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Benefit of Facilitated Percutaneous Coronary Intervention in High-Risk ST-Segment Elevation Myocardial Infarction Patients Presenting to Nonpercutaneous Coronary Intervention Hospitals

Howard C. Herrmann, MD,* Jiandong Lu, MD,† Bruce R. Brodie, MD,‡ Paul W. Armstrong, MD,§ Gilles Montalescot, MD, PHD,‖ Amadeo Betriu, MD,¶ Franz-Joseph Neuman, MD,# Mark B. Effron, MD,** Elliot S. Barnathan, MD,† Eric J. Topol, MD,†† Stephen G. Ellis, MD,‡‡ for the FINESSE Investigators

Philadelphia and Malvern, Pennsylvania; Greensboro, North Carolina; Edmonton, Alberta, Canada; Paris, France; Barcelona, Spain; Bad Krozingen, Germany; Indianapolis, Indiana; La Jolla, California; and Cleveland, Ohio

Objectives We hypothesized that patients most likely to benefit would be those at high risk with a shorter duration of acute ischemia and who required transfer for percutaneous coronary intervention (PCI).

Background The FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) study failed to demonstrate an improvement in the 90-day composite clinical end point of early treatment with abciximab plus half-dose reteplase (combination-facilitated PCI) or abciximab alone.

Methods We performed a retrospective analysis of 2,452 patients in this double-blind, placebo-controlled study. Patients were stratified by Thrombolysis In Myocardial Infarction (TIMI) risk score for ST-segment elevation myocardial infarction (STEMI), presentation to a spoke (no PCI available) or hub site, and symptom-to-randomization time. Outcomes included the primary composite end point of death, ventricular fibrillation after 48 h, cardiogenic shock, and congestive heart failure through day 90 as well as 1-year mortality.

Results Mortality for all patients at 1 year was directly related to TIMI risk score (23 of 1,223 = 1.9% in patients with score <3 and 145 of 1,229 = 11.8% with score ≥ 3, $p < 0.001$). Patients with TIMI risk score ≥ 3 and presentation to a spoke site with a symptom-to-randomization time ≤ 4 h had significantly better 1-year survival if treated with combination-facilitated PCI (hazard ratio [HR]: 0.351, $p = 0.01$) as well as 90-day composite outcome (HR: 0.45, $p = 0.009$). A trend for improved survival was also observed in patients with TIMI score ≥ 3 and spoke site alone (HR: 0.549, $p = 0.06$).

Conclusions Facilitation of PCI with a combination of abciximab and half-dose reteplase improved survival at 1 year in high-risk patients presenting to a spoke hospital with symptom-to-randomization time ≤ 4 h. Further prospective study of facilitated PCI in this subgroup of patients is warranted. (J Am Coll Cardiol Intv 2009;2:917–24) © 2009 by the American College of Cardiology Foundation

From the *Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; †Centocor Research & Development, Inc., Malvern, Pennsylvania; ‡LeBauer Cardiovascular Research, Greensboro, North Carolina; §University of Alberta Hospital, Edmonton, Alberta, Canada; ‖Hôpital Pitiè-Salpétrière, Paris, France; ¶Hospital Clinic i Provincial, Barcelona, Spain;

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Primary percutaneous coronary intervention (PCI) is more effective than thrombolytic therapy for the treatment of ST-segment elevation myocardial infarction (STEMI) when delivered by an experienced team soon after the onset of symptoms (1). However, performance of PCI in a timely fashion can be logistically challenging, and delays in time to reperfusion with primary PCI adversely affect outcome (2). This might become particularly important for patients who require transfer to another hospital where real world delays might greatly exceed those times observed in randomized trials (3,4).

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For these reasons, the FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) study was designed to test the hypothesis that early pharmacologic reperfusion before PCI could lead to myocardial salvage and better long-term outcomes. Although combination-facilitated PCI with abciximab plus half-dose reteplase improved early ST-segment resolution compared with abciximab alone (either early or in the catheterization laboratory), there was no significant reduction in the primary composite end point or 90-day mortality (5).

There were, however, trends to potential benefit with a facilitated strategy in patients with higher risk, shorter symptom onset to randomization time, and an intermediate door-to-balloon time (5). Therefore, we hypothesized that a facilitated approach might benefit high-risk patients (defined by Thrombolysis In Myocardial Infarction [TIMI] risk score) with a shorter duration of ischemia who also required transfer for PCI. Our goal was to determine whether a subgroup of patients could be identified at the time of presentation who would benefit from a facilitated PCI strategy.

Abbreviations and Acronyms

HR = hazard ratio

MI = myocardial infarction

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

Methods

The FINESSE study overview. The design of the FINESSE study has been previously reported (5). In brief, this international, double-blind, placebo-controlled trial randomized 2,452 patients who presented within 6 h of the onset of STEMI to receive 1 of 3 treatments: half-dose reteplase plus abciximab (combination-facilitated PCI), abciximab alone (abciximab-facilitated PCI), or placebo with abciximab administered in the catheterization laboratory just before PCI (primary PCI). Patients in the combination-facilitated PCI group received intravenous abciximab (0.25 mg/kg) and reteplase (2 5-U boluses separated by 30 min for those younger than 75 years of age or 1 5-U bolus for those 75 years of age or older); patients in the abciximab-facilitated group received an intravenous bolus of abciximab (0.25 mg/kg). All patients also received either low-molecular-weight or unfractionated heparin and aspirin. Approximately 60% of patients were enrolled at centers with PCI capability (hub sites), and the remainder were transferred to PCI sites from "spoke" centers.

The primary study end point in the FINESSE study was a composite of all-cause mortality, ventricular fibrillation occurring >48 h after randomization, cardiogenic shock, and congestive heart failure requiring hospital stay or emergency department visit within 90 days. Secondary end points included all-cause mortality at 90 days, ST-segment resolution of more than 70% at 60 to 90 min after randomization, and major or minor bleeding as assessed by the TIMI classification.

Study population. For this post hoc analysis, all 2,452 patients were initially included in the study population. Patients were then stratified by TIMI risk score for STEMI (6). The TIMI risk score for STEMI assigns points for age (2 points for ages 65 to 74 years, and 3 points for age ≥75 years), diabetes or hypertension or angina (1 point), systolic blood pressure <100 mm Hg (3 points), heart rate >100 (2 points), Killip class II to IV (2 points), weight <67 kg (1 point), anterior myocardial infarction (MI) or left bundle branch block (1 point), and time to treatment >4 h (1 point) to create a score from 0 to 14 points. A correlation between TIMI risk score and 1-year mortality has confirmed its predictive value in STEMI patients undergoing both fibrinolysis and primary PCI (6,7).

In addition, we investigated 2 other supplementary terms: 1) patients presenting to a spoke site that did not have PCI capability, thus requiring transfer for primary PCI; and 2) stratification by symptom-to-randomization time. Finally, the TIMI risk score was modified by not including the "time-to-treatment" variable, which assigns 1 point for time-to-treatment >4 h in order to include symptom-to-randomization as a patient-related variable. Outcomes for this analysis included the primary composite end point at 90 days, 1-year mortality, and TIMI major or minor bleeding through discharge or day 7, whichever was earlier.

#Herz-Zentrum bad Krozingen, Bad Krozingen, Germany; **Eli Lilly and Company, Indianapolis, Indiana; ††The Scripps Research Institute and Scripps Clinic, La Jolla, California; and the ‡‡Cleveland Clinic Foundation, Cleveland, Ohio. The FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) trial was supported by Centocor, Inc., and Eli Lilly, Inc. Several of the authors (Drs. Lu, Effron, and Barnathan) are employees of these companies. The other authors received research funding to participate in the trial. Dr. Herrmann did not receive research funding, and no additional funding was provided for this analysis.

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Statistical analysis. Efficacy analyses were conducted on the basis of the intention-to-treat principle, and safety analyses were performed according to the treatment received. Cox proportional hazards model was used to investigate the patient characteristics measured by modified TIMI STEMI risk score; whether patients presented to a spoke site that did not have PCI capability, thus requiring transfer for primary PCI; and symptom-to-randomization time and their relationship to both the composite 90-day primary end point and to 1-year mortality. Interaction p values between treatment (combination-facilitated PCI vs. primary PCI) and any of these factors were used to guide the refinement of the model to identify the subgroups with better survival benefit by combination-facilitated PCI. Comparisons between the combination-facilitated PCI group and the abciximab-facilitated PCI or primary PCI groups for particular subgroups were performed with Cox model stratified by the modified TIMI score with a significance level of 0.05. Kaplan-Meier analyses were performed to estimate the rate of mortality and primary composite end point over time by treatment groups. No multiple comparison adjustment was made for any p value reported.

Results

Baseline characteristics of the study population. We first explored the distribution of patients in the overall study population by modified TIMI risk score (all components except time to treatment >4 h), which is shown in Figure 1A. Approximately one-half of the patients had a TIMI risk score ≥3. Mortality at 1 year was directly related to TIMI risk score (Fig. 1B) at 1.9% for patients with a score <3 (23 of 1,223 patients) and 11.8% with score ≥3 (145 of 1,229 patients) ($p < 0.001$). Outcomes for the 90-day composite end point and mortality to 1 year for each treatment arm with various TIMI risk score cutoffs are shown in Tables 1 and 2, respectively. The choice of the dichotomous cut point of ≥3 was data driven and provided adequate sample size with a significantly higher mortality with some evidence of treatment effect.

Among this higher-risk group, we next explored the subgroup of patients presenting to non-PCI (i.e., "spoke") hospitals, because in these centers, subjects were randomized and given study medications and then had a longer time until PCI could occur. These subjects again seemed to have a greater treatment benefit from combination therapy (Table 2). Finally, on the basis of the hypothesis that early reperfusion was most likely to have demonstrable effect in subjects with short acute ischemic times, we explored the additional effect of stratifying the population by time from symptom onset to randomization time. Beyond 4 h, treatment effect seemed to fall off. Using 3 h gave similar results with less power in the analysis due to smaller sample size. Therefore, we chose a subgroup consisting of 397 patients (16%) with a TIMI risk score ≥3, presentation at a spoke site, and a symptom-to-randomization time ≤4 h as a high-risk subset for analysis. Baseline characteristics of this high-risk subgroup in comparison with the entire FINESSE study population are shown in Table 3.

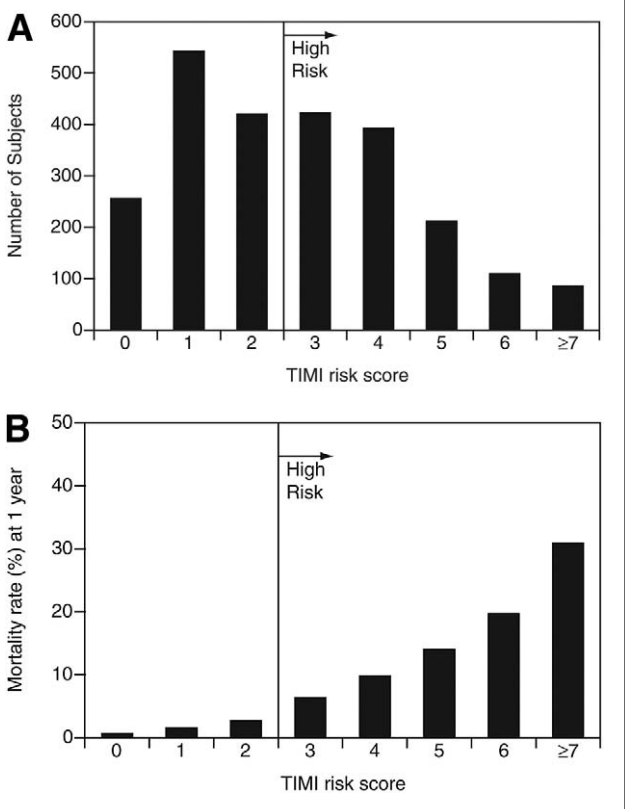

Figure 1. Number of Patients and 1-Year Mortality Stratified by Modified TIMI Risk Score

(A) The distribution of patients in the overall study population by modified Thrombolysis In Myocardial Infarction (TIMI) risk score (all components except time to treatment >4 h are shown). Approximately one-half of the patients had a modified TIMI risk score ≥3. Mortality at 1 year was directly related to the modified TIMI risk score **(B)** at 1.9% for patients with a score <3 (23 of 1,223 patients) and 11.8% with score ≥3 (145 of 1,229 patients) ($p < 0.001$).

Mortality through 1 year for each treatment group for the entire study and subgroups as outlined earlier are shown (Table 2, Fig. 2). There were no significant differences between treatment arms for 1-year mortality, either with respect to all patients (Fig. 2A) or in those with TIMI score ≥3 (Fig. 2B), although the combination-facilitated PCI group demonstrated a trend to a lower mortality rate in patients with a modified TIMI score ≥3 (10.1%) as compared with the primary PCI group (12.5%) (hazard ratio [HR]: 0.78; 95% confidence interval: 0.52 to 1.17, $p = 0.231$).

Influence of site and time to randomization. Forty percent of patients were enrolled at spoke sites without PCI capability. The median door-to-balloon time was 120 min at hub sites and 155 min at spoke sites, which included a median

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Table 1. Outcomes for 90-Day Composite End Point for Subgroups With Various Combinations of Cutoffs

Cutoffs	Combo-Facilitated PCI	Abciximab-Facilitated PCI	Primary PCI	Combo vs. Primary	Abciximab vs. Primary
TIMI ≥2	67/555 (12.1)	76/550 (13.8)	77/546 (14.1)	0.814 (0.586–1.130)	0.921 (0.671–1.265)
TIMI ≥3	59/414 (14.3)	67/415 (16.1)	70/400 (17.5)	0.776 (0.548–1.098)	0.874 (0.625–1.223)
TIMI ≥4	51/270 (18.9)	51/276 (18.5)	53/259 (20.5)	0.871 (0.592–1.280)	0.869 (0.591–1.277)
TIMI ≥5	33/145 (22.8)	35/140 (25.0)	32/126 (25.4)	0.892 (0.548–1.453)	0.949 (0.588–1.534)
TIMI ≥3 and spoke	26/177 (14.7)	27/167 (16.2)	34/158 (21.5)	0.606 (0.363–1.012)	0.681 (0.410–1.131)
TIMI ≥3 and spoke and time ≤2 h	7/57 (12.3)	8/67 (11.9)	10/53 (18.9)	0.810 (0.299–2.191)	0.872 (0.328–2.320)
TIMI ≥3 and spoke and time ≤3 h	15/112 (13.4)	11/103 (10.7)	26/103 (25.2)	0.429 (0.224–0.821)	0.378 (0.186–0.770)
TIMI ≥3 and spoke and time ≤4 h	18/137 (13.1)	19/135 (14.1)	29/125 (23.2)	0.453 (0.249–0.824)	0.531 (0.296–0.955)
TIMI ≥3 and spoke and time ≤5 h	24/161 (14.9)	25/155 (16.1)	31/139 (22.3)	0.586 (0.342–1.004)	0.654 (0.384–1.113)

Values are n/n (%) and hazard ratio (95% confidence interval). Comparison of various combinations of cutoffs for Thrombolysis In Myocardial Infarction (TIMI) risk, presentation at a spoke site without percutaneous coronary intervention (PCI) capability, and times from symptom onset to randomization on the 90-day composite end point in all 3 treatment arms.

CI = confidence interval; Combo = combination (half-dose reteplase plus abciximab).

transfer time of 35 min (5). There was no significant difference between the incidence of the primary 90-day composite end point at spoke sites in combination-facilitated (10.7%) and primary-PCI groups (12.0%, HR: 0.88; 95% confidence interval: 0.56 to 1.39) (5). However, a trend for benefit of combination-facilitated PCI was observed when TIMI risk score ≥3 was combined with presentation at a spoke site (Table 2). In this subgroup of patients, the 90-day end point was 21.5% in the primary PCI group compared with 14.7% in the combination-facilitated PCI group (p = 0.091); 1-year mortality was 15.2% and 9.0% in the primary-PCI and combination-facilitated PCI groups, respectively (HR: 0.549, p = 0.064) (Table 2, Fig. 2C).

The addition of a third stratification variable, time-to-randomization, demonstrated further benefit with a facilitated approach (Table 2). After analyzing various symptom-to-randomization cut points, a cutoff of ≤4 h versus >4 h was selected to obtain the most significant interaction p value (p = 0.044) between symptom-to-randomization time and treatment group (combination-facilitated PCI vs. primary PCI). Patients with a modified TIMI risk score of ≥3 who presented to a spoke site and had a symptom-to-randomization time ≤4 h did significantly better as measured by the primary composite outcome in both facilitated groups compared with primary PCI (combination-facilitated PCI, HR: 0.45, p = 0.009; abciximab-facilitated PCI, HR: 0.53, p = 0.035) (Table 1, Fig. 3). One-year mortality in this subgroup was only significantly reduced for the combination-facilitated PCI group (HR: 0.35, p = 0.01) (Fig. 2D).

Safety. Bleeding was assessed with the TIMI classification through discharge or day 7, whichever occurred sooner. In the overall study, nonintracranial TIMI major or minor bleeding occurred in 14.5%, 10.1%, and 6.9% of patients in the combination-facilitated PCI, abciximab-facilitated PCI, and primary-PCI groups, respectively (p < 0.001 for the comparison of combination with primary PCI) (5). In the subgroup of patients with modified TIMI risk score ≥3, spoke site, and

Table 2. Outcomes for 1-Year Mortality for Subgroups With Various Combinations of Cutoffs

	Mortality at 1 Year				
Cutoffs	Combo-Facilitated PCI	Abciximab-Facilitated PCI	Primary PCI	Combo vs. Primary	Abciximab vs. Primary
TIMI ≥2	47/555 (8.5)	56/550 (10.2)	54/546 (9.9)	0.815 (0.551–1.206)	0.998 (0.687–1.451)
TIMI ≥3	42/414 (10.1)	53/415 (12.8)	50/400 (12.5)	0.778 (0.516–1.173)	1.009 (0.686–1.486)
TIMI ≥4	38/276 (13.8)	43/270 (15.9)	37/259 (14.3)	0.938 (0.596–1.477)	1.108 (0.714–1.720)
TIMI ≥5	23/145 (15.9)	30/140 (21.4)	26/126 (20.6)	0.760 (0.433–1.333)	1.059 (0.626–1.791)
TIMI ≥3 and spoke	16/177 (9.0)	24/167 (14.4)	24/158 (15.2)	0.549 (0.291–1.036)	0.924 (0.524–1.632)
TIMI ≥3 and spoke and time ≤2 h	4/57 (7.0)	6/67 (9.0)	8/53 (15.1)	0.591 (0.175–2.003)	0.957 (0.314–2.914)
TIMI ≥3 and spoke and time ≤3 h	9/112 (8.0)	13/103 (12.6)	18/103 (17.5)	0.410 (0.182–0.922)	0.725 (0.353–1.490)
TIMI ≥3 and spoke and time ≤4 h	9/137 (6.6)	18/135 (13.3)	20/125 (16.0)	0.351 (0.159–0.777)	0.824 (0.432–1.573)
TIMI ≥3 and spoke and time ≤5 h	13/161 (8.1)	21/155 (13.5)	20/139 (14.4)	0.515 (0.255–1.040)	0.921 (0.497–1.709)

Values are n/n (%) and hazard ratio (95% confidence interval). Comparison of various combinations of cutoffs for TIMI risk, presentation at a spoke site without PCI capability, and times from symptom onset to randomization on the 1-year mortality in all 3 treatment arms.

Abbreviations as in Table 1.

Table 3. Comparison of Variables Between the Overall Trial Population and the Study Subgroup

	All Patients	Study Population
n (%)	2,452 (100)	397 (16)
Female	642 (26.2)	154 (38.8)
Age ≥75 yrs	388 (15.8)	142 (35.8)
Previous MI	266 (10.8)	46 (11.6)
Diabetes	380 (15.5)	89 (22.4)
Anterior infarction	1,173 (47.8)	209 (52.6)
Killip class II–IV	241 (9.8)	71 (17.9)
Symptom-to-randomization time, h		
≤2	787 (32.1)	177 (44.6)
2–4	1,101 (44.9)	220 (55.4)
>4	564 (23.0)	0 (0.0)
Randomization-to-balloon time ≤1 h	251 (10.2)	1 (0.3)
Modified TIMI risk score ≥3	1,229 (50.1)	397 (100)
Spoke site	984 (40.1)	397 (100)

Values are n (%).
MI = myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction.

symptom-to-randomization time ≤4 h, the rates of nonintracranial TIMI major or minor bleeding occurred in 15.3%, 11.9%, and 10.4% for the same 3 treatment groups, respectively. Compared with primary PCI, the bleeding rate was similar for abciximab-facilitation (p = 0.85) and trended higher with combination therapy (p = 0.32) (Table 4). Thrombocytopenia, in this subgroup, was higher in the abciximab-facilitated group compared with the other treatment groups (Table 4), although this was not observed in the trial overall (5).

Discussion

Improving outcomes with pharmacologic therapy for the treatment of acute MI before planned primary PCI in order to combine the benefits of early drug reperfusion with later and more complete mechanical reperfusion has great theoretic appeal (8). Despite the absence of benefit with a facilitated PCI strategy in the FINESSE study, we retrospectively sought to determine whether a subset of patients could be indentified upon presentation that would be more likely to benefit. In this study we demonstrated that, in a subgroup of 397 high-risk patients presenting to non-PCI hospitals within 4 h of symptom onset, combination-facilitated PCI reduced 1-year mortality compared with primary PCI.

Previous studies. Early studies exploring the facilitated PCI concept focused on determining whether an invasive strategy and the timing of such a strategy could demonstrate an improvement over a conservative strategy after the administration of a thrombolytic agent. (9). No benefit was demonstrated, but these trials were performed in advance of the availability of stents and before the routine use of

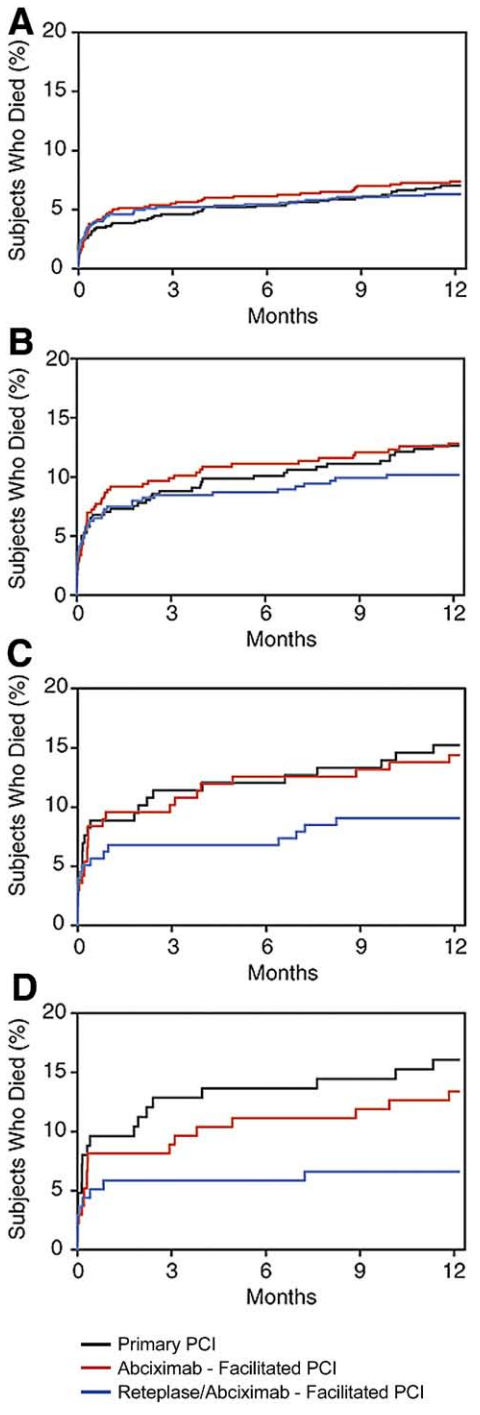

Figure 2. 1-Year Mortality in the FINESSE Study and Subgroups for Each Treatment Arm

Estimates of mortality at 1-year are shown for each treatment group in: **(A)** all patients (n = 2,452); **(B)** patients with a modified Thrombolysis In Myocardial Infarction (TIMI) risk score ≥3 (n = 1,229); **(C)** patients with a modified TIMI risk score ≥3 and spoke site randomization (n = 502); and **(D)** patients with a modified TIMI risk score ≥3, spoke site, and symptom-to-randomization time ≤4 h (n = 397). PCI = percutaneous coronary intervention.

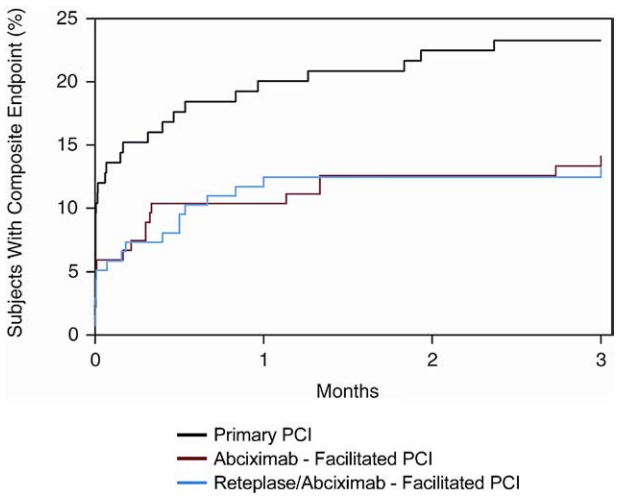

Figure 3. Primary End Point in High-Risk Subgroup for Each Treatment Arm

The primary composite end point (all-cause mortality, ventricular fibrillation occurring >48 h after randomization, cardiogenic shock, and congestive heart failure requiring hospital stay or emergency department visit within 90 days) is shown by treatment group for the subgroup of patients with modified TIMI risk score ≥3, spoke site, and symptom-to-randomization time ≤4 h. Abbreviations as in Figure 2.

glycoprotein IIb/IIIa inhibitors and thienopyridines (1). Several recent trials have suggested benefit for early PCI with stenting after thrombolysis (SIAM-III [Southwest German Interventional Study in Acute Myocardial Infarction], GRACIA-1 [Grupo de Analisis de la Cardiopatia Isquemica Aguda], CAPITAL-AMI [Combined Angioplasty and Pharmacological Intervention versus Thrombolysis Alone in Acute Myocardial Infarction]), but these studies were limited, because they were open-label and had small sample sizes (9).

The ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy with PCI) trial was a larger randomized contemporary trial of full-dose tenecteplase before PCI (10). This trial was discontinued early, due to worse outcomes in the facilitated PCI arm, despite higher TIMI flow grade 3 before PCI in the tenecteplase arm. The rapid drug-to-balloon time and lack of adequate antiplatelet therapy before PCI might have contributed to the worse outcomes observed.

In the CARESS (Combined Abciximab RE-teplase Stent Study) in acute MI trial, 600 high-risk patients receiving half-dose reteplase and abciximab were randomized to PCI versus conservative care. The composite end point of death, MI, and refractory ischemia at 30 days was reduced from 10.4% to 4.4% with early PCI (11). In the TRANSFER-AMI (Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute MI), urgent transfer for PCI after fibrinolysis was associated with a reduction in reinfarction and the 30-day composite of death, MI, and recurrent ischemia (12). In this study, all patients received a loading dose of clopidogrel, and 73% received glycoprotein IIb/IIIa inhibitors during PCI.

Several trials have examined the use of glycoprotein IIb/IIIa inhibition without fibrinolysis administered early to acute MI patients after the first demonstration of benefit in a randomized trial with abciximab (13). Similarly, in an observational registry of 1,066 higher-risk patients who received abciximab before transfer for primary PCI, 30-day mortality was reduced by 50% (14). However, in a randomized study of tirofiban, no improvement occurred in either TIMI flow or perfusion, possibly due to inadequate dosing, too short a time between drug administration and angiography, or the lack of high-risk patients (15).

Finally, a single center observational analysis of facilitated PCI was recently published (16). In 786 patients treated at a community hospital with a glycoprotein IIb/IIIa inhibitor and/or intravenous fibrinolytic before transfer for PCI with a door-to-balloon time between 90 and 150 min, 50% fewer major adverse clinical events were observed as compared with 767 patients undergoing primary PCI at the tertiary center despite a longer door-to-balloon time (16).

Rationale and results of the present investigation. In the FINESSE trial, neither facilitation of PCI with half-dose reteplase plus abciximab nor facilitation with abciximab alone significantly improved clinical outcomes, as compared with abciximab given at the time of PCI (5). However, the benefits of PCI are time-related (17) and lost more quickly in higher-risk patients (18). A reperfusion strategy should be selected not only on the basis of the benefits and

Table 4. Comparison of TIMI Major and Minor Bleeding in the 3 Treatment Arms in the Study Population

	Primary PCI (n = 125)	Abciximab-Facilitated PCI (n = 135)	Combination-Facilitated PCI (n = 137)
Nonintracranial major or minor TIMI	13 (10.4)	16 (11.9)	21 (15.3)
TIMI major (including ICH)	3 (2.4)	8 (5.9)	7 (5.1)
Stroke			
ICH	0	0	0
Ischemic	3 (2.4)	1 (0.7)	2 (1.5)
Transfusion			
pRBC	4 (3.2)	6 (4.4)	11 (8.0)
Platelets	0	2 (1.5)	0
Thrombocytopenia			
<100k	3 (2.4)	10 (7.4)	3 (2.2)
<50k	1 (0.8)	6 (4.4)	2 (1.5)
<20k	0	3 (2.2)	0

Values are n (%).

ICH = intracranial hemorrhage; PCI = percutaneous coronary intervention; pRBC = packed red blood cell; TIMI = Thrombolysis In Myocardial Infarction.

limitations of the reperfusion strategy and time delays (both presentation delay and PCI-related delay) but also patient characteristics.

We hypothesized that the patients most likely to benefit from a facilitated strategy would be those at high risk with a shorter duration of ischemia who required transfer for PCI. To make an analysis of such patients clinically useful, we focused on information that would be readily available at patient's presentation. In this regard, the TIMI risk score for STEMI is easily calculated and has been validated in patients treated with fibrinolysis and primary PCI (6,7). Because patients with very short door-to-balloon times are unlikely to benefit from pharmacologic reperfusion before PCI, we limited our analysis to patients presenting at a spoke site requiring transfer for PCI. Finally, because fibrinolysis is more effective in less mature thrombotic lesions (19), we included only patients with a symptom-to-randomization time ≤4 h.

The benefit we observed in 90-day composite outcome and 1-year mortality in the high-risk group treated with a facilitated approach was associated with a trend to greater bleeding (Table 4). However, nonintracranial TIMI major and minor bleeding were not significantly different in this high-risk subgroup as compared with the overall study population but trended higher in the primary PCI group (10.4% in our subgroup vs. 6.9% in the overall study population). This might reflect the high-risk characteristics of these patients or be related to chance variation in a small subgroup of patients.

Study limitations. This is a retrospective, post-hoc analysis of a randomized trial. Therefore, our conclusions are exploratory and require validation in a prospective randomized trial. We are hopeful that future trials of facilitation for PCI in acute MI will consider inclusion of the subset of patients we have identified as a pre-planned analysis. The lack of pre-specified clopidogrel administration is an additional study limitation.

The TIMI risk score was modified to exclude the "time-to-treatment" variable in order to allow inclusion of time-to-treatment as a patient-related variable. Therefore, previous studies of the predictive value of the unmodified TIMI risk score might not be directly comparable. We also examined higher cut points for TIMI risk, which revealed a similar effect on 1-year mortality (e.g., 1.9% for score <5 vs. 18.3% for score ≥5) but reduced the overall number of patients available and the statistical power for analysis. Similarly, using a shorter symptom-to-randomization time (e.g., 3 h) resulted in a similar benefit for 1-year mortality with combination therapy (HR: 0.41, p = 0.03) but reduced power for analysis (Table 1). Future prospective analyses of this subgroup will need to test various TIMI risk scores and time points.

Conclusions

In a subgroup of patients in the FINESSE trial identified as high risk on the basis of a modified TIMI risk score ≥3, presentation to a spoke site without PCI capability, and with a symptom-to-randomization time ≤4 h, facilitation of PCI with early administration of a combination of abciximab and half-dose reteplase or abciximab alone may reduce 90-day clinical outcomes compared with abciximab given just before PCI. Furthermore, combination-facilitated PCI significantly reduced 1-year mortality as compared with primary PCI. We believe that further prospective evaluation of this high-risk subgroup of acute MI patients is warranted.

Reprint requests and correspondence: Dr. Howard C. Herrmann, 9038 West Gates Building, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104. E-mail: howard.herrmann@uphs.upenn.edu.

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