 0/1	TIMI 2	TIMI 3	p-value
Infarct location				
anterior	16/146 (10.9 %)	8/129 (6.2 %)	11/363 (3.0 %)	< 0.0001
inferior	14/259 (5.4 %)	5/123 (4.1 %)	7/476 (1.5 %)	0.0048
Total	30/405 (7.4 %)	13/252 (5.1 %)	18/839 (2.1 %)	< 0.0001

The infarct location as determined by the baseline ECG was anterior in 42.6 % and inferior in 57.4 %, while the mortality was 5.5 % and 3.1 % in patients with anterior and inferior infarctions, respectively (p = 0.035). The mortality rates according to TIMI flow at 90 minutes in patients with anterior and inferior infarct location are shown in Table 2. The mortality difference between TIMI 0/1 and TIMI 3 flow was statistically significant for the entire group (p < 0.0001) and the subgroups of patients with inferior (p = 0.006) and anterior infarct location (p = 0.0007). Between TIMI 0/1 and TIMI 2 flow there was neither a statistically significant difference in the entire group (p = 0.33) nor in the subgroups of patients with anterior (p = 0.2) or inferior (p = 0.8) infarct location. The mortality difference between TIMI 2 and TIMI 3 flow was statistically significant in the entire group (p = 0.01), borderline significant in patients with inferior infarcts (p = 0.07), but not significant in patients with anterior infarct location (p = 0.11).

Discussion

This is the first analysis which investigates the influence of infarct location on the prognostic value of the 90-minute TIMI flow on short-term mortality. Previous studies have shown that not only a patent epicardial artery but also an unimpaired flow (TIMI grade 3 flow) 90 minutes after the initiation of thrombolytic therapy is required to limit infarct size and to reduce mortality in patients with acute myocardial infarction [2–3, 13–15]. However, in a recent meta-analysis performed in 4687 pooled patients with 90-minute angiography (Figure 1), a significant better survival was observed in patients with TIMI 2 flow compared to patients with an occluded infarct vessel (TIMI 0/1 flow), although TIMI 2 flow was not equivalent to TIMI 3 flow [16]. This clinical benefit of TIMI 2 flow might be different in patients with different mortality risk, eg, inferior and anterior infarct location. In our analysis a mortality-benefit of thrombolysis in patients with inferior infarctions was seen only in patients with TIMI grade 3 flow, while there was a comparable mortality of 4–5 % in patients with TIMI 0/1 and 2 flow. In contrast, in patients with anterior infarctions the achievement of vessel patency, even with an compromised anterograde flow (TIMI 2), was associated with a better prognosis than an occluded infarct vessel. While

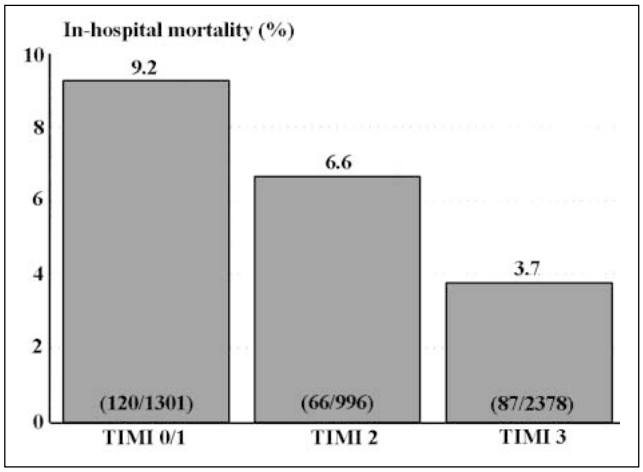

Figure 1. In-hospital mortality related to 90-minute TIMI patency after thrombolysis in 4687 patients with acute myocardial infarction [16] (TIMI 0/1 *versus* TIMI 2, p = 0.029; TIMI 0/1 *versus* TIMI 3, p < 0.0001; TIMI 2 *versus* TIMI 3, p = 0.0003)

in most of the previous studies mortality in patients with TIMI 2 flow was closer or even similar to the mortality with TIMI 0/1 flow, this is the first analysis to show a benefit of TIMI 2 flow in this subgroup of patients with a higher mortality risk. In the GUSTO-I study about 2/3 of the patients with TIMI 2 flow at 90 minutes had improved to TIMI 3 flow at follow-up, while only 6 % had an occluded artery at the 5–7 day angiography [17]. Patients with TIMI 2 at 90 minutes and TIMI 3 at 5–7 days demonstrated a measurable improvement in left ventricular function, which was intermediate between that of patients with vessels that were persistently closed and those who had persistently TIMI 3 flow. These data suggest that early TIMI 2 flow may be sufficient to provide prolonged myocyte viability, which will further improve if flow normalizes, and this mechanism might be especially important in patients with anterior infarcts.

Therefore, although TIMI 3 patency still is the primary aim of any reperfusion therapy, achievernent of TIMI 2 patency in patients with anterior infarcts should no longer be considered as therapy failure [18].

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