



LUND UNIVERSITY

Outcomes 1 year after thrombus aspiration for myocardial infarction.

Lagerqvist, Bo; Fröbert, Ole; Olivecrona, Göran; Gudnason, Thórarinn; Maeng, Michael; Alström, Patrik; Andersson, Jonas; Calais, Fredrik; Carlsson, Jörg; Collste, Olov; Göteborg, Matthias; Hårdhammar, Peter; Ioanes, Dan; Kallryd, Anders; Linder, Rickard; Lundin, Anders; Odenstedt, Jacob; Omerovic, Elmir; Puskar, Verner; Tödt, Tim; Zelleröth, Eva; Östlund, Ollie; James, Stefan K

Published in:
New England Journal of Medicine

DOI:
[10.1056/NEJMoa1405707](https://doi.org/10.1056/NEJMoa1405707)

2014

[Link to publication](#)

Citation for published version (APA):

Lagerqvist, B., Fröbert, O., Olivecrona, G., Gudnason, T., Maeng, M., Alström, P., Andersson, J., Calais, F., Carlsson, J., Collste, O., Göteborg, M., Hårdhammar, P., Ioanes, D., Kallryd, A., Linder, R., Lundin, A., Odenstedt, J., Omerovic, E., Puskar, V., ... James, S. K. (2014). Outcomes 1 year after thrombus aspiration for myocardial infarction. *New England Journal of Medicine*, 371(12), 1111-1120.
<https://doi.org/10.1056/NEJMoa1405707>

Total number of authors:
23

General rights

Unless other specific re-use rights are stated the following general rights apply:
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

ORIGINAL ARTICLE

Outcomes 1 Year after Thrombus Aspiration for Myocardial Infarction

Bo Lagerqvist, M.D., Ph.D., Ole Fröbert, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Thórarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Patrik Alström, M.D., Jonas Andersson, M.D., Ph.D., Fredrik Calais, M.D., Jörg Carlsson, M.D., Ph.D., Olov Collste, M.D., Matthias Götberg, M.D., Ph.D., Peter Hårdhammar, M.D., Dan Ioanes, M.D., Anders Kallryd, M.D., Rickard Linder, M.D., Ph.D., Anders Lundin, M.D., Jacob Odenstedt, M.D., Elmir Omerovic, M.D., Ph.D., Verner Puskar, M.D., Tim Tödt, M.D., Ph.D., Eva Zelleröth, M.D., Ollie Östlund, Ph.D., and Stefan K. James, M.D., Ph.D.

ABSTRACT

BACKGROUND

Routine intracoronary thrombus aspiration before primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) has not been proved to reduce short-term mortality. We evaluated clinical outcomes at 1 year after thrombus aspiration.

METHODS

We randomly assigned 7244 patients with STEMI to undergo manual thrombus aspiration followed by PCI or to undergo PCI alone, in a registry-based, randomized clinical trial. The primary end point of all-cause mortality at 30 days has been reported previously. Death from any cause at 1 year was a prespecified secondary end point of the trial.

RESULTS

No patients were lost to follow-up. Death from any cause occurred in 5.3% of the patients (191 of 3621 patients) in the thrombus-aspiration group, as compared with 5.6% (202 of 3623) in the PCI-only group (hazard ratio, 0.94; 95% confidence interval [CI], 0.78 to 1.15; $P=0.57$). Rehospitalization for myocardial infarction at 1 year occurred in 2.7% and 2.7% of the patients, respectively (hazard ratio, 0.97; 95% CI, 0.73 to 1.28; $P=0.81$), and stent thrombosis in 0.7% and 0.9%, respectively (hazard ratio, 0.84; 95% CI, 0.50 to 1.40; $P=0.51$). The composite of death from any cause, rehospitalization for myocardial infarction, or stent thrombosis occurred in 8.0% and 8.5% of the patients, respectively (hazard ratio, 0.94; 95% CI, 0.80 to 1.11; $P=0.48$). The results were consistent across all the major subgroups, including grade of thrombus burden and coronary flow before PCI.

CONCLUSIONS

Routine thrombus aspiration before PCI in patients with STEMI did not reduce the rate of death from any cause or the composite of death from any cause, rehospitalization for myocardial infarction, or stent thrombosis at 1 year. (Funded by the Swedish Research Council and others; TASTE ClinicalTrials.gov number, NCT01093404.)

From the Department of Medical Sciences, Cardiology Section, and Uppsala Clinical Research Center, Uppsala University, Uppsala (B.L., O.O., S.K.J.), Department of Cardiology, Örebro University Hospital, Örebro (O.F., F.C.), Department of Coronary Heart Disease, Skane University Hospital, Clinical Sciences Section, Lund University, Lund (G.K.O., M.G., A.L.), Department of Cardiology, Karolinska Institutet, Södersjukhuset (P.A., O.C.), and Department of Cardiology, Karolinska Institutet, Danderyd (R.L.), Stockholm, Department of Cardiology, Umeå University Hospital, Umeå (J.A.), Section of Cardiology, Kalmar County Hospital and Linnaeus University, Kalmar (J.C.), Department of Cardiology, Halmstad Hospital, Halmstad (P.H.), Department of Cardiology, Sahlgrenska University Hospital, Gothenburg (D.I., J.O., E.O.), Department of Cardiology, Skaraborgs Hospital, Skövde (A.K.), Department of Radiology, Ryhov Hospital, Jönköping (V.P.), Department of Cardiology, Linköping University Hospital, Linköping (T.T.), and Department of Radiology, Mälarsjukhuset, Eskilstuna (E.Z.) — all in Sweden; Department of Cardiology and Cardiovascular Research Center, Landspítali University Hospital, Reykjavik, Iceland (T.G.); and the Department of Cardiology, Aarhus University Hospital, Skejby, Aarhus, Denmark (M.M.). Address reprint requests to Dr. James at the Department of Medical Sciences, Uppsala University, 751 85 Uppsala, Sweden, or at stefan.james@ucr.uu.se.

This article was published on September 1, 2014, at NEJM.org.

N Engl J Med 2014;371:1111-20.

DOI: 10.1056/NEJMoa1405707

Copyright © 2014 Massachusetts Medical Society.

ACUTE ST-SEGMENT ELEVATION MYOCARDIAL infarction (STEMI) is often caused by intracoronary thrombus formation with blockage of antegrade coronary flow leading to myocardial ischemia and cell death.¹ Thrombus burden, reduced coronary flow, and reduced myocardial perfusion are important predictors of a poor clinical outcome, including recurrence of myocardial infarction, stent thrombosis, and death.² Prompt initiation of antithrombotic therapy in combination with percutaneous coronary intervention (PCI) is the preferred approach to optimize myocardial perfusion and clinical outcomes.³ Coronary-artery thrombus aspiration before PCI reduces the thrombus burden and improves ST-segment resolution and coronary flow.^{4,5} To our knowledge, however, no adequately powered randomized clinical trial has shown improvement in short-term clinical outcomes. Neither the single-center Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study (TAPAS),⁴ which involved 1071 patients, nor our multicenter, randomized clinical trial Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE),⁶ which involved 7244 patients, showed a significant reduction in mortality or in the incidence of other clinical events at 30 days of follow-up.

TAPAS showed a significant reduction in the rate of death from any cause at 1 year with thrombus aspiration,⁷ but this finding must be considered to be hypothesis-generating, since the trial was underpowered for hard clinical end points. In the TASTE trial, the rates of stent thrombosis and rehospitalization for myocardial infarction at 30 days were numerically lower after thrombus aspiration than after PCI alone, but the difference was not significant. Here we report the clinical results at 1 year in the TASTE trial.

METHODS

STUDY DESIGN

The design of the TASTE trial has been reported previously.^{6,8} In summary, TASTE was a multicenter, prospective, randomized, controlled, open-label clinical trial comparing routine thrombus aspiration before PCI with PCI alone in patients with STEMI. The trial used the national comprehensive Swedish Coronary Angiography and Angioplasty Registry (SCAAR), which is part of the Internet-based Swedish Web System for Enhance-

ment and Development of Evidence-based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry,⁹ for the identification of patients, randomization, collection of baseline and procedural variables, and follow-up (see the Supplementary Appendix, available with the full text of this article at NEJM.org, for details about the SWEDEHEART registry). Regional ethics review boards in Uppsala, Sweden, Iceland, and Denmark approved the study. Trial administration, data management, and statistical analyses were performed at the Uppsala Clinical Research Center at Uppsala University.

The first three authors and the last author designed the TASTE study. All the authors vouch for the integrity and completeness of the data and analyses and for the fidelity of this report to the trial protocol, available at NEJM.org. The funding agencies had no access to the study data and no role in the study design or in the interpretation or reporting of the data.

PATIENT POPULATION

Patients were eligible for enrollment if PCI was planned for the treatment of acute STEMI. Acute STEMI was defined as chest pain of less than 24 hours' duration, electrocardiographic changes with new ST-segment elevation in two or more contiguous leads (≥ 0.2 mV in lead V2 or V3 or ≥ 0.1 mV in other leads) or a left bundle-branch block that was thought to be new, and a corresponding culprit-artery lesion on angiography. Exclusion criteria included the need for emergency coronary-artery bypass grafting and an inability to provide oral informed consent.

STUDY PROCEDURES

Patients fulfilling all the inclusion criteria and none of the exclusion criteria were asked to provide oral informed consent as described in the Supplementary Appendix. After providing oral informed consent, patients were randomly assigned, in a 1:1 ratio, either to thrombus aspiration followed by PCI or to PCI alone. Randomization was performed by means of an online randomization module within the SCAAR database. Within 24 hours, patients were asked to confirm informed consent to participation in writing.

Medical therapy was left to the discretion of the treating physician. For patients randomly assigned to thrombus aspiration, the protocol recommended the use of manual continuous suction

during at least four proximal-to-distal passes with 6-French-compatible, low-profile catheters. Balloon dilation was permitted up to a nominal diameter of 2.0 mm. Patients randomly assigned to PCI alone were treated according to the standard of care with optional balloon dilation.¹⁰ Stenting was encouraged in both randomized groups, with optional balloon dilation after stenting. Crossover from one group to the other was discouraged. Stent type and the duration of treatment with P2Y₁₂ inhibitors were at the physician's discretion.

END POINTS AND DEFINITIONS

Data on clinical end points were obtained from national health registries and were not centrally adjudicated. No study-specific clinical follow-up was done. The primary end point was all-cause mortality at 30 days, the results of which have been reported previously.⁶ For the 1-year follow-up, we report the following prespecified secondary end points: death from any cause, rehospitalization for myocardial infarction, stent thrombosis, target-vessel revascularization, and target-lesion revascularization. In addition, we report the events of a post hoc-defined composite of death from any cause, rehospitalization for myocardial infarction, or stent thrombosis.

Data regarding deaths were obtained from the national population registries. Data on hospitalization for myocardial infarction were obtained from the SWEDEHEART registry, and defined according to *International Classification of Diseases, 10th Revision*, codes I21 and I22 (as described in the Supplementary Appendix). Definite stent thrombosis was defined according to the Academic Research Consortium definition.¹¹ Target-lesion revascularization was defined as a new PCI procedure in the same coronary segment as the index procedure or coronary-artery bypass surgery after the index procedure. Thrombus grade was classified by the study investigators according to Thrombolysis in Myocardial Infarction (TIMI) criteria,¹² with reclassification of total occlusions after the initial restoration of flow according to the criteria of Sianos et al.¹³

STATISTICAL ANALYSIS

The sample-size calculation and group-sequential design for the primary outcome at 30 days have been described previously.^{6,8} The results were analyzed according to the intention-to-treat principle. Kaplan-Meier curves are used to show the

event rates over time, classified according to randomization assignment. Hazard ratios were calculated with the use of a Cox proportional-hazards model with treatment as the only factor and are reported with the nominal 95% confidence interval from the Cox proportional-hazards model and the nominal two-sided P value from a log-rank test. Chi-square tests were used to test differences between categorical variables. Subgroup analyses were performed with the use of proportional-hazards models, with proper tests for interaction. All analyses were conducted with the use of SAS software, version 9.3 (SAS Institute).

RESULTS

STUDY POPULATION

All PCI centers in Sweden (29 centers) and Iceland (1 center), along with 1 PCI center in Denmark, participated in the trial. During the study period, 11,956 patients underwent PCI for STEMI, and 7244 were enrolled (Fig. S1 in the Supplementary Appendix).

During 2 years and 9 months of enrollment, 59.7% of all the patients presenting with STEMI and referred for PCI, and 76.9% of all the patients potentially eligible for enrollment in Sweden and Iceland, underwent randomization. The most prevalent reasons for not enrolling patients, as reported by the investigators, were the patient's inability to provide oral informed consent mainly owing to severe medical conditions (37.6% of patients), an inability to perform thrombus aspiration for anatomical reasons (16.0%), or a judgment that thrombus aspiration was inappropriate (11.3%) or not indicated (7.2%).

Baseline clinical and procedural characteristics as well as discharge medications for all the patients who underwent randomization and those who did not undergo randomization are listed in Table 1, and in Tables S1 and S2 in the Supplementary Appendix. Of particular note is the frequent use of radial-artery access (in 66.4% of the patients), bivalirudin (in 78.8%), potent new P2Y₁₂ inhibitors (in 43.7% of the patients at PCI and in 36.6% at discharge), and new-generation drug-eluting stents. None of the patients who underwent randomization and none of the patients in Sweden or Iceland who did not undergo randomization were lost to follow-up for the primary end point at 1 year; follow-up data were not obtained for patients in Denmark who did not undergo randomization.

Table 1. Characteristics of the Patients at Baseline, According to Randomization Status and Treatment Group.*

Characteristic	Patients Who Underwent Randomization		Patients Who Were Not Enrolled in the Trial†	
	PCI Only (N=3623)	PCI and Thrombus Aspiration (N=3621)	PCI Only (N=3543)	PCI and Thrombus Aspiration (N=1169)
Age — yr	65.9±11.7	66.5±11.5	69.4±12.5	66.8±13.5
Male sex — no. (%)	2703 (74.6)	2721 (75.1)	2366 (66.8)	835 (71.4)
Diabetes mellitus — no. (%)	453 (12.5)	448 (12.4)	636 (18.0)	163 (13.9)
Current smoking — no. (%)	1173 (32.4)	1083 (29.9)	880 (24.8)	318 (27.2)
Previous myocardial infarction — no. (%)	440 (12.1)	402 (11.1)	645 (18.2)	191 (16.3)
Previous PCI — no. (%)	362 (10.0)	337 (9.3)	438 (12.4)	138 (11.8)
Previous CABG — no. (%)	74 (2.0)	70 (1.9)	167 (4.7)	66 (5.6)
Fibrinolysis before PCI — no. (%)	69 (1.9)	68 (1.9)	100 (2.8)	16 (1.4)
Procedure-related medication — no. (%)				
Acetylsalicylic acid	3542 (97.8)	3546 (97.9)	3378 (95.3)	1102 (94.3)
Clopidogrel or ticlopidine	2395 (66.1)	2384 (65.8)	2222 (62.7)	760 (65.0)
Ticagrelor	1015 (28.0)	1050 (29.0)	964 (27.2)	357 (30.5)
Prasugrel	538 (14.8)	562 (15.5)	414 (11.7)	103 (8.8)
Heparin	3074 (84.8)	3063 (84.6)	2951 (83.3)	941 (80.5)
Low-molecular-weight heparin	142 (3.9)	147 (4.1)	144 (4.1)	80 (6.8)
Bivalirudin	2835 (78.3)	2874 (79.4)	2377 (67.1)	769 (65.8)
Glycoprotein IIb/IIIa inhibitor	630 (17.4)	558 (15.4)	516 (14.6)	324 (27.7)
Time from diagnostic ECG to PCI — min				
Median	66	67	72	65
Interquartile range	47–93	48–95	50–108	47–95
Killip class ≥2 — no. (%)	183 (5.1)	198 (5.5)	539 (15.2)	195 (16.7)
Radial-artery approach — no. (%)	2415 (66.7)	2394 (66.1)	1954 (55.2)	634 (54.2)
Type of disease — no. (%)				
One-vessel disease	1940 (53.5)	1946 (53.7)	1585 (44.7)	607 (51.9)
Two-vessel disease	1072 (29.6)	1010 (27.9)	982 (27.7)	276 (23.6)
Three-vessel disease	498 (13.7)	558 (15.4)	680 (19.2)	194 (16.6)
Left main coronary artery disease	105 (2.9)	98 (2.7)	277 (7.8)	89 (7.6)
Data not available	8 (0.2)	9 (0.2)	19 (0.5)	3 (0.3)
TIMI flow grade 0 or 1 — no. (%)	2811 (77.6)	2821 (77.9)	NA	NA
Thrombus grade — no. (%)‡				
G0	543 (15.0)	490 (13.5)	NA	NA
G1	809 (22.3)	733 (20.2)	NA	NA
G2	329 (9.1)	341 (9.4)	NA	NA
G3	818 (22.6)	887 (24.5)	NA	NA
G4	863 (23.8)	903 (24.9)	NA	NA
G5	215 (5.9)	235 (6.5)	NA	NA
Unknown	46 (1.2)	32 (0.9)	NA	NA

* Plus-minus values are means ±SD. Between-group differences were calculated with the use of the chi-square test or Student's t-test as appropriate. There were no significant between-group differences, except as specified. In the group of patients who underwent randomization, there were significant differences between the treatment groups with respect to the following characteristics: age, current smoking, and use of a glycoprotein IIb/IIIa inhibitor. In the group of patients who were not enrolled in the trial, there were significant differences between the treatment groups with respect to the following characteristics: age, sex, presence of diabetes mellitus, current smoking, previous myocardial infarction, fibrinolysis before percutaneous coronary intervention (PCI), procedure-related medication with the exceptions of acetylsalicylic acid and bivalirudin, and type of disease. CABG denotes coronary-artery bypass grafting, ECG electrocardiogram, NA not available, and TIMI Thrombolysis in Myocardial Infarction.

† The group of patients who were not enrolled in the trial included only Swedish and Icelandic patients. Patients in Denmark who were not enrolled were not available for follow-up.

‡ Thrombus grades are defined as follows: G0 indicates no thrombus, G1 possible thrombus, G2 small thrombus, G3 medium thrombus, G4 large thrombus, and G5 vessel occlusion.

UPDATE OF 30-DAY REGISTRY DATA

An update of the registry data for events within the first 30 days included one death that had not previously been identified or reported.⁶ Three events previously reported as new hospitalizations for myocardial infarction within 30 days were reclassified as part of the index hospitalization. Completion of a previously incomplete registry entry for PCI resulted in the reporting of one additional case of target-lesion revascularization and target-vessel revascularization within 30 days. A total of 15 additional patients in Sweden and Iceland were identified who had been potentially eligible for inclusion but had not undergone randomization in the TASTE study.

CLINICAL END POINTS

The rate of death from any cause at 1 year was 5.3% (191 of 3621 patients) in the thrombus-aspiration group, as compared with 5.6% (202 of 3623) in the PCI-only group (hazard ratio, 0.94; 95%

confidence interval [CI], 0.78 to 1.15; $P=0.57$) (Table 2 and Fig. 1A); the results were similar for the interval from day 31 to day 365 (Table S3 in the Supplementary Appendix). The rate of rehospitalization for myocardial infarction at 1 year was 2.7% and 2.7% in the two groups, respectively (hazard ratio, 0.97; 95% CI, 0.73 to 1.28; $P=0.81$) (Fig. 1B), and the rate of stent thrombosis was 0.7% and 0.9%, respectively (hazard ratio, 0.84; 95% CI, 0.50 to 1.40; $P=0.51$) (Fig. 1C). The incidences of target-vessel revascularization and target-lesion revascularization were similar in the two randomized groups (Table 2). The incidence of the composite of death, rehospitalization for myocardial infarction, or stent thrombosis was 8.0% in the thrombus-aspiration group and 8.5% in the PCI-only group (hazard ratio, 0.94; 95% CI, 0.80 to 1.11; $P=0.48$) (Table 2).

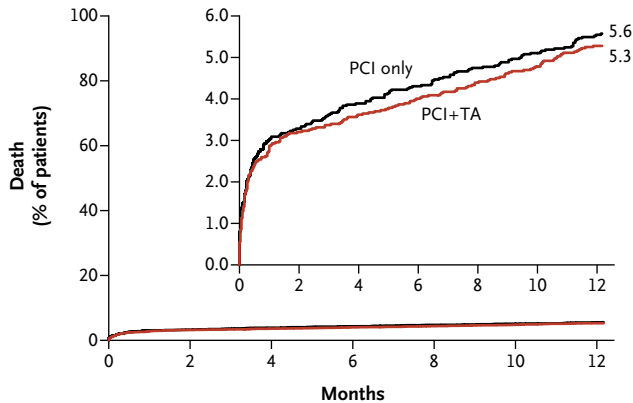
The median duration of follow-up from enrollment of the first patient to completion of 1 year of follow-up for the last patient enrolled was 858

Table 2. End Points at 365 Days and during Total Duration of the Trial.

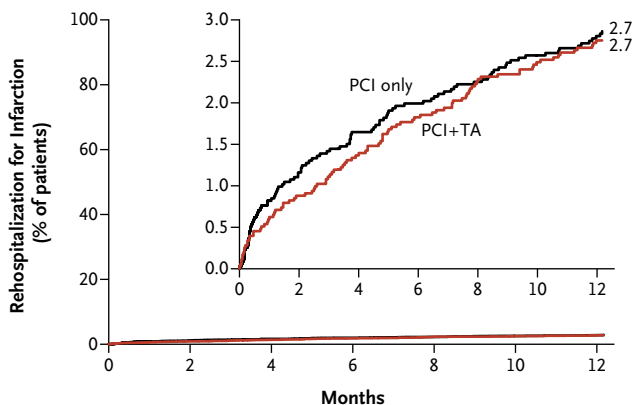
End Point	Patients Who Underwent Randomization		Hazard Ratio (95% CI)	P Value	Patients Who Were Not Enrolled in the Trial	
	PCI Only (N=3623)	PCI and Thrombus Aspiration (N=3621)			PCI Only (N=3543)	PCI and Thrombus Aspiration (N=1169)
	no. (%)				no./total no. (%)	
At 365 days						
Death from any cause	202 (5.6)	191 (5.3)	0.94 (0.78–1.15)	0.57	541/3450 (15.7)*	188/1145 (16.4)*
Rehospitalization for myocardial infarction	99 (2.7)	96 (2.7)	0.97 (0.73–1.28)	0.81	132/3543 (3.7)	45/1169 (3.8)
Death from any cause or rehospitalization for myocardial infarction	295 (8.1)	280 (7.7)	0.95 (0.80–1.12)	0.51	653/3450 (18.9)*	228/1145 (19.9)*
Stent thrombosis	32 (0.9)	27 (0.7)	0.84 (0.50–1.40)	0.51	28/3543 (0.8)	9/1169 (0.8)
Death from any cause, rehospitalization for myocardial infarction, or stent thrombosis	307 (8.5)	289 (8.0)	0.94 (0.80–1.11)	0.48	660/3450 (19.1)*	232/1145 (20.3)*
Target-vessel revascularization	178 (4.9)	160 (4.4)	0.90 (0.72–1.10)	0.31	189/3543 (5.3)	58/1169 (5.0)
Target-lesion revascularization	128 (3.5)	117 (3.2)	0.91 (0.71–1.17)	0.47	133/3543 (3.8)	40/1169 (3.4)
During total duration of trial†						
Death from any cause	316 (8.7)	295 (8.1)	0.93 (0.80–1.10)	0.40	693/3450 (20.1)*	240/1145 (21.0)*
Death from any cause, rehospitalization for myocardial infarction, or stent thrombosis	490 (13.5)	448 (12.4)	0.91 (0.80–1.04)	0.16	866/3450 (25.1)*	300/1145 (26.2)*

* Data include only Swedish patients.

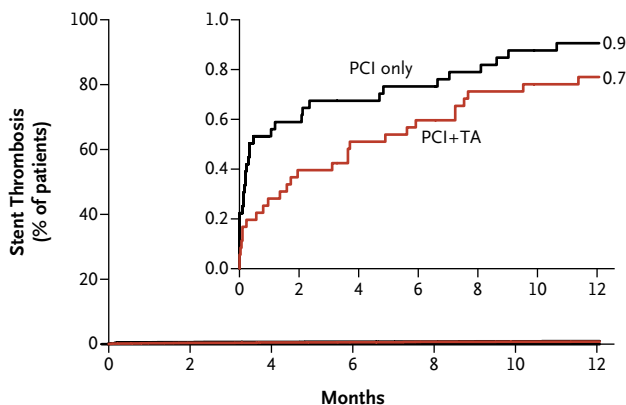
† The total duration of the trial was the time from enrollment of the first patient to completion of 1 year of follow-up for the last patient enrolled. The duration of follow-up varied, with a maximum of 1416 days.

A Cumulative Risk of Death**No. at Risk**

PCI+TA	3621	3500	3485	3470	3456	3440	3425
PCI only	3623	3503	3481	3466	3450	3435	3420

B Cumulative Risk of Rehospitalization for Infarction**No. at Risk**

PCI+TA	3621	3473	3441	3412	3384	3360	3336
PCI only	3623	3463	3424	3398	3374	3349	3327

C Cumulative Risk of Stent Thrombosis**No. at Risk**

PCI+TA	3621	3487	3467	3450	3432	3416	3400
PCI only	3623	3485	3460	3443	3425	3407	3392

Figure 1. Time-to-Event Curves for Events Occurring up to 365 Days after the Intervention.

Kaplan–Meier time-to-event curves show the cumulative risk of death from any cause among patients who were randomly assigned to undergo percutaneous coronary intervention (PCI) alone and among those who were randomly assigned to undergo thrombus aspiration (TA) and PCI (Panel A), the cumulative risk of rehospitalization for myocardial infarction in the two groups (Panel B), and the cumulative risk of stent thrombosis in the two groups (Panel C). The insets show the same data on an enlarged y axis.

days (interquartile range, 597 to 1096), with a maximum of 1416 days. When the entire follow-up period was analyzed, the rate of death was 8.1% (295 of 3621 patients) in the thrombus-aspiration group as compared with 8.7% (316 of 3623 patients) in the PCI-only group (hazard ratio, 0.93; 95% CI, 0.80 to 1.10; $P=0.40$). The composite of death, rehospitalization for myocardial infarction, or stent thrombosis during the entire follow-up period occurred in 448 and 490 patients in the two groups, respectively (hazard ratio, 0.91; 95% CI, 0.80 to 1.04; $P=0.16$) (Table 2 and Fig. 2).

In a per-protocol analysis that included only patients who received the randomly assigned therapy, the hazard ratio for death at 1 year was 0.95 (95% CI, 0.77 to 1.16; $P=0.60$) and the hazard ratio for the composite of death, rehospitalization for myocardial infarction, or stent thrombosis was 0.94 (95% CI, 0.80 to 1.11; $P=0.48$). The results were consistent across all prespecified subgroups and several post hoc subgroups, including those based on hospital size and enrollment rate, and subgroups associated with high thrombotic risk, such as patients who had a TIMI flow grade of 0 or 1, a thrombus grade of G4 or G5, a proximal lesion, or a short delay from symptom onset to PCI and those who smoked (Fig. 3, and Fig. S2 in the Supplementary Appendix).

OUTCOMES FOR PATIENTS NOT ENROLLED IN THE STUDY

Patients not enrolled in TASTE during the enrollment period had a higher proportion of risk indicators than enrolled patients (Table 1). The incidence of the composite of death, rehospitalization for myocardial infarction, or stent thrombosis and the incidences of the individual components were higher among the unenrolled patients than among

the enrolled patients. However, among patients who were not enrolled, outcomes were similar in patients who underwent thrombus aspiration and in those treated with PCI alone (Table 2).

DISCUSSION

The main finding of the 1-year follow-up of the TASTE study is that a strategy of routine use of thrombus aspiration before PCI, as compared with PCI alone, in patients with an acute STEMI, did not result in a lower rate of death from any cause, a lower risk of the composite of death, rehospitalization for myocardial infarction, or stent thrombosis, or a lower risk of any of these component end points separately. The absence of any benefit of thrombus aspiration as an adjunct to PCI was consistent for all outcomes in the prespecified intention-to-treat analyses, in the per-protocol analyses, and in all the patient subgroups, regardless of baseline clinical or angiographic characteristics. On a national basis, the TASTE trial enrolled a very high proportion of all the patients with STEMI for whom PCI was planned and who were eligible to provide oral informed consent. The trial is therefore truly representative of the overall population of patients in our region with STEMI who undergo PCI.

The similar rates of death at 30 days and 1 year in the two groups are consistent with the absence of a difference in infarct size with thrombus aspiration and without thrombus aspiration, as shown in multiple trials.¹⁴ Because thrombus aspiration is an intervention performed only in the acute phase of myocardial infarction and there is no ongoing therapy, a late effect is not likely in the absence of an early benefit. The 1-year follow-up findings in the TASTE trial do not suggest that thrombus aspiration might result in a long-term reduction in mortality.

At 30 days, the rates of both rehospitalization for myocardial infarction and definite stent thrombosis tended to be lower after thrombus aspiration and PCI than after PCI alone. The differences between the study groups decreased over time, and at 1 year, the rates were very low and were similar in the two groups. The low rate of stent thrombosis is consistent with the frequent use of new-generation drug-eluting stents^{15,16} and potent platelet inhibition.

In TAPAS, a single-center trial that was not designed for the evaluation of clinical outcomes,

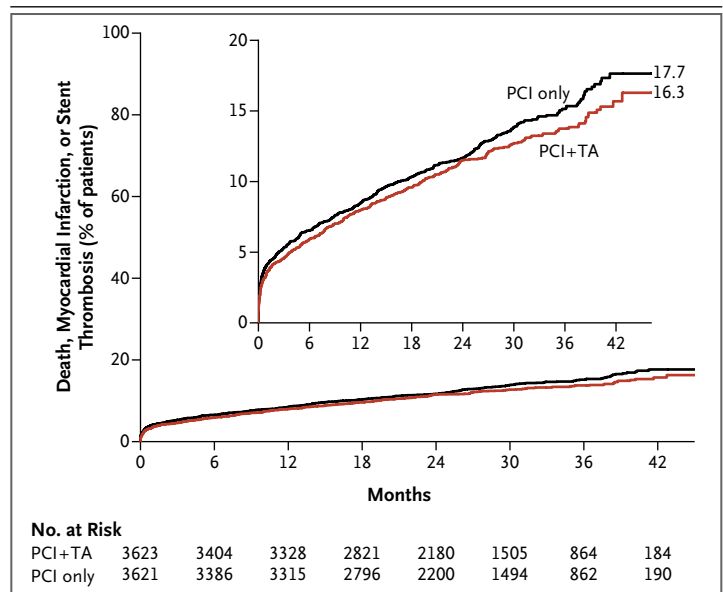


Figure 2. Time-to-Event Curves for the Total Duration of Follow-up after the Intervention.

Kaplan–Meier time-to-event curves show the cumulative risk of the composite of death from any cause, rehospitalization for myocardial infarction, or stent thrombosis after PCI alone or PCI and TA during the total period of follow-up, from enrollment of the first patient to completion of 1 year of follow-up for the last patient enrolled. The duration of follow-up varied, with a maximum of 1416 days. The inset shows the same data on an enlarged y axis.

thrombus aspiration was associated with a significant 40% relative reduction in all-cause mortality at 1 year of follow-up.⁴ The observed reduction was based on a total of 66 events. Furthermore, the reduction in mortality occurred immediately after randomization, with a nonsignificant 48% reduction in the rate of death from any cause at 30 days and with no further separation of the event curves up to 1 year.

In contrast to TAPAS, the TASTE trial was a large, multicenter study designed to have statistical power for the evaluation of all-cause mortality at 30 days. The evaluation of mortality at 1 year was based on 393 events, and the evaluation of the triple composite end point was based on 596 events. There was a nonsignificant 6% relative difference in mortality between the two randomized groups both at 30 days and at 1 year. Unlike the patients in TAPAS, the patients in the TASTE trial underwent randomization after angiography, which led to a lower crossover rate in the thrombus-aspiration group (6.1%, vs. 10.8% in TAPAS⁴) (Table S1 and Fig. S1 in the Supplementary Appendix). Mortality at 1 year in the

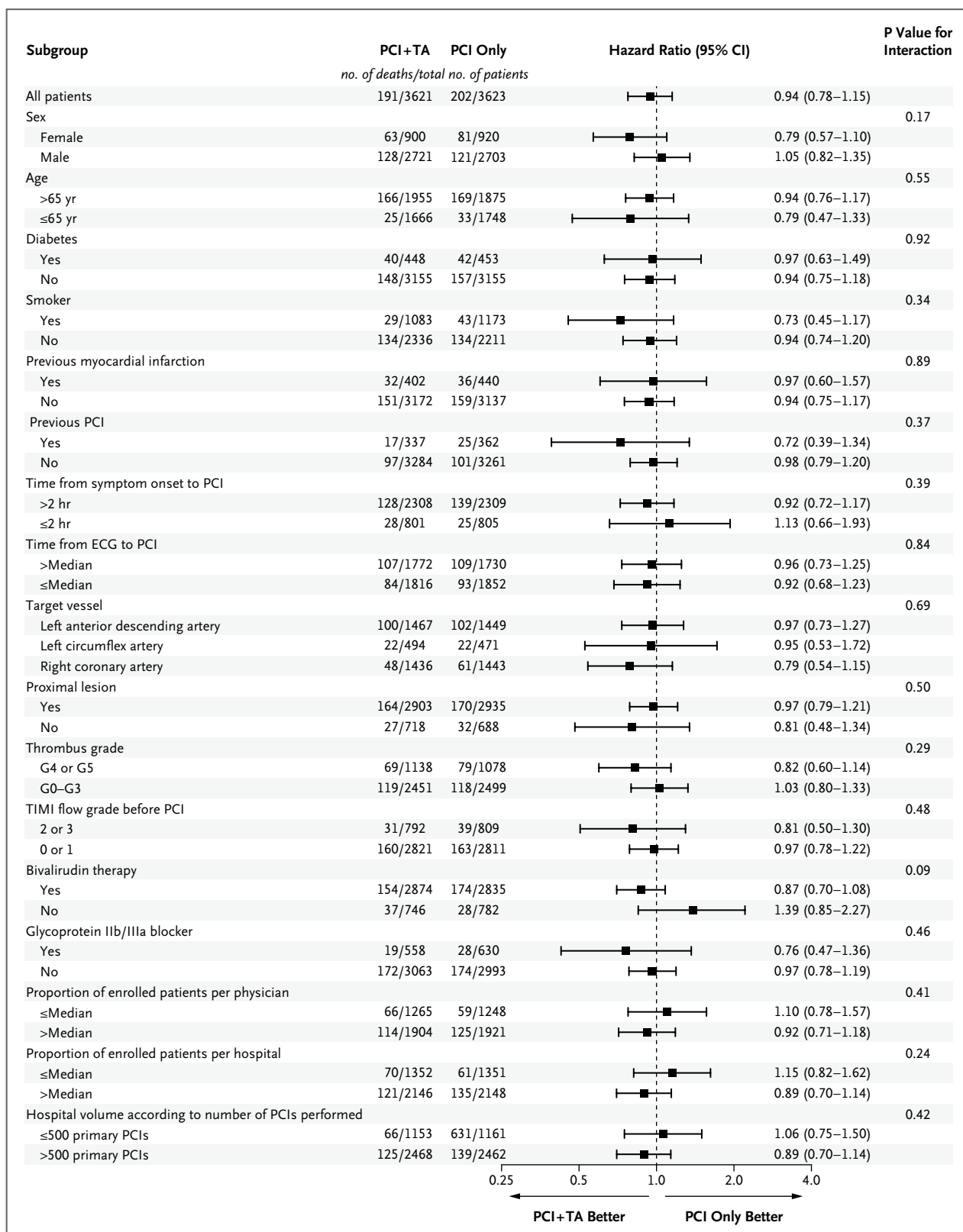


Figure 3 (facing page). Hazard Ratios for Death within 365 Days after the Intervention, According to Subgroup.

Hazard ratios for death within 365 days after PCI alone or PCI and TA are shown with 95% confidence intervals according to prespecified and post hoc subgroups; the last five groups were post hoc. Continuous variables were dichotomized at the median. Hospital volume was reported per study site during the course of the trial. Thrombus scores are defined as follows: G0 indicates no thrombus, G1 possible thrombus, G2 small thrombus, G3 medium thrombus, G4 large thrombus, and G5 vessel occlusion. ECG denotes electrocardiography, and TIMI Thrombolysis in Myocardial Infarction.

conventional PCI group was lower in the TASTE study than in TAPAS (5.6% vs. 7.6%),⁷ which may reflect continued improvements in other treatment strategies such as the frequent use of radial-artery access, bivalirudin, and secondary preventive medications, including potent second-generation P2Y₁₂ inhibitors.

In the INFUSE-AMI (Intracoronary Abciximab and Aspiration Thrombectomy in Patients with Large Anterior Myocardial Infarction) trial, which involved 452 high-risk patients with proximal or mid occlusion of the left anterior descending coronary artery, thrombus aspiration was not associated with a reduction in ischemic events at 30 days but was associated with a significant reduction in rehospitalization for heart failure and a nonsignificant reduction in reinfarction at 1 year.^{17,18} Mortality at 1 year in the thrombus-aspiration group (4.9%) was similar to that in the TASTE trial (5.3%) and was not significantly different from that in the PCI-only group of the INFUSE-AMI trial (7.0%). Recently, observational data from 1498 patients with STEMI that was identified in a randomized trial of treatment with drug-eluting stents showed that clinical outcomes with thrombus aspiration were similar to those with stenting alone.¹⁹

Several meta-analyses of randomized trials of thrombus aspiration have had inconsistent results with respect to mortality and other clinical outcomes.^{5,12,14} The findings of these meta-analyses are dominated by the results of TAPAS and the TASTE trial. A further evaluation of the effect of thrombus aspiration on clinical outcomes will be performed in the multicenter, randomized Trial of Routine Aspiration Thrombectomy with Percutaneous Coronary Intervention (PCI) versus PCI

Alone in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary PCI (TOTAL; ClinicalTrials.gov number, NCT01149044), which has a target enrollment of 10,700 patients.²⁰

The lack of a clinical benefit of thrombus aspiration in the TASTE trial was seen even in subgroups with a high thrombotic burden, suggesting that manual aspiration may not have a sufficient effect on the thrombus itself to influence clinical outcomes. In TAPAS, 23% of the patients did not have evidence of any thrombotic material in the aspirate,⁴ and in a study involving patients with non-STEMI, optical coherence tomography did not detect a decrease in intracoronary thrombus burden in the culprit coronary artery after manual thrombus aspiration.¹² A TAPAS substudy showed that thrombus aspiration had no effect on visible distal embolization, which was noted in 6.7% of the patients in the thrombus-aspiration group and 6.0% of those in the PCI-alone group.²¹

The most important limitation of the TASTE trial is that outcome events were recorded on the basis of registry data and were not systematically adjudicated. For this reason, the ascertainment of outcome events may have been less accurate than in a conventional randomized trial. However, there is no reason to assume skewed reporting between the two treatment groups. The SCAAR requires reporting of stent thrombosis in all patients undergoing angiography for any reason, making the underreporting of stent thrombosis minimal.²² In the SWEDEHEART registry, rehospitalization for myocardial infarction is registered with a high level of completeness.^{9,23,24} Owing to the mandatory use of personal identification numbers, death registries in the Nordic countries have a high degree of completeness but without discrimination between cardiac and non-cardiac causes. The results cannot necessarily be extrapolated to very high-risk patients who would not have been eligible for inclusion.

In conclusion, this multicenter, randomized, registry-based trial, which was powered for the evaluation of mortality among patients with STEMI, showed that a strategy of routine manual thrombus aspiration before PCI, as compared with PCI alone, did not reduce all-cause mortality or the composite of death from any cause, rehospitalization for myocardial infarction, or stent thrombosis up to 1 year.

Supported by unrestricted research grants from the Swedish Research Council, the Swedish Association of Local Authorities and Regions, Terumo Medical, Medtronic, and Vascular Solutions, by grants from the Swedish Heart-Lung Foundation (20100178, to Dr. Fröbert; and B0010401, to Dr. James), and by the Landspítali University Hospital Research Fund (to Dr. Gudnason).

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank the staff at all the centers participating in the Swedish Coronary Angiography and Angioplasty Registry collaboration for their continuous data collection and commitment to this study.

REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012; 60:1581-98.
2. Stone GW, Peterson MA, Lansky AJ, Dargas G, Mehran R, Leon MB. Impact of normalized myocardial perfusion after successful angioplasty in acute myocardial infarction. *J Am Coll Cardiol* 2002; 39:591-7.
3. Steg PG, James SK, Gersh BJ. 2012 ESC STEMI guidelines and reperfusion therapy: evidence-based recommendations, ensuring optimal patient management. *Heart* 2013;99:1156-7.
4. Svilaas T, Vlaar PJ, van der Horst IC, et al. Thrombus aspiration during primary percutaneous coronary intervention. *N Engl J Med* 2008;358:557-67.
5. Costopoulos C, Gorog DA, Di Mario C, Kukreja N. Use of thrombectomy devices in primary percutaneous coronary intervention: a systematic review and meta-analysis. *Int J Cardiol* 2013;163:229-41.
6. Fröbert O, Lagerqvist B, Olivecrona GK, et al. Thrombus aspiration during ST-segment elevation myocardial infarction. *N Engl J Med* 2013;369:1587-97.
7. Vlaar PJ, Svilaas T, van der Horst IC, et al. Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study. *Lancet* 2008;371:1915-20.
8. Fröbert O, Lagerqvist B, Gudnason T, et al. Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial): a multicenter, prospective, randomized, controlled clinical registry trial based on the Swedish Angiography and Angioplasty Registry (SCAAR) platform: study design and rationale. *Am Heart J* 2010;160:1042-8.
9. Jernberg T, Attebring MF, Hambræus K, et al. The Swedish Web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies (SWEDEHEART). *Heart* 2010;96:1617-21.
10. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on myocardial revascularization. *Eur Heart J* 2010;31:2501-55.
11. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;115:2344-51.
12. Gibson CM, de Lemos JA, Murphy SA, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. *Circulation* 2001; 103:2550-4.
13. Sianos G, Papafaklis MI, Serruys PW. Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. *J Invasive Cardiol* 2010;22:Suppl B:6B-14B.
14. Kumbhani DJ, Bavry AA, Desai MY, Bangalore S, Bhatt DL. Role of aspiration and mechanical thrombectomy in patients with acute myocardial infarction undergoing primary angioplasty: an updated meta-analysis of randomized trials. *J Am Coll Cardiol* 2013;62:1409-18.
15. Sarno G, Lagerqvist B, Nilsson J, et al. Stent thrombosis in new-generation drug-eluting stents in patients with STEMI undergoing primary PCI: a report from SCAAR. *J Am Coll Cardiol* 2014;64: 16-24.
16. Sarno G, Lagerqvist B, Fröbert O, et al. Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J* 2012;33:606-13.
17. Stone GW, Maehara A, Witzenbichler B, et al. Intracoronary abciximab and aspiration thrombectomy in patients with large anterior myocardial infarction: the INFUSE-AMI randomized trial. *JAMA* 2012;307:1817-26.
18. Stone GW, Witzenbichler B, Godlewski J, et al. Intralesional abciximab and thrombus aspiration in patients with large anterior myocardial infarction: one-year results from the INFUSE-AMI trial. *Circ Cardiovasc Interv* 2013;6:527-34.
19. Fernández-Rodríguez D, Regueiro A, Brugaletta S, et al. Optimization in stent implantation by manual thrombus aspiration in ST-segment-elevation myocardial infarction: findings from the EXAMINATION trial. *Circ Cardiovasc Interv* 2014;7:294-300.
20. Jolly SS, Cairns J, Yusuf S, et al. Design and rationale of the TOTAL trial: a randomized trial of routine aspiration Thrombectomy with percutaneous coronary intervention (PCI) versus PCI Alone in patients with ST-elevation myocardial infarction undergoing primary PCI. *Am Heart J* 2014;167(3):315.e1-321.e1.
21. Fokkema ML, Vlaar PJ, Svilaas T, et al. Incidence and clinical consequences of distal embolization on the coronary angiogram after percutaneous coronary intervention for ST-elevation myocardial infarction. *Eur Heart J* 2009;30:908-15.
22. Lagerqvist B, Carlsson J, Fröbert O, et al. Stent thrombosis in Sweden: a report from the Swedish Coronary Angiography and Angioplasty Registry. *Circ Cardiovasc Interv* 2009;2:401-8.
23. Chung SC, Gedeberg R, Nicholas O, et al. Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK. *Lancet* 2014;383:1305-12.
24. Hammar M, Alfredsson L, Rosén M, Spetz CL, Kahan T, Ysberg AS. A national record linkage to study acute myocardial infarction incidence and case fatality in Sweden. *Int J Epidemiol* 2001;30:Suppl 1:S30-S34.

Copyright © 2014 Massachusetts Medical Society.