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Clinical Investigations

Long-Term Prognosis of Young Patients after Myocardial Infarction in the Thrombolytic Era

JÖRG-UWE FÜLLHAAS, M.D., PETER RICKENBACHER, M.D., MATTHIAS PFISTERER, M.D.,* RUDOLF RITZ, M.D.

Divisions of Intensive Care Medicine and *Cardiology, Department of Internal Medicine, University Hospital, Basel, Switzerland

Summary

Background: Myocardial infarction (MI) in young adults is a rare event. In the Framingham study, the 10-year incidence rate of MI per 1,000 was 12.9 in men 30–34 years old. Overall, 4–8% of patients with acute MI are ≤40 years old.

Hypothesis: It was the purpose of this study to assess the in-hospital and long-term morbidity and mortality in patients ≤40 years old with acute myocardial infarction compared with older patients in the thrombolytic era.

Methods: A consecutive series of 75 patients aged ≤40 years (mean 35.0 ± 4.8) with acute myocardial infarction was compared with an equally sized group of patients aged >40 years (mean 65.1 ± 9.8).

Results: Thrombolysis or direct percutaneous transluminal coronary angioplasty was performed in 52 versus 24% (p = 0.0004) and 5.3 versus 2.7% (p = NS) in younger and older patients, respectively. Significantly fewer young patients had multivessel disease (28 vs. 64%, p < 0.004). No in-hospital mortality was observed in patients with reperfusion therapy irrespective of age. After a mean followup time of 47 ± 35 months, cardiac mortality was 0 and 11% (p < 0.03), respectively, in young and older patients with, and 3 versus 24% (p < 0.02) without reperfusion therapy, respectively. In addition, significantly fewer patients in the younger age group developed recurrent angina pectoris (12 vs. 39%, p = 0.0004) or congestive heart failure (9 vs. 34%, p = 0.0005) irrespective of reperfusion therapy.

Conclusion: Our observations demonstrate that long-term prognosis after myocardial infarction in young patients is excellent in the thrombolytic era.

Address for reprints:

Peter Rickenbacher, M.D.
Division of Intensive Care Medicine
Department of Internal Medicine
University Hospital
Petersgraben 4
CH-4031 Basel, Switzerland

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Introduction

Myocardial infarction (MI) in young adults is a rare event. In the Framingham study,[1] the 10-year incidence rate of MI per 1,000 was 12.9 in men 30–34 years old. Overall, 4–8% of patients with acute MI are ≤40 years old.[2]

Several earlier studies have demonstrated significant differences in risk factor profile,[3–14] angiographic appearance,[4–7, 15–22] and outcome in younger and older patients with MI.[4, 8, 11, 13, 23–31] However, whether the better long-term survival of young patients is maintained in the thrombolytic era is unknown. Therefore, it was the purpose of this study to assess the in-hospital and long-term morbidity and mortality in a consecutive series of patients ≤40 years old, with acute MI, in the thrombolytic era and to compare them with a control group of patients >40 years old.

Methods

Patients

From January 1986 to December 1995, 75 consecutive patients ≤40 years old (mean 35.0 ± 4.8 years) admitted to the coronary care unit of the University Hospital Basel with confirmed acute MI were retrospectively identified from our coronary care unit (CCU) registry and formed the study population (Group 1). For each index patient, the next patient >40 years old (mean 65.1 ± 9.8 years), hospitalized with acute MI, was included in an equally sized control group (Group 2). The diagnosis of MI was based on two or more of the following criteria: typical chest pain of >30 min duration, characteristic cardiac enzyme level elevation, and typical electrocardiographic (ECG) changes.

Treatment during the CCU phase was standardized according to written, yearly updated guidelines. Thrombolytic therapy was implemented in these guidelines in March 1986 and direct percutaneous transluminal coronary angioplasty (PTCA) was performed in selected cases with contraindications to thrombolytic therapy.

The following demographic and clinical parameters were recorded during the hospital stay: age, gender, cardiovascular risk factors, history of previous MI, blood pressure and Killip on admission, treatment in the CCU, peak creatine kinase

(CK)-MB values, infarct localization, complications, coronary angiographic findings, interventions [PTCA, coronary artery bypass grafting (CABG)], and cardiac mortality.

Follow-Up

Follow-up information regarding cardiac events (angina, symptoms of congestive heart failure, reinfarction) and revascularization procedures was obtained by telephone interviews with the patient, the treating physician and/or family members, and from review of hospital records in May 1996. Information concerning death was obtained from hospital records, treating physician, family members, and/or official death registries.

Patients living in other countries (n = 4, one in Group 1, three in Group 2) were excluded from follow-up, but with that exception, follow-up was complete in all patients.

Statistical Analysis

Results are presented as mean ± 1 standard deviation for clinical and as mean ± 1 standard error for actuarial data. The younger (Group 1) and older (Group 2) patient groups were compared using the chi-square test for discrete variables and the unpaired *t*-test for continuous variables. Actuarial survival in the two groups was examined with Kaplan-Meier procedures to contrast absolute survival differences and by log rank test to assess for equality of survival curves. Subgroup analyses were performed in patients with thrombolysis/direct coronary angioplasty (reperfusion therapy). A p value of < 0.05 was considered statistically significant. Commercially available statistics software (Statview 4.01, Abacus Concepts, Inc.) was used.

TABLE I Baseline characteristics

	Group 1 (n = 75)	Group 2 (n = 75)	p Value
Age (years)	35.0 ± 4.8	65.1 ± 9.8	< 0.0001
Male gender (%)	85	72	0.04
Current smokers (%)	75	50	< 0.002
Arterial hypertension (%)	19	37	< 0.02
Hypercholesterolemia (%)	53	49	< 0.7
Diabetes mellitus (%)	7	15	< 0.2
Family history of CAD (%)	33	22	< 0.2
Previous MI (%)	9	23	< 0.03

Abbrevations: CAD = coronary artery disease, MI = myocardial infarction.

TABLE II Coronary care unit course

	Group 1 (n = 75)	Group 2 (n = 75)	p Value
Systolic BP at entry (mmHg)	134 ± 24	135 ± 28	<0.9
Heart rate at entry (beats/min)	81 ± 17	78 ± 17	<0.3
Killip class I at entry (%)	95	61	<0.0001
Killip class II at entry (%)	4	32	
Killip class III at entry (%)	0	3	
Killip class IV at entry (%)	1	4	
Maximal CK-MB (U/l)	213 ± 167	202 ± 235	<0.8
Q-wave infarction (%)	67	60	<0.5
Anterior infarction (%)	39	37	<0.9
Inferior infarction (%)	55	47	<0.4
Thrombolysis (%)	52	24	0.0004
Direct coronary angioplasty (%)	5	3	<0.5
Beta blockers (%)	84	64	<0.005

Abbreviations: BP = blood pressure, CK = creatine phosphokinase.

Results

Baseline Characteristics

Baseline characteristics of the two groups are shown in Table I. Younger (Group 1) compared with older (Group 2) patients were significantly more often of male gender (85 vs. 72%, p = 0.04) and current smokers (75 vs. 50%, p<0.002). Arterial hypertension (19 vs. 37%, p<0.02) and a history of previous myocardial infarction (9 vs. 23%, p<0.03) were significantly less prevalent in the younger group.

Hospital Course

Findings during the CCU course are shown in Table II. On admission, significantly more Group 1 patients were in Killip class I (95 vs. 61%, p < 0.0001). Thrombolysis was performed in 52 versus 24% (p = 0.0004) of patients, and 5.3 versus 2.7% (p = NS) underwent direct PTCA in Group 1 and Group 2, respectively. The remaining Group 1 and 2 patients were not eligible for thrombolysis for the following reasons: contraindications (28 vs. 16%), delayed admission to hospital (19 vs. 40%), no ECG criteria on admission (11 vs. 35%), and miscellaneous reasons (42 vs. 9%). Maximal CK-MB values, infarct location, and proportion of Q-wave infarctions were similar between the two groups. More patients in Group 1 were treated with beta-blocking agents (84 vs. 64%, p < 0.005) compared with Group 2.

In the 91 patients undergoing coronary angiography [63 (84%) in Group 1, 28 (37%) in Group 2], significantly fewer patients in Group 1 had multivessel disease (28 vs. 64%, p < 0.004) and no-vessel disease (< 50% diameter stenosis) was found in 14% of Group 1 but not in Group 2 patients (Table III). Coronary angioplasty or CABG during the initial hospitalization was performed in 48% of Group 1 versus only in 16% of Group 2 patients (p < 0.0001).

In-hospital complications in Groups 1 and 2 (Table IV) and in the subgroups of patients with and without reperfusion therapy (Table V) were comparable, with the exception of a higher prevalence of congestive heart failure in Group 2 patients (20 vs. 4%, p = 0.02), mainly in the subgroups without reperfusion therapy (24 vs. 6%, p = 0.03). No in-hospital mortality was observed in patients with reperfusion therapy irrespective of age, whereas 6.2 and 7.2% of Group 1 and Group 2 patients without reperfusion therapy died during hospitalization.

Table III Angiographic findings

	Group 1 (n = 63)	Group 2 (n = 28)	p Value
LVEF (%)	60 ± 11	59 ± 12	< 0.8
No vessel disease (%) [a]	14	0	< 0.004
Single-vessel disease	58	36	
Double-vessel disease	20	36	
Triple-vessel disease	8	28	

[a] Diameter stenosis 0– < 50%.
Abbreviation: LVEF = left ventricular ejection fraction.

Table IV In-hospital complications

	Group 1 (n = 75)	Group 2 (n = 75)	p Value
Angina (%)	36	41	<0.6
Reinfarction (%)	4	3	<0.7
Congestive heart failure (%)	4	20	0.02
Cardiogenic shock (%)	5	8	<0.6
Cardiac death (%)	3	5	<0.5

The medication at discharge included aspirin (78 vs. 72%, p = NS), warfarin (11 vs. 22%, p = NS), beta-blocking agents (48 vs. 52%, p = NS), nitrates (4 vs. 23%, p = 0.0006), and diuretics (1.3 vs. 38%, p ≤ 0.0001) in Group 1 and Group 2 patients, respectively.

Follow-Up

The mean follow-up time was 49.1 ± 35.6 months in Group 1 and 44.1 ± 34.7 months in Group 2.

Significantly fewer Group 1 patients developed recurrent angina pectoris (12 vs. 39%, p = 0.0004) and congestive heart failure (9 vs. 34%, p = 0.0005). Late PTCA was performed in 19% of Group 1 and 3% of Group 2 patients (p < 0.006); however, the combined frequency of revascularization procedures (CABG and PTCA) was comparable in the two groups as shown in Table VI. Furthermore, cardiac mortality was significantly lower in Group 1 patients (1 vs. 21%, p < 0.0001). One and 5-year actuarial survival rates for Group 1 and Group 2 patients were 100 and 97% versus 91 and 77%, respectively, as shown in Figure 1.

In the subgroups of patients with and without reperfusion therapy, respectively, (Table VII), Group 1 patients had a better outcome than Group 2 patients with respect to recurrent angina [10 vs. 31% (p < 0.05), and 15 vs. 43% (p < 0.02)], congestive heart failure [10 vs. 38% (p < 0.02), and 7 vs. 33% (p < 0.02)] as well as cardiac death [0 vs. 11% (p < 0.03), and 3 vs. 24% (p<0.02)]. Long-term survival was favorable in Group 1 patients irrespective of reperfusion therapy and in Group 2 patients only with reperfusion therapy. Survival was significantly worse in Group 2 patients without reperfusion therapy compared with the other subgroups (Fig. 2).

Discussion

Young patients with MI have been shown to have a favorable prognosis compared with that in older patients.[3,4,8,11,13,23–27,31] However, most of these studies have been performed in the prethrombolytic era, and to the best of our knowledge no comparison of the long-term outcome of younger patients with and without thrombolysis has been published. Since thrombolysis and direct PTCA have become a well established standard in the treatment of acute MI in the past decade,[32,33] it seemed appropriate to address this question. The main results of the present analysis demonstrate that young patients ≤ 40 years with acute MI had a favorable in-hospital course and long-term prognosis irrespective of reperfusion therapy. In the older age group survival was worse, particularly in patients without reperfusion therapy.

Baseline Characteristics

We observed significant differences in the cardiovascular risk factor profile between the two groups. This is in accordance with a number of previous studies showing that current smoking is more prevalent in younger patients, whereas hypertension and diabetes are less frequent.[3–14] Inconsistent results have been reported with respect to a family history of premature coronary artery disease and hyperlipidemia.[3–5,7,8,11,12]

Table V In-hospital complications in the subgroups of patients with and without thrombolysis/direct coronary angioplasty

	Reperfusion therapy			No reperfusion therapy		
	Group 1 (n = 43)	Group 2 (n = 20)	p Value	Group 1 (n = 32)	Group 2 (n = 55)	p Value
Angina (%)	37	35	< 0.9	34	44	< 0.4
Reinfarction (%)	0	5	< 0.2	9	2	< 0.2
Congestive heart failure (%)	2	10	< 0.2	6	24	0.03
Cardiogenic shock (%)	2	10	< 0.2	9	7	< 0.8
Cardiac death (%)	0	0	1	6	7	< 0.9

TABLE VI Long-term follow-up

	Group 1 (n = 72)	Group 2 (n = 68)	p Value
Follow-up time (months)	49.1 ± 35.6	44.1 ± 34.7	< 0.5
Angina pectoris (%)	12	39	0.0004
Reinfarction (%)	13	19	< 0.4
Congestive heart failure (%)	9	34	0.0005
Cardiac death (%)	1	21	< 0.0001
PTCA (%)	19	3	< 0.006
CABG (%)	9	16	< 0.2
PTCA or CABG (%)	23	18	< 0.5

Abbreviations: PTCA = percutaneous transluminal coronary angioplasty, CABG = coronary artery bypass grafting.

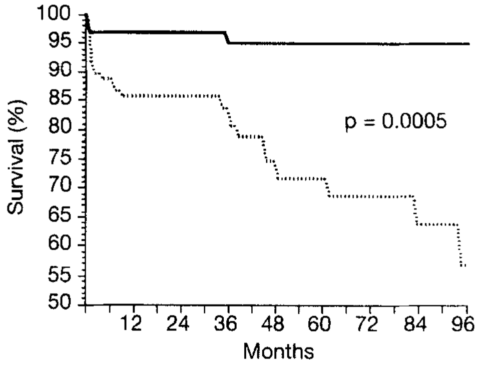

FIG. 1 Comparison of actuarial long-term survival in patients ≤ 40 years (Group 1) and > 40 years (Group 2) with acute myocardial infarction. —— = Group 1, – – – – = Group 2.

In the present study, we found no association of these two risk factors with age. In our study as in others,[3] patients in the younger age group were more often of male gender and had a lower prevalence of previous MI.

Hospital Course

In the present analysis, 57% of the young patients versus 27% of the older patients underwent thrombolysis or direct PTCA. In the large U. S. National Registry of Myocardial Infarction,[34] 37% of patients received reperfusion therapy and the overall usage of thrombolysis was 40–50% in patients < 65 years and < 20% in those > 65 years. In our study, thrombolysis was withheld mainly because of delayed admission and ECG criteria in the older age group. It is well known that, for unknown reasons, elderly patients present later than younger patients[33, 35] despite the fact that a larger number of them have had the experience of a previous infarction.

Maximal CK-MB levels, infarct locations, and Q-wave infarctions were not significantly different between the two groups and left ventricular ejection fraction in those undergoing coronary angiography was similar in our study. Older patients have been reported to have smaller infarcts than younger patients based on CK levels.[35, 36] This difference could relate to the lesser muscle mass in elderly patients. The more cardiac-specific CK-MB isoenzyme used in our analysis was not reported in most previous studies. In accordance with other reports,[3, 4] we found a lower Killip class at entry in the younger age group, and fewer young patients developed congestive heart failure during the hospital course. Other hospital complications were comparable between our two study groups despite the fact that significantly fewer patients in Group 1 had multivessel disease. The latter finding was not unexpected.[4, 5, 7, 11, 12, 15, 35, 37, 38] As in our study, angiographically normal or minimally diseased coronary arteries have been described in up to 30% of young patients with acute MI.[4–6, 15–22, 35] It has been hypothesized that the mechanisms responsible for coronary obstruction leading to MI might be different with a higher prevalence of thrombotic obstruction and vasospasm in younger patients and fixed atherosclerotic lesions in older patients.[39–42] Despite the angiographic differences, 48% of young patients but only 16% of older patients underwent additional revascularization procedures during the initial hospitalization.

In contrast to younger patients, those in the older age group presented later in the hospital with less specific ECG changes, had a higher incidence of previous MIs, profited less often from early reperfusion therapy, had a higher incidence of mul-

TABLE VII Long-term follow-up in the subgroups of patients with and without thrombolysis/direct coronary angioplasty

	Reperfusion therapy			No reperfusion therapy		
	Group 1 (n = 42)	Group 2 (n = 18)	p Value	Group 1 (n = 30)	Group 2 (n = 50)	p Value
Angina pectoris (%)	10	31	< 0.05	15	43	< 0.02
Reinfarction (%)	10	29	< 0.07	18	16	< 0.8
Congestive heart failure (%)	10	38	< 0.02	7	33	< 0.02
Cardiac death (%)	0	11	< 0.03	3	24	< 0.02
PTCA (%)	14	12	< 0.8	25	0	0.0004
CABG (%)	7	24	< 0.09	11	13	< 0.8
PTCA or CABG (%)	20	29	< 0.5	29	13	< 0.2

Abbreviations as in Table VI.

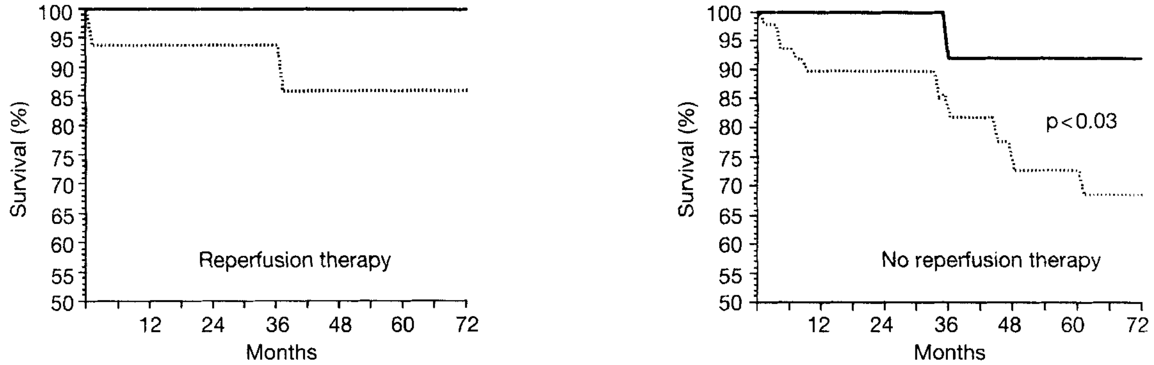

FIG. 2 Comparison of actuarial long-term survival in the subgroups of patients ≤40 years (Group 1) and >40 years (Group 2) with and without reperfusion therapy (thrombolysis or direct percutaneous transluminal coronary angioplasty). —— = Group 1, - - - - = Group 2.

tivessel disease, were less likely to undergo revascularization procedures in hospital, and developed congestive heart failure more often. This high-risk profile did not influence in-hospital mortality. However, the size of our population was not sufficient to identify small differences of in-hospital mortality as were observed in large studies.[3, 4, 35]

Follow-Up

During the long-term follow-up of hospital survivors, significantly fewer patients in the young age group experienced recurrent angina pectoris and congestive heart failure, whereas the rate of reinfarctions and coronary interventions was comparable. Cardiac mortality was significantly lower in the young age group. Overall, outcome was best for young patients with early reperfusion therapy and worst for older patients without reperfusion therapy. Although greater relative reductions in mortality have been observed with thrombolytic therapy in younger patients, greater absolute mortality reductions have been reported in older patients due to progressively greater absolute mortality rates with advancing age.[33, 35] Most trials of thrombolytic therapy versus control have concentrated on in-hospital or 30-day mortality, but recent updates have shown that the survival benefit from thrombolysis can be maintained long-term.[33, 43] Our results suggest that this is true particularly for young patients. In contrast, significant long-term mortality occurred in older patients, especially in those not undergoing thrombolysis. The favorable in-hospital results were not predictive for the future outcome in this group.

Limitations

First, patients were identified retrospectively from our CCU registry. Second, the young but not the older age group represented a consecutive series of patients. For each of the young patients, the next patient in the registry >40 years old with acute MI was selected to provide an equally sized control group and to minimize selection bias. Third, not all patients underwent coronary angiography. This reflects clinical practice, but the angiographic results must, therefore, be interpreted with caution.

Conclusions

Although patients ≤40 years who underwent reperfusion therapy had the best outcome in this analysis, prognosis was excellent in this age group irrespective of these interventions. In addition, favorable in-hospital outcome was maintained long-term in this group. Reperfusion therapy was more often performed in patients ≤40 years. Fewer patients in this group had multivessel disease, and they were more likely to undergo revascularization procedures during the initial hospitalization. Patients in the older age group had a significant long-term survival benefit from thrombolysis or direct PTCA; therefore, reperfusion therapy should be considered more often in older patients. In addition, these patients may benefit from more aggressive revascularization strategies during the initial hospitalization.

Our observations demonstrate that not only short-term but also long-term prognosis after myocardial infarction in young patients is excellent in the thrombolytic era.

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